H. H. Sheikh Hamdan Bin Rashid Al Maktoum

Deputy Ruler of Dubai, Minister of Finance, UAE

Patron of the Sheikh Hamdan Award for Medical Sciences

CONTENTS

04 **Messages**
- UAE Minister of Health
- President of the Conference & Chairperson, Scientific Committee
- Scientific Director

10 **Organizational Profiles**
- Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences
- Centre for Arab Genomic Studies
- Golden Helix Institute

14 **Conference Committees**
- Organizing Committee
- Scientific Committee

16 **Scientific Program**

24 **Abstracts**
- Keynotes
- Lectures
- Posters

116 **Workshop**
- RD-Connect

120 **Indices**
- Author Index
- Keyword Index
- Country Index

138 **Sponsors' Profiles**

HE Abdul Rahman Mohammed Al Owais

UAE Minister of Health
Chairman, Board of Trustees, Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences

It has been a decade since the establishment of the Centre for Arab Genomic Studies, under the aegis of the Sheikh Hamdan Award for Medical Sciences. Through the past ten years, the Centre has worked tirelessly towards its mission of reducing the burden of genetic diseases in the Arab World. Indeed, the field of study of human genetics has changed significantly in the past decade, and this is reflected in the shift in the activities of the Centre as well.

Under the able patronage of HH Sheikh Hamdan Bin Rashid Al Maktoum, Deputy Ruler of Dubai, and UAE Minister of Finance, the Centre has blossomed from being a local repository of information on genetic diseases to an international hub of resources pertaining to genetic disorders in the Arab World. This growth is in line with the UAE strategic plan implemented under the wise leadership of HH Sheikh Khalifa Bin Zayed Al Nahyan, President of the United Arab Emirates, HH Sheikh Mohammed Bin Rashid Al Maktoum, Vice-President and Prime Minister of the United Arab Emirates and the Ruler of Dubai, and Their Highnesses Members of the Supreme Council of Rulers of the Emirates.

Foremost of the services offered by the Centre is the Catalogue for Transmission Genetics in Arabs (CTGA) Database, which has grown steadily to become the largest ethnic based database on genetic disorders in the World. Alongside this, the Centre has organized a series of scientific conferences and workshops which have attracted numerous scientists and researchers in this field. The 5th Pan Arab Human Genetics Conference is the latest addittion in this well-establishment tradition of conferences.

I welcome all the participants of this conference to Dubai and hope you have a successful and enlightening conference meeting.

Abdul Rahman Mohammed Al Owais

Prof. Najib Al-Khaja
President of the Conference

Dr. Mahmoud Taleb Al Ali
Chairperson, Scientific Committee

It gives us great pleasure to welcome you to the 5th Pan Arab Human Genetics Conference (PAHGC). First of all, we would like to thank you for your continued interest and participation in the conference. Through the organization of the PAHGCs, the Centre for Arab Genomic Studies (CAGS) has successfully brought together diverse regional and international expertise on human medical genetics, and created a platform for discussion and mutual collaboration on issues relevant to researchers, medical professionals, and patients in this region. CAGS happens to be celebrating its tenth anniversary this year, and we are doubly proud to bring you the 5th edition of the conference in this special year with the theme 'Genomics Into Healthcare'.

The response and participation towards the PAHGC seems to grow with every edition. We have received over 170 abstracts for presentation at this conference. These presenters come not only from across the Arab World, but also from many other countries in Asia, Europe, and North America. The large number of abstracts received has, in fact, necessitated the use of parallel sessions, in order to accommodate the maximum number of presentations. The quality of these abstracts keeps increasing, and we are fairly confident in saying that this year's conference program is capable of rivaling other international genetics conference.

A constellation of prominent international and local geneticists will set the tone for the conference with their oral presentations. The program will see lectures on topics ranging from contemporary issues, such as cancer genetics and epigenetics to the role of genomics in public health. There will also be sessions dealing with the latest technologies in genetics research, such as next generation sequencing. In addition, each day of the conference will witness poster sessions, providing an opportunity for the participants to have a more detailed interaction with young researchers in this field. RD-Connect, a global project linking up databases, registries, and biobanks related to rare disease research, will host a special session highlighting their efforts in creating a central bioinformatics resource for rare disease researchers worldwide.

Special thanks are due to the Organizing and Scientific Committees of the conference, who have worked hard to bring this conference to fruition. We would also like to thank the members of the Arab Council and Executive Board of CAGS, who have guided and helped us over the years.

We hope that you enjoy and benefit from the many sessions that the conference has to offer, and find time to network with other participants of the conference.

Najib Al-Khaja **Mahmoud Taleb Al Ali**

Dr. George P. Patrinos
Scientific Director; The Golden Helix Foundation, London, United Kingdom

We are very pleased to welcome you to Dubai for the joint 5th Pan Arab Human Genetics Conference and the 2013 GOLDEN HELIX Symposium® with the theme "Genomics into Healthcare".

Genomic Medicine is expected to play a pivotal role in future medical practice. Recognizing the challenges that are emerging from the recent advances in genomics and their impact on human health, this joint conference features lectures by several internationally renowned scientists and covers all aspects of this field, including recent developments from deciphering the human genome, genomics of rare disorders, pharmacogenomics, next-generation sequencing, cancer and population genomics and the requirements to bring genomics in the clinic.

The Golden Helix Symposia® are international high-profile scientific conferences in the field of genomic medicine, organized by the Golden Helix Foundation, a registered UK-charity aiming to catalyze collaborative research and to promote knowledge transfer and education in the area of genomic medicine. This year, the 2013 Golden Helix Symposium® will be held jointly with the 5th Pan-Arab Human Genetics Conference, the most prestigious scientific conference on human genetics in the Arab world that provides a platform for regional and international researchers and professionals in genetics to have a constructive dialogue and share their views. This joint conference is the result of a fruitful collaboration between scientists from the Center for Arab Genomic Studies and the Golden Helix Foundation and the generous support from H H Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences.

We are committed to setting the highest standard for symposia in the field of human genomics and personalized medicine, and look forward to a very successful conference and, at the same time, to experience the warmth of Arab hospitality in the beautiful city of Dubai.

George P. Patrinos

10 Organizational Profiles

11 Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences

12 Centre for Arab Genomic Studies

13 Golden Helix Institute

Sheikh Hamdan Bin Rashid Al Maktoum
Award for Medical Sciences

Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences

On the 10th of April 1999, the late Sheikh Maktoum Bin Rashid Al Maktoum, UAE Vice President, and Prime Minister and Ruler of Dubai, issued the Supreme Decree No. (5) to establish the Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences, with the objective of honouring scientists from every part of the world who tirelessly pursue distinctive medical research that serves the larger interests of humanity. The Board of Trustees and the General Secretariat of Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences was formed on the 1st of May 1999, under the directives of H.H. Sheikh Hamdan Bin Rashid Al Maktoum, Deputy Ruler of Dubai and Minister of Finance.

Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences is one of the most outstanding awards from the GCC countries, and has consistently acted as a motivating force towards promoting the medical services by honouring the scientists and the distinct working parties in academic and therapeutic scopes alongside with medical and humanitarian services all over the world.

The Award clearly recognizes the importance of scientific research in boosting the progress of UAE, and plays a proactive role in funding domestic health researches through a pioneering program. The Award has proved to be widely successful, as it has been recognized by international observers and was testified by leading researchers vying for the award.

This success reflects on the foundation's international reputation and its high scientific credibility and level of performance.

www.hmaward.org.ae

المركز العربي للدراسات الجينية
CENTRE FOR ARAB GENOMIC STUDIES

Centre for Arab Genomic Studies

In the Arab World, genetic diseases represent a major public health problem. The vision of H.H. Sheikh Hamdan Bin Rashid Al Maktoum to alleviate human suffering from genetic diseases in the Arab World crystallized in the establishment of the Centre for Arab Genomic Studies (CAGS) to characterize and prevent genetic disorders and transfigure the future practice of health care in the region.

Some of the priority objectives of the Centre for Arab Genomic Studies are to educate the public and professionals alike on the important impact of genetic diseases in the Arab World and the methods and benefits of early genetic diagnosis. The Centre for Arab Genomic Studies also plans to provide comprehensive genetic services by translating research achievements into well-integrated patient treatment programs. Concurrently, it will also address the ethical, legal, and social issues that may arise with the implementation of such programs.

CAGS includes two scientific committees: The Executive Board of CAGS is composed of a number of local scientists and it represents the governing body and the legal trustee of all activities of the centre. The Council of CAGS includes a number of regional scientists and it facilitates the exchange of information on genetic disorders occurring in Arab countries. Countries represented in the Council of CAGS currently include: Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Sudan, Tunisia, and the United Arab Emirates. In the future, CAGS aims to extend memberships to a larger group of scientists and include other Arab countries.

One of the major projects of CAGS is the Catalogue for Transmission Genetics in Arabs (CTGA), an online, freely accessible database of genetic disorders reported from the Arab World. CAGS has been involved in the Human Variome Project as a representative of the Arab region, and has been one of the first organizations to take an active lead in working on the project. CAGS organizes the Pan Arab Human Genetics Conference every alternate year, to provide a platform for discussion and education on genetic issues in the region. The Centre also publishes various books and booklets on genetics aimed at the scientific community and the general public.

www.cags.org.ae

Golden Helix Institute of Biomedical Research

Golden Helix Institute of Biomedical Research

The Golden Helix Institute of Biomedical Research, established in 2003, is an international non-profit scientific organization active in Europe, Asia and Latin America. As a non-profit organization, the mission of the GHI is the transfer of knowledge and scientific results among local researchers and internationally renowned scientists to the scientific community and the society through participation in collaborative scientific projects, a variety of scientific symposia and educational events, and establishment of public health policies in the field of pharmacogenomics and personalized medicine.

The Golden Helix Institute of Biomedical Research is the regional coordination center of the Pharmacogenomics for Every Nation Initiative in Europe, in an effort to integrate pharmacogenomics in developing and other countries. Also, the Institute has been involved in the development of several National/Ethnic Genetic databases and related web services to document the genetic heterogeneity in different populations worldwide.

Educational activities of the Golden Helix Institute of Biomedical Research include the organization of the Golden Helix Symposia® and the Golden Helix Pharmacogenomics Days. The Golden Helix Symposia are high profile international research meetings, organized in the field of genomic medicine. The Golden Helix Pharmacogenomics days are international educational events organized in major cities with large academic hospitals

Finally, the Golden Helix Institute of Biomedical Research has encouraged the creation and actively supports the operations of the Genomic Medicine Alliance (www.genomicmedicinealliance.org), an international initiative aiming to create collaboration ties between academics, researchers, regulators, and the general public interested in all aspects of genomics and personalized medicine.

www.goldenhelix.org

14 CONFERENCE COMMITTEES

President of the Conference

Prof. Najib Al Khaja

Scientific Committee

Dr. Mahmoud Taleb Al Ali
(Chairperson)
Dr. Abdul Rezzak Hamzeh
(Vice-Chairperson)
Prof. Lotfi Chouchane
(Qatar)
Dr. Fahd Al-Mulla
(Kuwait)
Dr. Ahmad Al-Marzouqi
(UAE)
Dr. Myles Axton
(USA)
Prof. Milan Macek
(Czech Republic)
Dr. George Patrinos
(Greece)
Dr. Fatima Bastaki
(UAE)
Dr. Fatima Al Jassmi
(UAE)
Prof. Hanan Hamamy
(Switzerland)

Organizing Committee

Mr. Abdulla Bin Souqat
(Chairperson)

Dr. Abdul Rezzak Hamzeh

Dr. George P Patrinos

Prof. Paolo Fortina

Dr. Federico Innocenti

Prof. Larry J Kricka

Event Organizer

meeting minds
EXPERTS

Dubai Media City
Shatha Tower, Office 3113
P.O. Box 502464, Dubai
United Arab Emirates
Tel.: +9714-4270492
Fax: +9714-4270493
meetingmindsdubai.com

16

SCIENTIFIC PROGRAM

17 Scientific Program

Day 1	Sunday, November 17, 2013
09:00 – 09:45	Registration
09:45 – 10:30	**Key Note Session** *Chairperson: Mahmoud Taleb Al Ali*
09:45 – 10:30	**Key Note Speech – David N. Cooper** The Molecular Basis of Reduced Penetrance in Human Inherited Disease
10:30 – 11:30	Opening Ceremony
11:30 – 12:30	**Session 1: Cancer Genomics and Epigenetics** *Chairpersons: Mouza Sharhan, Paolo Fortina*
11:30 – 12:00	Breast Cancer in Arab Populations: Molecular Characteristics and Disease Management Implications Lotfi Chouchanne
12:00 – 12:15	Role of sema3C in breast cancer progression and its effects on cancer cells proliferation, adhesion and invasion Muhammad Malik
12:15 – 12:30	A novel method to identify imprinted genes in nasopharyngeal carcinoma pathogenesis Ismail Alhwij
12:30 – 13:30	Lunch Break
13:30 – 14:30	**Session 2: Genomic and Epigenomic Studies** *Chairpersons:*
13:30 – 14:00	The Molecular Functions of Chromatin Modifiers Ahmad Al Marzouqi
14:00 – 14:30	High Throughput Genetic Studies and Advanced Functional Analyses of _Brugada Syndrome Patients Maurizio Ferrari
14:30 – 16:30	**Session 3: Genomics of Blood and Metabolic Disorders** *Chairpersons: Nabil Sulaiman, Abdul Rezzak Hamzeh*
14:30 – 15:00	Advances in Prenatal Diagnosis of Hemoglobinopathies: Focus on UAE Erol Baysal
15:00 – 15:15	Novel Missense mutation in ANKRD26 gene cause Familial Thrombocytopenia. Walid Dridi
15:15 – 15:30	Genetically influenced metabotype and human metabolic individuality Karsten Suhre
15:30 – 16:00	Coffee Break and Poster Session 1

16:00 – 16:30	Novel Aspects Regarding the Molecular Basis of Thalassemia Douglas R Higgs
16:30 – 17:30	RD-Connect Workshop NeurOmics: omics research for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases – an EU-funded FP7 project Olaf Riess

Day 2	Monday, November 18, 2013
09:00 – 11:00	**Session 4: Cytogenetic Diagnosis and Molecular Profiling** *Chairpersons: Mansour Al Zarouni, and Kemal Khazanehdari*
09:00 – 09:30	Search for the Genetic Modifiers of Disease Severity in Tibial Hemimelia in a large multigenerational Arab Family: Progress and Future Directions. Mohammed Naveed
09:30 – 10:00	Population prevalence of Birth Defects and Genetic Conditions in Oman Anna Rajab
10:00 – 10:30	Coffee Break and Poster Session 2
10:30 – 10:45	A distinct clinical phenotype associated with ATP1A2 gene mutation Amal Al Hashem
10:45 – 11:00	Advantages of FISH in the Diagnosis of Cytogenetics Abnormalities Suzan Roshdi Ismail
11:30 – 12:00	A Success Story of the Centre for Arab Genomic Studies at its 10th Anniversary; the CTGA Database: Challenges and Prospects Abdul Rezzak Hamzeh
12:00 – 12:30	Industry Symposia: Changing the face of Patient Diagnostics: Affymetrix Solutions Fiona Sara Togneri
12:30 – 13:30	Lunch
13:30 – 15:30	**Session 5: Next Generation Sequencing** *Chairpersons: Andre Megarbane, George Patrinos*
13:30 – 14:00	Next-Generation Sequencing in the Clinic: Enabling Genomic Medicine Radoje Drmanac
14:00 – 14:30	Personal Genomes are Personalised Jun Wang
14:30 – 15:00	Next Generation Sequencing, Genomic Medicine and You Fahd Al Mulla
15:00 – 15:30	Comprehensive elucidation and diagnosis of intellectual disability and related disorders Hilger Ropers

15:30 – 16:00	Coffee Break and Poster Session 3
16:00 – 17:30	**Session 6: Consanguinity and Hereditary Diseases** *Chairpersons: Rabah Shawky, Sadika Al Awadi*
16:00 – 16:30	NGS Platforms and Hereditary Disorders in Highly Inbred Populations Moien Nihad Kanaan
16:30 – 16:45	Mutation in EZR inhibits the Ras/MAP pathway and causes autosomal recessive intellectual disability Rami Abou Jamra
16:45 – 17:00	Chromosomal microarray as a first-tier clinical diagnostic test for children with dysmorphology, malformations, developmental delay and idiopathic mental retardation: GCC experience Zafar Nawaz
17:00 – 17:30	Consanguineous Marriages: Past, Present and Future Trends in Counseling Hanan Hamamy

Day 3	Tuesday, November 19, 2013
09:00 – 10:30	**Session 7: Clinical Genomics** *Chairpersons: Moiz Bakheit, Moeen Al Sayed*
09:00 – 09:30	Translational Genomics and the Future of Medical Genetics in the Middle East Aida Al Aqeel
09:30 – 10:00	Neurotrophins as Therapeutic Targets for Neurodegenerative Diseases, Achilleas Gravanis
10:00 – 10:30	Aldehyde Dehydrogenases as Novel Therapeutic Targets for Metabolic Diseases and Cancer Stem Cells Vasilis Vasiliou
10:30 – 11:00	Coffee break and poster session 4
11:00 – 12:00	**Session 8A: Clinical Applications and Pharmacogenomics** *Chairpersons: Federico Innocenti, Taher Rizvi*
11:00 – 11:30	Clinical Implementation of Pharmacogenomics Ron H. van Schaik
11:30 – 12:00	Pharmacogenomics and personalized medicine in the global village George Patrinos
12:00 – 12:15	The VCORK1 Alleles Involved in the Pharmacogenetics of Warfarin Anticoagulant among Emiratis Hayat Aljeibeji
12:15 – 12:30	The rescue of cellular trafficking-defective mutants resulting in Congenital Myasthenic Syndrome and Familial Exudative Vitreoretinopathy Reham Milhem
12:30 – 13:30	Lunch

1200 – 1230	**Session 8B: Selected Abstracts** *Chairpersons: Laila Abdel Wareth, Fatma Bastaki*
12:00 – 12:15	Role of HCV core protein in expression of the human telomerase reverse transcriptase (hTERT) gene in hepatoma cell lines Hussain Abdulla
12:15 – 12:30	A novel ALMS1 splice mutation in a non-obese juvenile-onset insulin-dependent syndromic diabetic patient May Sanyoura
12:30 – 12:45	Inactivation of RIZ1 Gene by Promoter Hypermethylation is Associated with Disease Progression and Resistance to Imatinib in Indian Chronic Myelogenous Leukemia Patients, First Study from India Rashid Mir

13:30 – 16:00	**Session 9A: Selected Abstracts** *Chairpersons: Ghazi Tadmouri, Emily Niemitz*
13:30 – 13:45	Contribution of copy number variants (CNVs) in congenital unexplained intellectual and developmental disabilities in 149 patients: the first Lebanese study leading to new findings in CNVs. Andre Megarbane
13:45 – 14:00	Recurrent hydatidiform mole: detection of two novel mutations in the NLRP7 gene in two Egyptian families Ebtesam Abdalla
14:00 – 14:15	Prenatal Diagnosis of Genetic Disorders in UAE –Collaborative Experience of Dubai and Delhi Renu Saxena
14:15 – 14:30	Identification Of Genes Causing Monogenic Diabetes By Deep Sequencing Of Accessible Coding Regions Of The Human Genome Anette Gjesing
14:30 – 14:45	The Use of Whole Exome Sequencing (WES) to Unravel Disease Genes Causing Autosomal Recessive Disorders in the Population of Qatar Tawfeg Ben-Omran
14:45 – 15:00	Identification of Known and Novel Variants Associated with Paediatric Disorders using Whole Exome Sequencing and Array-CGH Arif Anwar
15:00 – 15:15	Whole-Exome Sequencing (WES) Deciphers Rare Recessive Disorders Segregating in Consanguineous Families from the United Arab Emirates (UAE) Nadia Akawi
15:30 – 16:00	Coffee break and poster session 5
16:00 – 17:30	**Session 10: Genomics in Public Health** *Chairpersons: Shaikha Al Arrayed, Larry Kricka*
16:00 – 16:30	Quantification of Genome Sharing in Consanguineous Couples with or Without Affected Child by Autosomal Recessive Disease and Impact on Genetic Counseling Habiba Chaaboun
16:30 – 16:45	Ethical issues in genomic research and limits of the informed consent Rachida Roky
16:45 – 17:30	**Keynote Speech – Angela Brand** Genomics and Public Health
17:30	Closing Ceremony

13:30 – 15:00	**Session 9B: Selected Abstracts** *Chairpersons: Makia Marafie, Fatima Al Jassmi*
13:30 – 13:45	Association of APOA5 56C>G gene polymorphism with both hypertriglyceridemia and risk of coronary artery disease (CAD) in Arterial Hypertensive Moroccan patients Sanaa Outau
13:45 – 14:00	Infantile Ascending Spastic Paralysis caused by a novel ALS2 mutation identified by Homozygosity Mapping. Salma Majid
14:00 – 14:15	Homozygous mutation in fatty acyl CoA reductase 1 FAR1 causes autosomal recessive intellectual disability with early epilepsy and constipation Rebecca Buchert
14:15 – 14:30	Mutations in the DDHD2 gene Cause a Recessive Form of Complex Hereditary Spastic Paraplegia Salma Ben Salem
14:30 – 14:45	Documentation of inherited disorders in the Moroccan population in the Moroccan National Mutation database Ilham Ratbi
14:45 – 15:00	Lessons learned from whole exome sequencing data analysis of rare diseases:non-coding variants and copy number variations Somayyeh Fahiminiya
15:00 – 15:15	New findings in a global approach to dissect the whole phenotype of PLA2G6 gene mutations Hamid Azzedine

24 ABSTRACTS

26 Keynotes

28 Lectures

38 Oral Presentations

55 Posters

KEYNOTE LECTURES

K1

The Molecular Basis of Reduced Penetrance in Human Inherited Diseases

David N. Cooper
Professor of Human Molecular Genetics,
Cardiff University School of Medicine, Cardiff, UK

Some individuals with a particular disease-causing mutation or genotype fail to express most if not all features of the disease in question, a phenomenon that is known as 'reduced (or incomplete) penetrance'. Reduced penetrance is not uncommon; indeed, there are many known examples of 'disease-causing mutations' that fail to cause disease in at least a proportion of individuals who carry them. Reduced penetrance may therefore explain not only why genetic diseases are occasionally transmitted through unaffected parents but also why healthy individuals can harbour quite large numbers of potentially disadvantageous variants in their genomes without suffering any obvious ill effects. Reduced penetrance can be a function of the specific mutation(s) involved or allele dosage. It may also be influenced by differential allelic expression, copy number variation or the modulating influence of additional genetic variants in cis or in trans. The penetrance of some pathogenic genotypes is known to be age- and/or sex-dependent. Penetrance may also reflect the action of unlinked modifier genes, epigenetic changes or environmental factors. At least in some cases, complete penetrance appears to require the presence of one or more genetic variants at other loci. In this lecture, I shall seek to demonstrate that reduced penetrance is a widespread phenomenon in human genetics and will explore some of the molecular mechanisms that may help to explain this enigmatic characteristic of human inherited disease.

K2

Genomics in Public Health

Angela Brand
Institute for Public Health Genomics (IPHG), Cluster Genetics and Cell Biology, GROW, Maastricht University, The Netherlands

Rapid scientific advances in genomics such as in the light of epigenomics, microbiomics and systems biology supported by new ICT solutions not only contribute to the understanding of disease mechanisms, but also provide the option of new promising applications in human health management during the whole life-course of a person. What was little time ago a vision for a new era of public health, in which advances from the -omic sciences would be integrated into strategies aiming at benefiting population health, is now responding to the very pressing need for the development of effective personalized healthcare going even beyond personalized medicine.

So far, all stakeholders including policy-makers and the private sector are struggling to translate the emerging knowledge into public health.

Public Health Genomics (PHG) is the area of public health ensuring that scientific advances in genomics ("from cell...") triggered by innovative technologies are timely, effectively and responsibly translated into health policies and practice for the benefit of population health ("...to society").The implementation of PHG requires increased concerted activities. The Institute for Public Health Genomics (IPHG) at Maastricht University aims to fulfil this task in all European Member States by hosting the European Centre for Public Health Genomics (ECPHG) and coordinating the Public Health Genomics European Network (PHGEN). Furthermore, it is actively involved in the FP7 CSA on Personalised Medicine (PerMed) funding bodies, as well as in the European Flagship Pilot ITFoM on the future of medicine that aims to achieve the visionary goal of the "virtual human".

INVITED LECTURES

L1

Breast Cancer in Arab Populations: Molecular Characteristics and Disease Management Implications

Jingxuan Shan, Konduru Sastry, Lotfi Chouchane
Professor of Genetic Medicine, Weill Cornell Medical College in Qatar, Qatar

Breast cancer incidence and prognosis differs among racial and ethnic groups. Breast cancers in women from Arab populations have different characteristics to those reported in individuals from Europe and the USA. For example, affected patients are at least a decade younger, they have a more advanced stage of disease at first presentation, and their tumour size is larger.

While socioeconomic, psychological, and lifestyle issues are undoubtedly important in such disparities, genetic factors may also play roles as shown by findings of genome-wide association and gene expression profiling studies. In this communication, I summarize recent investigations on breast cancer genes in Arab populations and report our recent findings unveiling the function of TNRC9 in breast cancer that highlights a new paradigm in BRCA1 regulation.

L2

Pharmacogenomics and Personalized Medicine in the Global Village

George Patrinos
University of Patras, School of Health Sciences, Department of Pharmacy, Patras, Greece

Medicine prioritization is a high stakes undertaking for developing countries and pharmacogenomics promises to materialize personalized treatment. Many developing countries currently lack the knowledge and/or the resources to individualize drug therapy. Here, we propose a multi-step approach for the implementation of pharmacogenomics in developing countries, focusing on emerging European countries. This approach includes (a) Collection of DNA samples from healthy volunteers to determine the various pharmacogenomic markers allele frequencies in this population, using a 2-tiered approach (b) Conduct a comprehensive health economic analysis to illustrate the cost-effectiveness of pharmacogenomic testing, (c) Survey the level of awareness and education of several stakeholders over genetics, including genetic laboratories, pharmacists, the general public and healthcare professionals, (d) Organization of education activities to disseminate pharmacogenomics knowledge to society, and (e) Establishment of national guidelines for medication prioritization. Since 2009, this approach is being implemented in the Hellenic population. DNA from 45 healthy donors of Hellenic origin was isolated with consent, and subsequently genotyped to determine the allele frequencies in 1,936 pharmacogenomic markers in 220 pharmacogenes, using the DMET+ microarray (Affymetrix, Santa Clara, CA, USA). We identified 46 pharmacogenomic markers that display divert allele frequencies compared to those of the Caucasian population ($p<0.05$), that are currently being confirmed in 500 healthy donors of Hellenic origin. We are also concluding a cost-benefit analysis to demonstrate the usefulness of integrating pharmacogenomics in everyday clinical decision-making process, to adjust the acenocoumarol-dosing scheme, while since 2009 we have initiated a pharmacogenomics educational meeting series for healthcare professionals and regulators in Greece and elsewhere abroad (the Golden Helix Pharmacogenomics Days). This approach is currently being replicated in other developing countries enabling integration of pharmacogenomics in healthcare decision-making process, provision of guidelines for medication prioritization for individual countries, using pharmacogenomic information and development of local infrastructure for future pharmacogenomic research studies.

INVITED LECTURES

L3

Advances in the Prenatal Diagnosis of Hemoglobinopathies in the UAE

Erol Baysal
Dubai Genetic and Thalassemia Center, Dubai Health Authority, Dubai, UAE

Advances in chorionic villus sampling (CVS) and in DNA-based diagnostics has provided impetus for successful implementation of prenatal diagnosis (PND) of hemoglobinopathies in the UAE. Direct detection of mutant genes has enabled many couples to seek DNA diagnostic services in the first trimester of pregnancy. The procedure empowers couples to consider options under informed consent. In the UAE, PND has been employed since 2005 as a principal diagnostic to determine fetal DNA status for beta-thalassemia.

INTRODUCTION: Advances in chorionic villus sampling (CVS) have rendered the first trimester PND a standard practice. The ability to detect mutant globin genes in CVS has provided a rapid, safe, accurate and reliable methodology for the early detection of many fatal genetic diseases. The genetic information enables the couples to reach a decision compatible with their beliefs and family planning criteria.

METHODOLOGY: DNA diagnostic services utilize the most advanced diagnostic tools mainly PCR and DNA Sequencing and include Thalassemias (alpha & beta-thal), Sickle Cell Disease (SCD) and Abnormal Hemoglobins. The DNA is extracted from CVS using Qiagen kits and is amplified by PCR using specific primers. The amplicons are sequenced on an ABI Genetic Analyzer 3130. The results are reported within 24 hours. Maternal contamination is excluded for each sample with STR Cofiler.

RESULTS & DISCUSSION: Since 2005, PND has been available for pregnancies at risk for virtually all inherited hemoglobin disorders in the UAE. Nearly 200 couples have been tested using the CVS and subsequent DNA analyses involving PCR and DNA Sequencing. The couples were predominantly from the UAE. Others were from Bahrain, Kuwait, India, Pakistan and other countries in the region. The couples with affected fetuses were counselled and given appropriate available options.

CONCLUSION: Accurate detection and counselling of at-risk couples is a promising way to reduce the mortality and morbidity from beta-thalassemia in countries where it is prevalent.

L4

The Relationship between Genome Structure and Function: Lessons from the Globin Loci

Douglas R Higgs
Director, MRC Molecular Haematology Unit, Weatherall Institute of Molecular Medicine, Oxford, UK

We have studied how transcriptional and epigenetic programmes are played out on chromatin spanning the terminal 500kb of human chromosome 16 (16p13.3) as hematopoietic cells undergo lineage fate decisions and differentiation. This region includes the alpha globin cluster and its regulatory elements, which are silenced via the Polycomb system in early progenitors, poised for expression in later progenitors and fully expressed during terminal erythroid differentiation. Other genes in this region are also up-regulated in an erythroid specific manner. Using a variety of approaches we have established the order in which silencing factors are removed, activating transcription factors bind and epigenetic modifications occur. In addition we have shown how chromosomal conformation and nuclear sub-localisation change during hematopoiesis. Natural cis and trans acting mutations (involving transcription factors and chromatin associated proteins) that cause alpha thalassaemia provide additional insight into how the long range regulatory elements may interact with the promoters of the globin genes and other flanking genes to activate their expression. Together these observations establish some of the general principles by which genes within their natural chromosomal environment are switched on and off during hematopoiesis. These findings add to our general understanding of the relationship between genome structure and function.

INVITED LECTURES

L5

Search for the Genetic Modifiers of Disease Severity in Tibial Hemimelia in a Large Multigenerational Arab Family: Progress and Future Directions

Mohammed Naveed
Director of Planning & Operations, H.H. Sheikh Sultan Bin Khalifa Al Nahyan Humanitarian & Scientific Foundation, UAE

Split-hand/foot malformation with long-bone deficiency (SHFLD [MIM 119100]), a rare and severe limb deformity, is also known as tibial aplasia (TA) with split-hand/split foot deformity. It is characterized by hypoplasia or aplasia of tibia, with relatively intact fibula, associated with split-hand/split-foot deformity that more often affects the upper limb. The incidence of SHFLD has been estimated to be ~1 per million live births. Genomic regions with evidence of linkage for SHFLD were identified SHFLD1 and SHFLD2 and SHFLD3 loci on various chromosomal regions including two of our identified loci residing at 1q42.2-q43 and 6q14.1 in a large multigenerational Arab family which most likely contain novel susceptibility genes for autosomal SHFLD. Additionally, six suggestive loci with evidence of linkage on 1p36.13, 1q31.1, 1q42.3, 4q34.3, and 6q14.1 and 17p13.1 regions have identified using a high resolution SNP array in the same Arab family (Am. J. Hum. Genet.2007; 80:105–111). Considerable progress has been made recently in identifying genes that are responsible for SHFLD predisposition. Recently, we have identified microduplications on chromosome 17p13.3, a locus previously associated with SHFLD, has been found in sporadic and familial SHFLD patients, suggesting that a single gene, BHLHA9 within the duplication play an important role in SHFLD development (J Med Genet. 2012 Feb;49(2): 119-25). Additionally, reports from our recent exome sequence study of selected UAE SHFLD subjects showed that 2 polymorphic variants within the coding regions of on chromosomes 1q42.2-q43 and on 6q14.1 regions significantly affect SHFLD phenotype. The present analysis provides the understanding the pathophysiology of the disease and also providing definitive genetic diagnosis of the condition. Additionally, the data also help us in developing non-invasive methods of screening for the disorder in at-risk family members, in order to reassure those are not carrying the mutation and to plan prophylactic measures for those who are or will be affected. A detailed recent genetic data, future directions of studies of SHFLD will be presented.

L6

Next-Generation Sequencing in the Clinic: Enabling Genomic Medicine

Radoje Drmanac
Chief Scientific Officer, Complete Genomics, Inc., Mountain View, California, U.S.A.

Advanced massively parallel DNA sequencing using genomic nanoarrays enables to efficiently and accurately sequence entire genome of millions of people including tumor cells. This ultimate genetic test when broadly applied will provide a foundation for Genomic Medicine and Genomic Healthcare. Introduction: Our genomes encode a program for development and adaptive functioning of all our tissues in six billion DNA letters, three billion inherited from each parent with thousands of rare family variants and about one hundred de novo mutations as personal variants. Due to such complexity, highly accurate genome sequencing at low cost is critical for personalized disease prevention, diagnosis and treatment. Methodology: Genomic DNA nanoarrays continue to advance our ability to efficiently sequence a large number of individual human genomes at exceeding sensitivity and specificity, including separate sequence assembly of parental chromosomes (haplotyping) with less than 1 error per 10 million bases. Imaging advances allow several tera-bases per day per instrument. Furthermore, accurate whole genome sequencing (WGS) including comprehensive detection of de-novo mutations is now achievable from non-invasive micro-biopsies of IVF embryos or circulating fetal or tumor cells. Discussion: These advances in human WGS are shifting the bottleneck for broad use of genomic medicine from genome sequencing to genome interpretation. Sequencing genomes and determining other "omes" from millions of individuals and families with extensive clinical measurements will provide an urgently needed genomic knowledge base. We expect creation of such data base in a few years. Conclusions: We are approach an era when every person will have their genome sequenced even before birth, securely stored in computer memory and used for their entire life for personalized health management as well as personalized learning or parenting. WGS as the ultimate genetic test allows a long term standardization of health related industries and other industries.

INVITED LECTURES

L7

Personal Genomes are Personalised

Jun Wang
Director, BGI, Shenzhen, China

It is ten years since human genome project was drafted, yet we are still asking how genomes will help health care for people in general. The recent sequencing revolution has brought affordable personal genomes into practice in terms of cost and throughput, but it remains very difficult to interpret a genome to make sense for the owner. Scientists are still struggling in biomedical genomics studies to get the meaning of every nucleotide in the sequence, while missing heritability in complex diseases confuses researchers, and prevents disease modeling, prevention and prediction.

Our recent studies have proposed two possible explanations for the missing heritability. First, we have discovered an excess of rare, deleterious SNPs in the average human population, which are not designed into current genome-wide association study (GWAS) arrays. Second, we have identified extensive structural variations as well as individual-specific sequences among human individuals with potential functional impacts. In all, we believe each human genome is actually highly personalized, or private, as a personal genome. Continuing innovations in technology could finally prove that by complete de novo assembly of multiple private genomes we could find the key to human genomics for medical genomics and health care.

L8

Next Generation Sequencing, Genomic Medicine, and You

Fahd Al Mulla
Professor, Head of Molecular Pathology, Assistant Vice President for External Research Collaboration, Kuwait University, Kuwait

INTRODUCTION: Worldwide, breast cancer is the most common cancer in women. Susceptibility is thought to be polygenic and the risk tends to increase in women with positive family history of breast cancer. Breast cancer in the Gulf states seem to have a stronger tendency for familial clustering. Furthermore, many women are diagnosed with breast cancer at a relatively early age, so that the mean age of diagnosis in Kuwait is almost eleven years younger than in other comparable populations. Both of these factors suggest that at least one gene of major effect is operating to produce familial clustering of breast cancer, early-onset of breast cancer, or perhaps both.

METHODS: Current diagnostic and unpublished data do not support a major founder effect for the BRCA1/BRCA2 genes, especially with the fact that most breast cancers diagnosed in Kuwait and the region are estrogen receptor positive. We propose to undertake an ambitious study of approximately to exome sequence 100 women in a case-control format enriched for family history on the HiSeq 1000/2000 Illumina platforms to identify novel genes associated with breast cancer risk.

INVITED LECTURES

L9

Elucidation, Diagnosis and Prevention of Intellectual Disability: Meeting the Challenge

Hilger Ropers
Director, Max Planck Institute for Molecular Genetics, Berlin, Germany

INTRODUCTION: Intellectual disability (ID) is the most frequent reason for referral to Genetic Services and a major socio-economic burden, particularly in countries where parental consanguinity is common. Most severe forms of ID have specific genetic causes. Many hundreds of these have already been identified, but far more remain to be found, as a prerequisite for diagnosis, prevention and improved disease management. Yet, compared with other neuropsychiatric disorders where the role of genetic factors is less obvious, ID has been low on the agendas of policy makers including the WHO. As discussed here, diagnostic next generation sequencing (NGS) is an efficient strategy to solve this problem, and the time is ripe for it.

METHODOLOGY: Targeted enrichment and NGS is a fast and cost-effective procedure to establish the diagnosis in patients carrying mutations in established ID genes. Building on a previously described test for ~600 severe recessive childhood disorders (Bell et al, Science TranslMed 2010) and on a comprehensive list of genes implicated in ID, we have developed a novel diagnostic tool to detect mutations in most of the presently known ID genes. Data were analyzed with a novel, easy-to-use sequence analysis pipeline (Hao Hu et al, in preparation), comprising powerful subroutines for predicting the pathogenicity of missense mutations and for identifying medium-sized indels, which are a problem for widely used genome analysis software packages. In parallel, Whole Exome Sequencing (WES) in ID patients and families revealed numerous apparently causative mutations in novel ID genes, including de novo changes.

DISCUSSION AND CONCLUSION: Due to the extreme genetic heterogeneity of ID and the paucity of specific clinical signs, NGS is indispensable for the diagnosis of ID. Its clinical implementation will greatly accelerate the identification of clinically relevant mutations and genes and shed light on the molecular causes of ID and related conditions such as autism, schizophrenia and epilepsy, which are still largely unknown.

L10

Massively Parallel Sequencing Identification of Novel Genes and Mutations for Breast Cancer and Hereditary Hearing Loss in Palestine

Moien Nihad Kanaan
Professor of Molecular Genetics, Director of the Hereditary Research Lab, Bethlehem University, Palestine

BACKGROUND AND PURPOSE: Identification of inherited mutations has been an ongoing challenge in human medical genetics. Using advanced targeted DNA capture and massively parallel sequencing technologies, in conjunction with homozygosity mapping relevant for consanguinous families, we are meeting this challenge for hereditary hearing loss, Breast cancer and other genetic abnormalities. Our cohort consists of Palestinian Arab families of variable size, and onset of hearing loss and breast cancer .

METHODS AND MATERIALS: We constructed two custom design arrays of cRNA oligonucleotides containing 250 genes, responsible for both human and mouse deafness. and a custom array containing 38 breast and ovarian cancer (BROCA) associated genes We prepared paired-end libraries, followed by cluster amplification on v4 Illumina flow cells with our bar-coded multiplexed samples. A 2x72bp paired end recipe was used, resulting in a median base coverage of 300-572x and overall, 94.7% of our targeted bases covered by more than 10 reads, which was our cutoff for variant detection.

RESULTS: We generated SNP and indel calls for our samples and filtered the variants against those of dbSNP131 and the 1000 Genomes project to identify private and rare variants. Novel genes and mutations were discovered. Most compelling, a number of mutations were found in genes previously known only to be involved in mouse deafness. Protein structure predictions were made to provide insight into how the mutations lead to the predicted phenotypes.

CONCLUSION: Discovery of additional deafness, breast cancer genes and mutations will allow for early clinical diagnosis, enabling prediction of phenotypes and enhanced management. Characterization of the proteins encoded by these genes will enable a comprehensive understanding of the biological mechanisms involved in the pathophysiology of these disorders.

INVITED LECTURES

L11

Consanguineous Marriages: Past, Present and Future Trends in Counseling

Hanan Hamamy
Department of Genetic Medicine and Development, Geneva University, Switzerland

Young consanguineous couples contemplating marriage are nowadays seeking a scientifically sound answer to their questions:
"Will our children be physically or mentally abnormal?"
"How can we prevent having abnormal children?"

In a number of countries in the Middle East, premarital screening to detect high risk carrier couples for specific common autosomal recessive conditions such as hemoglobinopathies has been going on for the past two decades with examples of successful lowering of the birth rate of affected in some countries. However, consanguineous couples have an increased risk to have children that could be affected by any of the 2400 autosomal recessive conditions, most of which are rare disorders, when both partners share a pathogenic variant identical by descent from their grandparents.

The technological advances for rapid and inexpensive high throughput genome sequencing (HTS) and for the identification of copy number variants by comparative hybridization (aCGH) offer an unprecedented opportunity to identify a large number of known pathogenic variants. The presentation will discuss the feasibility of application of these technologies to detect shared known autosomal recessive pathogenic variants giving the chance for at risk couples to decide on their reproduction options aiming at the care and prevention of autosomal recessive disease in their offspring.

L12

Clinical Implementation of Pharmacogenetics

Ron H. van Schaik
Associate Professor Pharmacogenetics, Erasmus University Medical Center, Rotterdam, The Netherland

Personalized Medicine is an important topic in today's drug therapy. Adjusted dosing or alternative drugs based on genetic information seems possible today. However, the uptake of pharamcogenetics in a clinical setting is rather limited.

INTRODUCTION: Pharmacogenetics is the study of the impact of inherited DNA variants encoding metabolizing enzymes, drug transporters or target proteins on the effectively or adverse reactions on drug therapy. This information on individual metabolic capacity should enable a personalized approach to optimize drug therapy. The amount of publications identifying potential clinically relevant pharmacogenetic markers is high (>1,000 articles/year) and is increasing exponentially. In addition, new techniques like Next Generation Sequencing are rapidly evolving, facilitating access to complete genetic information in relation to drug metabolism.

METHODOLOGY: Our laboratory started offering pharmacogenetic tests for routine patient care in 2005. Based on literature, additional tests were developed. Interaction with clinical disciplines and in close collaboration with Hospital Pharmacy, this includes CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DPYD, SLCO1B1, TPMT, VKORC1, HLA-B*5701, HLA-B*1502 and HLA-A*3101 testing. Discussion: During our 7 years of experience, we have performed pharmacogenetic testing for 2,000 patients. The most frequently requested tests are TPMT, CYP2D6 and HLA-B*5701. Despite the promise of Personalized Medicine, the clinical implementation of pharmacogenetic tests is still going slowly. Currently, we are seeing an increase of 40-50% in test requests per year.

CONCLUSION: As a genetic test, pharmacogenetic analysis seems to be treated different from other laboratory tests in our experience in that a lot of evidence is requested before clinicians are willing to consider the test, especially as a screening tool. Awareness, education, clinical usefulness, consensus in literature, how to adjust therapy based on genetics and cost-effectiveness are factors that need to be addressed.

INVITED LECTURES

L13

High Throughput Genetic Studies and Advanced Functional Analyses of Brugada Syndrome Patients

Maurizio Ferrari

Vita-Salute San Raffaele University, San Raffaele Scientific Institute, Genomic Unit for the Diagnosis of Human Pathologies, Center for Translational Genomics and Bioinformatics, and Diagnostica e Ricerca San Raffaele SpA, Milan, Italy

Background and Purpose: Recent developments of next generation sequencing (NGS) represent a great opportunity to identify new candidate genes in genetically heterogeneous pathologies, allowing to increase the number of affected patients without a molecular diagnosis. Specifically, we performed targeted enrichment in a cohort of 91 Brugada patients to identify new candidate genes potentially involved in the Brugada Syndrome (BrS) pathogenesis. To assess of functional impact of mutations, we performed functional studies based on the use of heterologous systems in vitro and in silico, to establish a connection between genotype and electrical phenotype. We developed also disease models based on cardiomyocytes derived from iPS (CM-iPS) obtained from patient's skin fibroblasts, to improve our understanding of the mechanisms involved in arrhythmogenesis. Methods: We drawn a panel of 158 candidate genes. We used the Agilent Sureselect target enrichment protocol and the sequencing was performed on Illumina GA IIx. To manage the sequencing data, we developed an automated bioinformatics pipeline based on BWA aligner, which is able to map reads versus the hg19 reference. Results: We obtained a median of 273 protein-coding variations per sample considering only variants annotated in coding region. In order to select and prioritize candidate mutations, we filtered out all variations already known as common polymorphisms within the human population as well as the variations present in non-coding regions. We further analyzed three categories of variants: novel NS-SNVs possibly affecting protein function, previously reported rs-clinical variations in dbSNP137 and novel coding INDELs. In particular, 85 variants were reported as NS-SNVs, 60 mutations resulted already known as rs-clinical variations and 13 novel coding HQ-INDELs. Conclusions: The identification of these variants could be crucial for improving risk stratification and clinical management of asymptomatic patients. To date the predisposition to develop fatal arrhythmias cannot be easily predicted and no anti-arrhythmic drug is effective in preventing from life-threatening arrhythmias. such as autism, schizophrenia and epilepsy, which are still largely unknown.

L14

Aldehyde Dehydrogenases as Novel Therapeutic Targets for Metabolic Diseases and Cancer Stem Cells

Vasilis Vasiliou

University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

The aldehyde dehydrogenase (ALDH) superfamily comprises NADP-dependent enzymes that catalyze the oxidation of aldehydes to their corresponding carboxylic acids. To date, 19 ALDH genes have been identified in the human genome. In addition to aldehyde metabolizing capacity, ALDHs have additional catalytic (e.g. esterase and reductase) and non-catalytic activities. The latter include functioning as structural elements in the eye (crystallins) and as binding molecules to endobiotics and xenobiotics. Mutations in human ALDH genes are the molecular basis of several diseases, including gamma-hydroxybutyricaciduria, type II hyperprolinemia, Sjögren-Larsson syndrome, pyridoxine-dependent epilepsy as well as osteoporosis and gout. ALDH enzymes also play important roles in embryogenesis and development, neurotransmission, oxidative stress and cancer. One of the most exciting recent discoveries regarding ALDHs is their identification as markers of cancer stem cells and their involvement in cancer cell resistance to chemotherapy and radiotherapy. Thus, therapeutic targeting of ALDHs may represent a novel means of more effectively treating patients with cancer or metabolic disease and improving clinical outcomes.

INVITED LECTURES

L15

Recent Advances in Translational Genomics and the Future of Medical Genetics in the Middle East

Aida I. Al Aqeel
S. Consultant and Head Paediatric Medical Geneticist and Consultant Endocrinologist, Department of Paediatrics, Riyadh Military Hospital, Riyadh, Saudi Arabia

Although medical genetics has taken the lead in developing genetic technology and in translational research in clinical practice, this may become increasingly difficult as genetics goes "mainstream" and is incorporated in the different specialties. The information generated by genomic research will in the long-term have major benefits for the prevention, diagnosis and treatment of many diseases, e.g. cancer, diabetes, dementia, rheumatic diseases, neurological diseases & others. For example, we recognize that the sequence of the genome is only a part of the information required, and additional "omic dimensions" such as transcriptomics and epigenomics must be integrated. In addition, association data on large and adverse populations across these dimensions will be critical to attain highly predictive and personalized diagnostic information. In Saudi Arabia like other countries in the developing world first cousin marriages account for almost 60-70% of all marriages, leading to uniquely common disorders. A review of our patients files over 15 years period, documented more than 150 varieties of neurodegenerative disease among 2,000 children; 27 of which constitute more than half of these files. Some autosomal recessive disorders are common eg. sickle cell anaemia and thalassaemia. Others are unique eg. Al-Aqeel-Sewairi syndrome. Many of the advances in medical genetic can be predicted to be technology driven and the cost of genetic testing will fall rapidly. The impact of the next generation sequencing will change in many areas of diagnosis and prevention. One area will be prenatal testing on maternal blood sample by free fetal DNA. Another is cancer screening by oncogene mRNA. In addition there will be more accurate prediction of genetic risk which will lead to lifestyle counseling and personalized medicine. In Saudi Arabia medical Genetics has taken the lead in transitional research. For the last ten years pre- implantation genetic diagnosis and newborn screening for genetics metabolic disorders are the most important preventive programs. The Stem Cell Therapy Program was also established at King Faisal Specialist hospital and research centre with launching of ten projects. In conclusion: personalized medicine should not be limited to diagnostic and prognostic approaches, and must include personalized therapeutic strategies. Therefore we will explore the challenges as well as the progress and recent advances in the implementation of personalized transitional genomics in the clinical setting, including diagnostic and preventive strategies e.g. new born screening, pre implantation genetic diagnosis and new therapeutic strategies like stem cell therapy and personalized therapeutics strategies at the genomics level.

L16

Neurotrophins as Therapeutic Targets for Neurodegenerative Diseases

Achilleas Gravanis
Professor of Pharmacology, School of Medicine, University of Crete, Greece

Neurotrophins hold a central role in brain deve-lopment and maintenance as well as in various neurodegenerative conditions. Neurotrophins control neural cell fate and function after binding and activation of prosurvival tyrosine kinase Trk and pan-neurotrophin p75NTR receptors. However, their polypeptidic nature limits their potential applications in the pharmacological management of neurodegenerative diseases and brain trauma. We have recently shown that neurosteroiddehydroepiandrosterone (DHEA), prevents neuronal apoptosis (Charalampopoulos et al, PNAS 2004), through binding to TrkA and p75NTR receptors (Lazaridis et al, PLoSBiol 2011), activating prosurvival mir21 and anti-apoptotic Bcl-2 proteins, preventing thus the apoptotic loss of NGF receptor positive sensory and sympathetic neurons in NGF null mice. These findings suggest that neurosteroid DHEA may act as a small molecule with NGF receptor agonist properties. However, DHEA is metabolized in vivo to sex steroids, affecting the endocrine system and increasing the risk for hormone-dependent tumors. We have recently synthesized 17-spiro analogs of DHEA with strong neuroprotective properties (EC50 at nanomolar levels), and deprived of the endocrine ones (Calogeropoulou et al, J Med Chem 2009). These synthetic neurosteroidalmicroneurotrophins bind to NGF receptors, activate phosphorylation of TrkA and the interaction of RIP2 and RhoGDI effectors with p75NTR receptor. They also partially reverse apoptosis of NGF-dependent embryonic sensory neurons of NGF null mice. The neuroprotective actions of Microneurotrophins are now tested in various animal models of neurodegenerative diseases. Additionally, we test the neurogenic effects of Microneurotrophins in fetal and adult neural stem cells. In conclusion, Microneurotrophins may serve as lead molecules to develop blood brain barrier permeable neurotrophin-like small molecules with potential applications in the treatment of neurodegenerative diseases (Gravanis et al, Science Signaling 2012).

INVITED LECTURES

L17

Quantification of Genome Sharing in Consanguineous Couples with or without Affected Children by Autosomal Recessive Disease and Impact on Genetic Counseling

Habiba Bouhamed Chaabouni
Professor, Laboratory of Human Genetics, Faculty of Medicine of Tunis; Service of Hereditary Disorders, Hospital Charles Nicolle, Tunisia

Consanguineous marriages are associated more with multifactorial birth defects and a higher frequency of autosomal recessive disorders than marriages between unrelated individuals. Genetic counseling could establish the risk of having affected descendants for a consanguineous couple. It is commonly known that for a first-cousin couple an additional risk of 2 - 4% should be added to this basic risk that can increase if a family history of a genetic disorder exists. Beside consanguinity, endogamy is a risk factor too for autosomal recessive diseases that is why genetic counseling has to consider endogamy. Recent advances in genome analysis techniques and methodologies such as homozygosity mapping and exome sequencing have demonstrated the role of consanguinity in determining deleterious genotype status of patients born from related parents. We carried out a study of a cohort of 290 couples with a child affected by an autosomal recessive disorder. Genetic testing confirmed the molecular basis of the disease and established the genotype status of affected patients. More than 60% of non-consanguineous parents shared the same geographical origin. Furthermore 9% of patients born from consanguineous parents were found to be compound heterozygous and 68% of patients born to unrelated parents were homozygous for their identified mutation. These results demonstrate that homozygosity could result from Identity by Status (IBS) or from Identity by Descent (IBD) on top of that probably most of the affected patients from related parents are IBD. IBD evaluates the genome sequences shared by both parents. Genome-Wide Human SNP Array made possible the determination of shared genome sequences proportion between individuals. In a second study we analysed two groups of consanguineous parents. For this purpose we used Genome-Wide Human SNP Array 6.0, which is a single array that contains 906,600 SNPs. The same array also contains 945,826 copy number probes designed to interrogate CNVs in the genome. We analysed and compared shared genome sequences between these two groups of consanguineous couples. The first set included parents of at least one affected child with autosomal recessive disease and the second group included couples with no affected child that are parents of 3 or more normal children. Our conclusion is that consanguinity and endogamy are both at the origin of deleterious genotype responsible for recessive genetic disorders but the risk of affected siblings is related toshared deleterious genome status (quality genes) and not to shared quantity genome. Personalised genome analysis will be the best tool for genetic counseling and hereditary disorders prevention in high consanguineous population.

L18

Prevalence of Congenital and Genetic Disorders in the Sultanate of Oman. Steps towards Genetic Service needs assessment

Anna Rajab
Ministry of Health, Sultanate of Oman

It has been anticipated that improvement in quality of life, comprehensive healthcare facilities and successful control of communicable diseases in Oman would result in a change in disease pattern. Although genetic and congenital disorders are increasingly observed in medical practice, convincing data to support these observations is required.

An attempt to assess morbidity related to congenital and genetic disorders was made in order to aid future planning of the genetic services.

Interviewing mothers was assumed to be the most accurate rout of collecting data in the absence of centralized medical records. More than 3000 mothers had contributed with detailed histories of morbidity and mortality in their children and relatives. Maternal morbidity reports were verified with hospital records.

Significant mortality and childhood morbidity due to congenital and genetic disorders was reported. As much as 10% of interviewed mothers indicated morbidity from congenital and genetic causes, and a third of all morbidity reports were known AutosomalRecessive disorders.
The details of morbidity and mortality are discussed in view of planning genetic services and research.

INVITED LECTURES

L19

A Success Story of the Centre for Arab Genomic Studies at its 10th Anniversary; the CTGA Database: Challenges and Prospects

Abdul Rezzak Hamzeh
Senior Scientific Coordinator, Centre for Arab Genomic Studies, Dubai, UAE

As the largest ethnic-based database worldwide; the Catalogue for Transmission Genetics in Arabs (CTGA) has been going nonstop since 2004, providing free access, up-to-date information on genetic disorders in Arabs. Continuous growth in terms of quantity and quality of contents and records has been the hallmark of this unique database. Numbers of CTGA entries have been increasing considerably quicker, thus providing wider coverage of genetic loci that are involved in the pathogenesis of hereditary diseases.

Consequently, the number of online visitors seeking information on these disorders exhibited a parallel upward trend. With the bird's-eye view the CTGA database provides over scientific data from research performed on Arabs worldwide, it has been the basis for a large number of publications. Many of these publications focused on careful analysis of the huge wealth of data at hand and made use of the position of the Centre for Arab Genomic Studies as a melting pot for distinguished Arab geneticists. With the support of Sheikh Hamdan Bin Rashid Award for Medical Sciences, all of these publications are freely distributed, which further helps their wider dissemination. Moreover, the CTGA played an important role in the process of policymaking and featured frequently on national and international media. At this stage the software and hardware components of the CTGA database are undergoing a crucial revamp in order to cope with the increasing number of users and entries. This presentation sheds light on the content of the database, its past growth and its future prospects.

L20

The Molecular Functions of Chromatin Modifiers

Ahmed Al-Marzouqi
College of Medicine and Health Sciences, UAEU, UAE

In eukaryotes, the compaction of DNA into the nucleus inhibits the access of factors to DNA which leads to the repression of many important cellular processes required for maintenance and growth of the cell. To access the DNA and the genes, the nucleoprotein structure, called chromatin, which consists of DNA, histones, and non-histone proteins needs to be opened up or altered. This is accomplished as a result of DNA and histone modifications or by DNA binding protein. Many studies in the past few years have described conserved protein complexes whose function is to modulate the access of transcription factors to regulatory regions of genes relieving chromatin-mediated repression. The action of these complexes that are able to overcome the repressive effects of chromatin is an important step in the regulation of eukaryotic gene expression.

Research in my laboratory focuses on understanding how certain proteins can regulate gene expression by modifying the structure of chromatin or interacting with its components. We are interested in how different types of chromatin modifiers work in turning genes on or off. This is an important question since gene regulation can determine the amount of protein production required for important functions of all cells. This is also important since many subunits of these chromatin modifiers in humans have been implicated in the initiation of various diseases.

Phylogenetic analysis shows that these complexes share several common features including the presence of a distinct ATPase domain. Based on sequence homology to this domain, we have recently identified new candidate remodelers (i.e. Fun30, Irc5, and Irc20) in yeast Saccharomyces cerevisiae. We have previously reported that Fun30 is a homodimer with a molecular weight of about 250 kDa. Biochemical characterization of this complex revealed that it has ATPase activity stimulated by both DNA and chromatin. Consistent with this, Fun30 could also bind to both DNA and chromatin and exhibited activity in ATP-dependent chromatin remodeling assays. Interestingly, its activity in histone dimer exchange was high relative to the ability to reposition nucleosomes. We are also studying the functions of Irc5 and Irc20, two other potential remodelers with a role in DNA repair. Here, I will present some preliminary results on the functions of these potential chromatin remodelers.

ORAL PRESENTATIONS

01

Role of sema3C in Breast Cancer Progression and its Effects on Cancer Cells Proliferation, Adhesion and Invasion

[1,2]Muhammad Malik, [1]Lin Ye, [1]Wen G Jiang

[1]*Metastasis and Angiogenesis Research Group, Institute of Cancer and Genetics, Cardiff School of Medicine, Cardiff University, Heath Park, Cardiff, CF14 4XN, United Kingdom,* [2]*Department of Biosciences, COMSATS-Institute of Information Technology, Park Road, Chak Shazad, Islamabad, Pakistan*

BACKGROUND AND PURPOSE:
Involvement of sema3C in disease progression of certain solid tumours has been explored in the recent years. The aim of current study was to explore the role of sema3C using both breast cancer cohort and breast cancer cell lines.

METHOOLOGY AND RESULTS:
After RNA isolation and cDNA synthesis, sema3C expression was analyzed using real time PCR technique. Poorly differentiated tumour tissues showed higher sema3C expression when compared with well differentiated tissues (p=0.021 grade2 and grade3 vs grade1). No significant correlation of sema3C with TNM staging had been observed. ERa;(+) patients showed higher sema3C when compared with ERb (-) tissues (p=0.03). No significant association of sema3C with her-2 was observed. Knockdown of sema3c was performed in MDA-MB-23l and MCF-7 cells using ribozymes targeting sema3c mRNA. In the sema3c knockdown cells, a significant increase of cells attachment to basement membrane was observed (MDA-MB-231sema3Crib, p=0.04 vs. control cells and MCF-7 sema3Crib, p=0.04 vs. control cells). Cell proliferation was also reduced following the knockdown of sema3c (MDA-MB-231sema3Crib, p=0.02 vs. control cells and MCF-7 sema3Crib, p=0.01 vs. control cells). Furthermore, invasiveness of MCF-7sema3Crib and MDA-MB-231sema3Crib cells was also reduced compared with the controls (p=0.03, p=0.04 respectively).

CONCLUSION:
These findings suggest sema3C as a potential target molecule for breast cancer treatment.like small molecules with potential applications in the treatment of neurodegenerative diseases (Gravanis et al, Science Signaling 2012).

Keywords: Cancer, Semaphorins, Invasiveness

02

A Novel Method to Identify Imprinted Genes in Nasopharyngeal Carcinoma Pathogenesis

Ismail Alhwij, Ashley Soosay
University Sarawak Malaysia (UNIMAS), Sarawak, Malaysia

BACKGROUND AND PURPOSE:
Genomic imprinting is a normal unique process, occurs during the development of gametogenesis by heritable epigenetic modifications, in which monogenic expression happens. Imprinted genes are usually conserved between mouse and human. There are currently 120 human imprinted genes. Disruption of imprinting status has been reported in cancer. Loss of heterozygosity (LOH) is common in cancer, and imprinted genes are more likely to be affected by LOH due to their functional haploidy. Nasopharyngeal carcinoma (NPC) is a rare malignancy. It is an endemic disease in certain areas, including Southeast Asia and Northern Africa. Environmental factors, Epstein-Barr virus (EBV) infection, and genetics have been associated with NPC. This study aimed to unveil the profile of imprinted genes involved in NPC by using data mining from literature of genetic and cytogenetic analyses.

METHODS AND MATERIALS:
Six comparative genomic hybridization (CGH), and sixteen LOH studies were reviewed to identify the critical regions in primary NPC. Human imprinted genes (HIGs) database (http://www.geneimprint.com/site/genes-by-species) was extensively used to identify genes in the critical regions in primary NPC. Ensembl database (http://asia.ensembl.org/index.html) and computational prediction of the mouse imprinted genes study was utilized to delineate human orthologues genes. All polymorphic microsatellite markers (PMSMs) were authenticated on the current Ensembl database and Squencher 5.1 was used to build a comparative physical map of PMSMs, imprinted genes, and a reference human chromosome segment. RESULTS: Twenty-four critical regions in primary NPC were related to imprinted genes. Twenty-two genes from the HIGs and twenty-six human orthologues genes from syntenic analysis were identified. Eleven genes have been reported as imprinted whereas 25 genes are putative imprinted genes.

CONCLUSION:
The novel method used in this study has been a fruitful endeavour. However, further genetic and epigenetic analysis using NPC samples will clarify the power of this method in identifying imprinted genes in NPC pathogenesis.

Keywords: Nasopharynegeal carcinoma, Loss of heterozygosity, Comparative genomic hybridization, Imprinted genes

ORAL PRESENTATIONS

03

Novel Missense Mutation in ANKRD26 Gene cause Familial Thrombocytopenia

[1]Walid Dridi, [1]Saad Daama, [2]Lifeng Tian, [2]Patrick Sleiman, [2]Hakon Hakonarson, 1Yousef Housawi, [2]George Otieno, [2]Cuiping Hou, [2]Lyam Vasquez, [2]Cecilia Kim, [2]Mohammed Sager
[1]*King Fahad Specialist Hospital-Dammam, Saudi Arabia,*
[2]*Children Hospital Of Philadelphia, United States of America*

INTRODUCTION:
Inherited thrombocytopenias are heterogenous group of diseases that are characterized by decreased platelet count and an increased risk of bleeding. To date, mutations in at least 17 different genes have been associated. Autosomal dominant thrombocytopenia (THC2) was linked only to MASTL and ACBD5 genes. However, subsequent work cast doubt on the causality of both genes and implicated mutations in the 5'UTR of ANKRD26 as the underlying cause of the phenotype. Mutations have been described in the same 22 nucleotide stretch of the 5'UTR in a total of 21 pedigrees. Saudi Arabian family with apparent THC2 was investigated for the known molecular testing but was negative. OBJECTIVES: Detect and characterize mutations in this family which can be related to this mild form of THC2.

MATERIALS AND METHODS:
Whole Exome Sequencing was performed at Applied Genomic Center, Children Hospital Of Philadelphia, in two affected individuals from a large 4 generation Saudi Arabian family. Agilent SureSelect 2 target enrichment kit was used to prepare exome libraries for sequencing on an Illumina HiSeq 2000 instrument. Samples were sequenced to an average read depth of 40x. Reads were aligned and variants called using the GATK software package. Variants were annotated using ANNOVAR. RESULTS: Both affected individuals shared a heterozygous missense mutation in the ANKRD26 gene [c.A473G:p.D158G], which also segregated with the phenotype in the extended family.

CONCLUSION:
Mutations in the 5'UTR of the ANKRD26 gene have been previously associated with thrombocytopenia, leading to the hypothesis that increased ANKRD26 expression may result in the phenotype. Here, we report the first missense mutation in ANKRD26 causal of thrombocytopenia 2 (THC2). This finding supports the role of ANKRD26 in THC2, extends the range of mutations in the gene associated with THC2 and provides a mechanism for furthering our understanding of how mutations in ANKRD26 result in THC2.

Keywords: Platelet, Thrombocytopenia, TCH2, ANKRD26 gene, NGS

04

Genetically Influenced Metabotype and Human Metabolic Individuality

Karsten Suhre
Weill Cornell Medical College in Qatar, Qatar

BACKGROUND AND PURPOSE:
Genome-wide association studies (GWAS) have identified many genetic variants that predispose to complex disorders, such as Type 2 Diabetes, chronic kidney disease and cardiovascular heart disease. However, the effect sizes of these variants are typically small and do account only for a small portion of the heritable part of these diseases. Gene-gene and gene-environment interactions may explain part of this missing heritability. However, such effects are hard to identify without access to a more extensive characterization of the patients.

METHODS AND MATERIALS:
Metabolomics as the technique of determining ideally all relevant small molecules in a biological sample provides a quasi unbiased access to many intermediate metabolic phenotypes that lie on the path from genetic and environmental factors to the disease endpoints. We conducted a series of GWAS with metabolic traits in human blood and urine to identify the genetic basis of human metabolic individuality.

RESULTS:
We identified a series of genetically influenced metabotypes (GIM). These GIMs are genetic variants with typically large minor allele frequencies. They are often located in or near enzyme or transporter coding genes, and the associated metabolic traits most often matches the metabolic function of the gene. Maybe most importantly, many genetic variants that give rise to GIMs are also identified in GWAS with complex disorders, indicating that a specific GIM indeed plays a role in the pathway that leads to the disease. CONCLUSION: In this presentation I shall give an update about the fast moving field and report the latest. I shall discuss ideas about how these genetic variants can now be used more broadly in the biomedical context, such as for rational targeting of metabolic pathways in cancer and diabetes.

Keywords: Genome-wide association study, Metabolomics, Population study, Metabolic individuality, Genetic variance

ORAL PRESENTATIONS

05

Sensorineural Hearing Loss and Male Infertility A Case Report

[1]Bibhas Kar, [1]Sivamani S, [2]Kundavi S, [2]Thangam Varma
[1]*Centre for Genetic Studies & Research, The Madras Medical Mission,* [2]*Institute of Reproductive Medicine & Women Health, The Madras Medical Mission, Chennai, India*

Sensorineural hearing loss or deafness and male infertility is a condition characterized by hearing loss and inability to father children is commonly termed as deafness infertility syndrome (DIS) which is a new syndromic form of deafness caused by large contiguous gene deletions at 15q15.3. The aim of the present report is to highlight the possibility of genetic factors that could be responsible for primary sub fertility. We examined a couple, wife 21 years old and husband 33 years old, consanguineously married for 4 years who presented with primary sub fertility in which the husband was found to have deafness from child hood. A detailed pedigree analysis revealed a strong history of consanguinity among other family members including parents of the couple suggesting an autosomal recessive pattern of transmission. Various medical investigations like complete blood count, urine routine, blood sugar, hormonal assay, transvaginal ultrasound and karyotyping for female; and audiological testing, semen analysis and karyotyping for male partners were conducted. Audiogram confirmed the diagnosis as profound sensorineural hearing loss and semen analysis revealed sperm dysmotility with a diagnosis of asthenoteratozoospermia in the male partner. Karyotyping reports were normal in both the partner. Hence a final diagnosis was made which confirmed the male partner to be suffering from DIS. As DIS associated with the deletion of STRC (responsible for hearing loss) and CATSPER2 genes (responsible for sperm abnormalities and infertility) is consistent, a thorough molecular genetics studies is underway to unravel the causative factors correlated to our patient.

Keywords: Infertility, Deafness infertility syndrome, Karyotyping, Asthenoteratozoospermia, Molecular genetics

06

Advantages of FISH in the Diagnosis of Cytogenetics Abnormalities

Suzan Roshdi Ismail, Soha Kholeif, Nahla Nazmy, Rasha El Kharadly
Alexandria University, Egypt

This study reports the results of FISH application to detect chromosome abnormalities in the GCS Alexandria FISH was performed using specific probes on uncultured amniotic cells w' risk of a DS fetus, this allowed rapid detection of numerical chromosome anomalies and abnormalities not detected by conventional techniques. The study included 612 cases 30 prenatal diagnosis and 129 abnormal sex differentiation Amniotic fluid & Prenatal diagnosis On 30 amniotic fluid samples prenatal cytogenetic and FISH were performed.

The results of FISH showed XX signal in 18 cases, in 10 signal of XY while in one case X Y in 91% of cells and 2 X X detected in 9% of cells. In 29 cases 91% of cells showed 2 red signals 21 while in one case 3 red signals were present in most cells denoting trisomy 21 fetus. FISH, therefore allows a much more rapid result as it is used on uncultured amniotic cells it takes 48 hrs . It is also more accurate than conventional techniques. Sex chromosomes Anomalies) Conventional cytogenetics 40 pts with 45,X karyotype: 6 with structural abnormality of X: 34 mosaics 45,X/46,XX: 12 mosaics 45/46,XY 37 w' unidentified marker a total of 129 abnormal karyotypes. FISH on 40 cases with 45, X karyotype, a minor cell line was found in 18 cases, an XX cell line in 12, XY mosaicism in 6 cases and 45, X in 22 . FISH on the 37 markers showed X in13 and Y in 24 idic Y with a double hybridization sign. the risk of gonadoblastoma. The study concludes that FISH is a useful tool in detection of low frequency cell line and identification of the nature of unknown chromosome markers, it provides a sensitive, specific, rapid and informative technique Therefore, it should be present in all specialised centres

Keywords: FISH, Cytogenetic abnormalities, Diagnosis

ORAL PRESENTATIONS

07

Mutation in EZR Inhibits the Ras/MAP Pathway and causes Autosomal Recessive Intellectual Disability

[1]Hasan Tawamie, [2]Heinrich Sticht, [1]Andr´ Reis, [3]Helen Morisson, [1]Rami Abou Jamra, [3]Katja Geissler, [3]Lars Riecken, [1]Rebecca Buchert, [1]Steffen Uebe, [4]Johannes Schumacher, [1]Arif Bülent Ekici, [5]Amina Ismael,

[1]Institute of Human Genetics, Germany, [2]Institute of Biochemistry, Germany, [3]Leibniz Institute for Age Research, Germany, [4]Institute of Human Genetics, University of Bonn, Germany, [5]Praxis of Pediatrics, Jesser El Sheghour, Syria

We examined a large, Arabic consanguineous family with two sons with severe non-specific intellectual disability, early epilepsy, periventricular leukomalacia, cerebral atrophy, dysplasia of corpus callosum, and reduction in the white matter. We undertook autozygosity mapping and identified three candidate loci with a total length of 18.7 Mb. We then enriched the exome of the index patient with Agilent SureSelect Kit 50 Mb and sequenced it on SOLiD 5500XL. We identified a novel homozygous variant in EZR (p.A129T). The mutated alanine in EZR is highly conserved and in silico analysis predicted a pathogenic effect of the identified variant. Comprehensive molecular modelling on protein level showed that the mutation buries the hydrophilic threonine in the hydrophobic core and thus destabilizes the protein structure, probably leading to a strong effect on the protein function. The identified mutation is located in the FERM domain of the encoded protein ezrin, which has binding sites for many membrane and signaling molecules. Because we recently showed that ezrin is required for the activity control of the small GTPase Ras we measured the effect of the ezrin mutant specifically on Ras. We transfected NIH3T3 cells with the wild type or mutated EZR. NIH3T3 cells expressing mutant ezrin blocked growth factor induced Ras activity. As a consequence of the inhibition of Ras we observed a decrease in proliferation. These in vitro cellular assays show that this mutation has a drastic effect and expression of which leads to an abnormal cellular phenotype. Further experiments on neuronal cell lines are ongoing. The loss of function of the ezrin mutant with the observed defects in Ras signaling is in line with other phenotypes of neurodevelopmental disorders and defects in Ras/MAP pathway. Taken together, we were able to identify EZR as a novel gene causing severe autosomal recessive intellectual disability.

Keywords: EZR, RAS/MAPK, Intellectual disability, Inhibition, Autosomal recessive

08

The Rescue of Cellular Trafficking-Defective Mutants Resulting in Congenital Myasthenic Syndrome and Familial Exudative Vitreoretinopathy

[1]Reham Milhem, [2]Lihadh Al-Gazali, [1]Bassam Ali

[1]Department of Pathology, College of Medicine and Health Sciences, [2]Department of Paediatrics, College of Medicine and Health Sciences, United Arab Emirates University, United Arab Emirates

BACKGROUND AND PURPOSE: It is well-established that certain inherited mutations result in the retention of their proteins in the endoplasmic reticulum (ER) whilst en route through the secretory pathway to their final destinations. These mutations affect a proteins' conformational tertiary structure resulting in misfolding and degradation by the Endoplasmic Reticulum Associated Degradation (ERAD) machinery. We identified ER retained missense mutations in muscle, skeletal, receptor tyrosine kinase (MuSK) causing Congenital Myasthenic Syndrome (CMS) and frizzled family receptor (FZD4) causing Familial Exudative Vitreoretinopathy (FEVR).
METHODS AND MATERIALS: Mutants of MuSK and FZD4 were generated by site-directed mutagenesis. Expression in HeLa and Cos-7 cells coupled with confocal fluorescence microscopy imaging and western blotting were used to confirm the subcellular localization of the mutant proteins. To determine if the trafficking defect is correctable, cells were cultured at reduced temperatures and/or treated with chemical chaperones.
RESULTS: Confocal microscopy imaging showed that MuSK's P344R and FZD4's P33S, G36N, H69Y, M105T, C204R, C204Y and G488D mutants co-localize with the ER lectin chaperone calnexin unlike their respective wild-type proteins that co-localize on the plasma membrane. N-glycosylation profiles and immunoblotting of these mutants confirmed ER retention. In addition, FZD4's M105V and C181R exhibited delayed trafficking to the plasma membrane implicating an ER quality control hold on these proteins. The intracellular retained mutants are highly polyubiquitinated. Incubation at 28°C or treatment with glycerol, dimethyl sulfoxide and/or thapsigargin rescued the subcellular mis-localization of the mutant proteins. CONCLUSION: Our study highlights the importance of elucidating the cellular mechanisms of monogenic diseases. Prospective alternative treatments for patients suffering from diseases caused by excessive ERAD stringency are feasible. Treatments are suggestive that folding defects can be improved and folding correctors and/or pharmacological chaperones have yet to be identified.

Keywords: Muscle skeletal receptor tyrosine kinase (MUSK), Frizzled family receptor (FZD4), Endoplasmic Reticulum Associated Degradation (ERAD), Chemical chaperones, Protein misfolding

ORAL PRESENTATIONS

O 09

A Distinct Clinical Phenotype Associated with ATP1A2 Gene Mutation

Amal Al hashem, Brahim Tabarki
Prince Sultan Military and Medical City in Riyadh, Saudi Arabia

BACKGROUND AND PURPOSE:
ATP1A2 were shown to be more consistent with familial hemiplegic migraine disease (FHM) either isolated or in association with benign infantile convulsions. It is also identified in some familial cases of alternating hemiplegia of childhood (AHC). Here, we present clinical and molecular data from a Saudi kindred with a novel ATP1A2 gene mutation.

METHODS AND MATERIALS:
We have identified a novel heterozygous mutation in ATP1A2 gene (c.1766T>6 p, ile589Thr) causing atypical AHC in a Saudi consanguineous family. From this report and previous reports of AHC associated with ATP1A2 mutation, we characterize a clinically distinct phenotype characterized by: (1) familial cases, (2) the late age of presentation of hemiplegic attacks, usually after the age of 18 months; (3) the frequency of hemiplegic attacks, being in the lower range; (4) no clear resolution of hemiplegia during sleep; (5) the positive effect of flunarazine; (6) seizures are common, mainly triggered by fever, (7) no history of headache, (8) there is increased risk of stroke. RESULTS: Theses clinical features clearly distinguish this phenotype/syndrome from AHC and FHM.

CONCLUSION:
Our findings broaden the phenotype spectrum of patients with ATP1A2 mutation. Recognition of this distinct clinical phenotype is important as it allows a rapid genetic diagnosis in affected patients, management, prognosis and genetic counseling.

Keywords: Alternating hemiplegia of childhood, ATP1A2

O 10

Recurrent Hydatidiform Mole: Detection of Two Novel Mutations in the NLRP7 Gene in Two Egyptian Families

[1]Ebtesam Abdalla, [2]Bruce Hayward, [3]Ahmed Sahms, [4]Mona Nawar
[1]*Department of Human Genetics, Medical Research Institute, Alexandria University, Egypt,* [2]*Leeds Institute of Molecular Medicine, University of Leeds, UK,* [3]*Department of Obstetrics and Gynecology, Alexandria Faculty of Medicine, Egypt,* [4]*Madina Fertility Centre, Alexandria, Egypt*

BACKGROUND AND PURPOSE:
Hydatidiform mole is an aberrant pregnancy with hyperproliferative vesicular trophoblast and defective fetal development. In 2006, mutations in NLRP7 were found to be responsible for recurrent hydatidiform moles (RHM), but genetic heterogeneity has been demonstrated and mutations of C6orf221 were later reported in several families. Here we report a new Egyptian family in which two sisters had eleven and four molar pregnancies, respectively. The objective was to present the results of the mutation analysis of NLRP7 and C6orf221 genes in Egyptian women with RHM. STUDY DESIGN: Three women from two unrelated Egyptian families; two sisters and a previously described sporadic case, all presenting with RHM, were enrolled. The cases were subjected to detailed history taking, karyotyping and screening for mutations in NLRP7 and C6orf221.

RESULTS:
Two NLRP7 mutations have been detected, one in each family. In the first family, sequencing identified a homozygous 2 bp deletion in the seventh coding exon of NLRP7, while a homozygous G-to-A substitution in the third coding exon of NLRP7 was detected in the second family. Both of them result in a truncated protein. The two mutations have not been previously described in the literature. No mutations in C6orf221 were found in any of the samples.

CONCLUSION:
The detection of an NLRP7 mutation in both the familial and the apparently isolated case of RHM provides further evidence for the previously established role of NLRP7 mutations in the pathophysiology of RHM and increases the diversity of mutations described in the Egyptian population. Our results also expand further the spectrum of reproductive wastage associated with NLRP7 mutations to patients with recurrent spontaneous abortion.

Keywords: Molar pregnancy, Recurrent hydatidiform mole, NLRP7 gene, C6orf221 gene

ORAL PRESENTATIONS

O 11

Contribution of Copy Number Variants (CNVs) in Congenital Unexplained Intellectual and Developmental Disabilities in 149 Patients: The First Lebanese Study Leading to New Findings in CNVs

[1,2]Nancy Choucair Alam, [1,3]Andre Megarbane, [1]Joelle Abou Ghoch, [2,4]Laurent Villard, [1]Eliane Chouery

[1]*Unité de Génétique Médicale et Laboratoire Associé INSERM à l'Unité UMR_S 910, Faculté de Médecine, Université Saint-Joseph, Beirut, Lebanon,* [2]*Faculté de Médecine de la Timone, Aix-Marseille Université, Marseille, France,* [3]*Institut Jérôme Lejeune, Paris, France,* [4]*Institut National de la Santé et de la Recherche Médicale, U910, Marseille, France*

BACKGROUND AND PURPOSE:
Molecular karyotyping is nowadays the most adopted clinical test for patients with unexplained intellectual disability (ID) and developmental delay (DD). This study presents some de novo unreported pathogenic copy number variants (CNVs) and reviews for several described ones. It also exposes the strategy and the conditions of analysis leading to the determination of these causative.

METHODS AND MATERIALS:
We have applied this technique to a cohort of 149 Lebanese patients with ID/DD using the 2.7M array of Affymetrix. Confirmation of array findings was performed using quantitative PCR. Bioinformatical and statistical analysis (Student T-test..) were used in order to reduce false positive CNVs. RESULTS: Out of 149 Lebanese ID/DD patients, 28 causative abnormalities were found in 26 patients forming a detection rate of 18.8%. Sixteen of these aberrations were previously related to known microimbalances and the 12 others were considered as most probable/potential pathogenic. We also found 3 new homozygous deletions, in 3 out of 45 probands with consanguineous parents, touching genes that are for the first time described as causative. Furthermore criteria were set to improve the reliability of CNVs. When the latter is greater than 62 Kb and contains at least 49 markers, it is then considered as certainly existing.

CONCLUSION:
This is the first Lebanese CMA study of ID/DD patients. It has shown the importance of uncovering genomic imbalances in diagnostic and research approaches. All CNVs found will be a guide to clinicians, helping them in the diagnosis of further cases.

Keywords: Intellectual disability, Developmental delay, Copy number variants

O 12

Prenatal Diagnosis of Genetic Disorders in UAE–Collaborative Experience of Dubai and Delhi

[1]Ishwar Verma, [1]Renu Saxena, [1]Sudha Kohli, [2]Nadia AlSawalhee, [2]Fareeda Nikhat

[1]*Sir Ganga Ram Hospital, Center of Medical Genetics, Rajedner Nagar, India,* [2]*Dept of Obstetrics and Gynecology, Maternal & Fetal Medicine Unit, Al Wasl Hospital, United Arab Emirates*

BACKGROUND AND PURPOSE:
Preventing the birth of an affected child through prenatal diagnosis is a recognized option. Prenatal Diagnosis at Al Wasl Hospital, Dubai [Latifa Hospital] started in 2004 for chromosomal and single gene disorders. We present the data for prenatal diagnosis of single gene disorders.

METHODS AND MATERIALS:
Couples of various nationalities, who desired prenatal diagnosis, were evaluated in Al Wasl Hospital, and provided genetic counseling regarding risk of recurrence, the procedure for obtaining fetal tissue, risks involved, laboratory methods, and possible outcomes. The chorionic villus sampling was done in Dubai using the trans-abdominal double needle technique (17/19 gauge). The samples were couriered to Delhi. Mutations in the concerned gene were either known before, or were obtained by sequencing in Delhi center. Maternal cell contamination was analyzed in every case. The results were then conveyed to collaborators in Dubai who counseled the couple.
RESULTS:
Of the 90 couples enrolled from 2008 to April 2013, 66 (73.3%) were for hemoglobinopathies, four for congenital adrenal hyperplasia, three for spinal muscular atrophy and single cases of diverse disorders such as Swiss agammaglobulinemia, Omenn syndrome, GM1 gangliosidosis, GSD type III, mucolipidosis, MMA, Pompie's disease, cystic fibrosis, Crouzon disease, Sanjad-Sakati syndrome, Duchenne muscular dystrophy, and retinoblastoma. In alpha-thalassemia the commonest mutations observed were IVS1-5 G>C (38%), 25 bp deletion (10.6 %), Hb S (9%), IVS1-110 (5.6%), Frsh 8/9 (7%), and 17 other mutations. 38 % of fetuses were observed to be affected, 35 % were carriers, and 26 % were normal. The diagnosis was possible in all the cases.

CONCLUSION:
The study shows that many couples in UAE are willing to accept prenatal diagnosis, which was provided at a fraction of the cost that would have been incurred if these couples had travelled abroad for antenatal diagnosis.

Keywords: Prenatal diagnosis, Genetic counseling, Chorionic villus sampling

ORAL PRESENTATIONS

O 13

A Novel ALMS1 Splice Mutation in a Non-Obese Juvenile-Onset Insulin-Dependent Syndromic Diabetic Patient

[1,2]May Sanyoura, [1,2]Cedric Woudstra, [3]George Halaby, [4]Patirck Baz, [1,2]Valerie Senee, [1,2,5]Pierre-Jean Guillausseau, [6]Pierre Zalloua, [1,2]Cecile Julier

[1]Inserm UMR-S958, Medical Faculty Paris 7, site Villemin, Paris, France, [2]University Paris 7 Denis-Diderot, Paris, France, [3]Division of Endocrinology, Hotel Dieu Hospital, Beirut, Lebanon, [4]Department of Ophthalmology, Saint Joseph University, Beirut, Lebanon, [5]AP-HP, Department of Internal Medicine B, Lariboisiere Hospital, France, [6]Lebanese American University, School of Medicine, Beirut, Lebanon

BACKGROUND AND PURPOSE:
Insulin-dependent juvenile-onset diabetes may occur in the context of rare syndromic presentations suggesting monogenic inheritance rather than common multifactorial autoimmune type 1 diabetes. Here, we report the case of a Lebanese patient diagnosed with juvenile-onset insulin-dependent diabetes presenting ketoacidosis, early-onset retinopathy with optic atrophy, hearing loss, diabetes insipidus, epilepsy, and normal weight and stature, who later developed insulin resistance. Despite similarities with Wolfram syndrome, we excluded the WFS1 gene as responsible for this disease.

METHODS AND MATERIALS:
Using combined linkage and candidate gene study, we selected ALMS1, responsible for Alström syndrome, as a candidate gene.

RESULTS:
We identified a novel splice mutation in intron 18 located 3 bp before the intronexon junction (IVS18-3T4G), resulting in exon 19 skipping and consequent frameshift generating a truncated protein (V3958fs3964X).

CONCLUSION:
The clinical presentation of this patient significantly differed from typical Alström syndrome by the absence of truncal obesity and short stature, and by the presence of ketoacidotic insulin-dependent diabetes, optic atrophy and diabetes insipidus. Our observation broadens the clinical spectrum of Alström syndrome and suggests that ALMS1 mutations may be considered in patients who initially present with an acute onset of insulin-dependent diabetes.

Keywords: Diabetes, Genetic diagnosis, Monogenic disease, Wolfram syndrome, Alstrom syndrome

O 14

Mutations in the DDHD2 gene Cause a Recessive Form of Complex Hereditary Spastic Paraplegia

[3]Salma Ben Salem, [1]Janneke Schuurs-Hoeijmakers, [2]M.T Geraghty, [1]EJ Kamsteeg, [4]S.T de Bot, [1]B Nijhof, [1]Ivan de Vondervoort, [5]M van der Graaf, [1]S Vermeer, [6]A.C Smith, [2]P Humphreys, [7]J Schwartzentruber, [8]S.A. Al-Yahyaee, [3]S. Tariq, [3]T. Pramathan, [9]R. Bayoumi, [1]B.B.A de Vrie, [1]A.P.M. de Brouwer, [3]B.R. Ali, [3]L. Al-Gazali

[1]Radboud University Nijmegen Medical Centre, The Netherlands, [2]Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, Ontario, Canada, [3]Departments of Paediatrics and Pathology, Faculty of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates, [4]Departments of Pediatrics, Pediatric Neurology and Neurology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [5]Departments of Pediatrics and Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [6]OHRI, University of Ottawa, Ontario, Canada, [7]McGill University and Genome Quebec Innovation centre, Montreal, Quebec, Canada, [8]Department of Genetics, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman, [9]Department of Biochemistry, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

BACKGROUND:
Hereditary spastic paraplegias (HSP) are a genetically and phenotypically heterogeneous group of neurodegenerative disorders mainly characterized by lower limb spasticity and weakness. Patients with pure HSP display corticospinal tract dysfunction; syndromic cases show more widespread associated symptoms. To date over than 50 loci have been mapped and 28 genes have been identified.

METHODS:
We reassessed a large consanguineous Arab family of Omani origin with complex hereditary spastic paraplegia mapped previously to 8p12-p11.21. To identify the genetic defect, Sanger sequencing of several candidate genes within the interval was carried out. In parallel, exome sequencing was performed in two non-Arab families.

RESULTS:
Two nonsense and two compound heterozygous mutations were identified in the DDHD2 gene, segregating in all affected individuals. Interestingly, patients showed an abnormal lipid accumulation in the CNS, which is in line with the function of the DDHD2 protein in lipid metabolism. Functional studies on dDdhd-knockdown Drosophila models confirmed an essential role for DDHD2 in synaptic function.

ORAL PRESENTATIONS

CONCLUSION:
In this study, we showed for the first time the implication of a member of the phospholipase A 1 (iPLA1) in a complex form of HSP (SPG54). We demonstrate that all identified mutations are affecting the DDHD2 domain which would result in a loss of the iPLA1 enzymatic activity. The unusual lipid peak on proton MR spectrum can be used as a diagnostic marker to confirm the molecular diagnosis.

Keywords: SPG54, DDHD2, iPLA1, Spastic paraplegia, Metabolic disorders

O 15

Inactivation of RIZ1 Gene by Promoter Hypermethylation is Associated with Disease Progression and Resistance to Imatinib in Indian Chronic Myelogenous Leukemia Patients, First Study from India

Rashid Mir, Imtiyaz Najar, Jamsheed Javid, P C Ray, Alpana Saxena
Cancer Genetics Lab, Department of Biochemistry, Pathology Block, Maulana Azad Medical College and Associated Hospitals, Delhigate, New Delhi, India

BACKGROUND AND PURPOSE: The epigenetic impact of DNA methylation in chronic myelogenous leukemia (CML) is not completely understood. RIZ1 expression and activity are reduced in many cancers. In CML, blastic transformation is associated with loss of heterozygosity in the region where RIZ1 is located. RIZ1 is a PR domain methyltransferase that methylates histone H3 lysine 9, a modification important for transcriptional repression. In CML blast crisis cell lines RIZ1 represses insulin-like growth factor-1 expression and autocrine signaling. Together these observations suggest that RIZ1 may have a role in the chronic phase to blast crisis transition in CML.
METHODS AND MATERIALS: To examine whether promoter methylation is involved in the disease development and progression of CML, we investigated promoter methylation status of RIZ1 gene in 100 chronic myeloid leukemia's (CML) patients and 50 controls by MSP method.
RESULTS: The RIZ1 methylation was studied in 100 CML patients, 9 were cases were methylation positive cases, six of nine were in blastic phase, 2 in chronic phase and one patient in accelerated phase. It was seen that RIZ1 methylation was increased significantly from early to advanced phase. The higher frequency of RIZ1 methylation was reported in haematologically resistant cases (42% vs 2%) and molecularly resistant cases (16.77% vs 1.92%) than the responders. The higher frequency of RIZ1 methylation was found in CML patients who were treated with interferon initially followed by imatinib treatment. Also RIZ1 hypermethylation was associated with faster disease progression $p<0.003$ than the non methylated cases. No correlation was found between RIZ1 gene methylation with age, thrombocytopenia, types of bcr/abl transcripts of CML patients.
CONCLUSION: We conclude that epigenetic silencing of RIZ1 gene is associated with CML progression and imatinib resistance. Early detection of RIZ1 methylation could be a predictive marker for imatinib resistance and disease progression in CML.

Keywords: Promotor hypermethylation, Epigenetic modification, Chronic myelogenous leukemia, RIZ1, Disease progression

ORAL PRESENTATIONS

O 16

The VCORK1 Alleles Involved in the Pharmacogenetics of Warfarin Anticoagulant among Emiratis

[1]Hayat Aljaibeji, [2]Nadia Akawi, [3]Lihadh Al-Gazali, [2]Bassam Ali
[1]*Department of Pharmacology and Therapeutics, College of Medicine and Health Sciences, United Arab Emirates University, Al-ain,* [2]*Department of Pathology, College of Medicine and Health Sciences, United Arab Emirates University, Al-Ain,* [3]*Department of Paediatrics, College of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates*

BACKGROUND AND PURPOSE:
Warfarin is one of the most prescribed anticoagulant drugs used in the prevention and treatment of thrombo-embolic vascular diseases. However, warfarin has a low therapeutic index and therefore has high risk of side effects and/or therapeutic failure. Individual variation in drug response depends on variation in patient weight, height, gender, use of other anticoagulant drugs, co-medications, diet, patient compliance, and most importantly genetic variation. Recently, more studies are focusing on determining the initial warfarin dosing based on the genetic profile of these patients rather than a trial and error based dosing. Warfarin targets the Vitamin K epoxide reductase VKORC1 and blocks its activity and therefore any functional mutations in the gene encoding this enzyme will perturb the balance between the influence of warfarin and vitamin K on the enzyme activity. The purpose of this study is to determine the alleles and genotypes and their frequencies among UAE nationals.

METHODS:
Blood samples from Emirati subjects were collected and the promoter and all exonic and intronic regions were amplified by PCR and sequenced using Sanger Sequencing.

RESULTS:
The alleles harboring the -promoter region variant (-1639G >A,rs9923231) have been observed in a large proportion of the population. Other variants including rs7294, rs9934438 and rs2884737 have also been observed.

CONCLUSION:
In Emirati population the promoter variant -1639G >A is common. The A allele is associated with the need of lower doses than the G allele. Homozygous carriers of the A allele require a warfarin dose approximately 50% of that of an individual that is homozygous for the G allele.

Keywords: Pharamacogenetics, Warfarin, VKORC1

O 17

New Findings in a Global Approach to Dissect the Whole Phenotype of PLA2G6 Gene Mutations

[1]Mustafa Salih, [2]Arif O. Khan, [3]Mohammed Al-Owain, [3]Hamad Alzaidan, [4]Hamid Azzedine
[1]*Division of Pediatric Neurology, College of Medicine, King Saud University, Saudi Arabia,* [2]*Division of Paediatrics Ophthalmology, King Khaled Eye Specialist Hospital, Saudi Arabia,* [3]*Department of Medical Genetics, King Faisal specialist Hospital & Research Centre, Saudi Arabia,* [4]*Department of Medical Genetics, Faculty of Biology and Medicine, University of Lausanne, Switzerland*

Mutations in PLA2G6 gene have variable phenotypic outcome including infantile neuroaxonal dystrophy, atypical neuroaxonal dystrophy, idiopathic neurodegeneration with brain iron accumulation and Karak syndrome. The cause of this phenotypic variation is so far unknown which impairs both genetic diagnosis and appropriate family counseling. We report detailed clinical, electrophysiological, neuroimaging, histologic, biochemical and genetic characterization of 11 patients, from 6 consanguineous families, who were followed for a period of up to 17 years. Cerebellar atrophy was constant and the earliest feature of the disease preceding brain iron accumulation, leading to the provisional diagnosis of a recessive progressive ataxia in these patients. Ultrastructural characterization of patients' muscle biopsies revealed focal accumulation of granular and membranous material possibly resulting from defective membrane homeostasis caused by disrupted PLA2G6 function.

Enzyme studies in one of these muscle biopsies provided evidence for a relatively low mitochondrial content, which is compatible with the structural mitochondrial alterations seen by electron microscopy. Genetic characterization of 11 patients led to the identification of six underlying PLA2G6 gene mutations, five of which are novel. Importantly, by combining clinical and genetic data we have observed that while the phenotype of neurodegeneration associated with PLA2G6 mutations is variable in this cohort of patients belonging to the same ethnic background, it is partially influenced by the genotype, considering the age at onset and the functional disability criteria. Molecular testing for PLA2G6 mutations is, therefore, indicated in childhood-onset ataxia syndromes, if neuroimaging shows cerebellar atrophy with or without evidence of iron accumulation.

Keywords: Phenotypic spectrum, PLA2G6, Childhood-onset ataxia syndromes

ORAL PRESENTATIONS

O 18

Role of HCV Core Protein in Expression of the Human Telomerase Reverse Transcriptase (Htert) Gene in Hepatoma Cell Lines

[1]Hussein Abdalla, [2,3]Toshifumi Hara, [2]Masataka Nakamura
[1]*Faculty of Medicine, Mansoura University, Egypt,* [2]*Human Gene Sciences Center, Tokyo Medical and Dental University, Tokyo, Japan,* [3]*Genetics Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA*

BACKGROUND AND PURPOSE:
Hepatitis C virus is an oncogenic virus although the mechanisms responsible for this behavior are not clear. Malignant transformation from mortal, normal cells to immortal, cancer cells is usually associated with activation of telomerase and subsequent telomere maintenance. A major mechanism to regulate telomerase activity in human cells is transcriptional control of the human telomerase reverse transcriptase (hTERT) gene. The aim of this study was to investigate the effects of HCV core protein on the regulation of Telomerase expression in human hepatoma cell line.
METHODS:Transient transfection and luciferase assay were used to evaluate hTERT promoter activity in cells cotransfected with Luciferase reporter plasmids carrying different regions of hTERT promoter and expression plasmids of HCV core proteins. Reverse transcription-polymerase chain reaction (RT-PCR) and Immunofluorescence staining were used to analyze the expression of HCV core proteins. All experiments were repeated at least three times. Differences between means of various treatment and control groups were assessed for statistical significance by t-test. Values of $P<0.05$ were taken as statistically significant.
RESULTS: hTERT promoter activity was increased about 4 folds in HCV core protein expressing cells (pCMV-Core) compared to vector-only controls. By indirect immunofluorescence analysis, the core which was translated as a full-length protein of 191 amino acids (aa) was located in the cytoplasm. While the cores designed to be truncated as a polypeptide of 173 aa and 151 aa were detected more in the nucleus. Reporter assays with mutant fragments of the hTERT promoter further revealed that the hTERT promoter fragment (-86--46) contains an element that mediates HCV core protein-dependent expression of hTERT and its activation by HCV core protein is independent on Sp1.
CONCLUSION: Hepatitis C virus core protein activation of hTERT promoter independent on Sp1 may contribute to HCV induced malignant transformation.

Keywords: HCV core protein, Telomerase, hTERT, Sp1, Transcription

O 19

Modulation of Coxsackievirus B3 Replication by Host Cell MicroRNAS

[1,2]Maged Hemida, [1]Mohamed Al-Hammadi
[1]*King Faisal University, Saudi Arabia,* [2]*Kafrelsheikh Univeristy, Egypt*

BACKGROUND AND PURPOSE:
Coxsackievirus B3 is the most leading causes of viral myocarditis, a disease characterized by inflammation of the heart muscle and high mortality among affected patients. MicroRNAs, short (~22nt) RNA molecules regulate more than one-third of the human genome. They induce translation repression of the target gene through targeting their complementary sequences on the 3'UTR. Recent studies confirmed that miRNA may also function by targeting the conserved sites in coding regions of mRNA. Our goals are to identify some potential microRNAs that target the 5' UTR and different coding sequence within the CVB3 genome, and to study the impact of the identified miRNAs on CVB3 replication.

METHODS AND MATERIALS:
Bioinformatic search for the potential miRNA candidates targeting both the 5'UTR and the various coding sequences in CVB3 genome was conducted. Transfection of each miRNA along with miR-CL was done for 48 hrs then infection of cells with 10 MOI of CVB3 for 5 hrs. Morphology observation of the cells was conducted. Protein lystes from each miRNA transfected sample was subjected to Western blot using different signals (VP-1, pERK/TERK, p21, p27, p53, Bcl2, BclXl, Bcl-Xs, cycline E and B-actin served as loading control).

RESULTS:
Five miRNA candidates were sleeted including miR-(138, 324, 362, 483, and 512). Each miRNA has several target sites within CVB3 genome. The most conserved sites confirmed by at least two programs (Target scan and miRanda) were selected for further validation. Interestingly, miR-324 has a conserved target on the 5'UTR. Western blot showing marked upregulation of VP-1 in case of (miR-324, 3672) in contrast to downregulation in case of miR-(138 and 512) transfected cells. Those 5 miRNA candidates showed marked alteration in different cell cycle arrest, tumor suppressor, prosurvial and proapototic markers.

CONCLUSION:
Host Cell miRNAs can modulate CVB3 replication and have great impact on its pathogenesis.

Keywords: Coxsachievirus B3, MicroRNA, Modulation, Pathogenesis, Myocarditis

ORAL PRESENTATIONS

O 20

Chromosomal Microarray as a First-Tier Clinical Diagnostic Test for Children with Dysmorphology, Malformations, Developmental Delay and Idiopathic Mental Retardation: GCC Experience

Zafar Nawaz, Khitam Abu Khadija, Shabeer Padariyakam, Sarmad Ali

Cytogenetic and Molecular Cytogenetics Laboratory, Hamad Medical Corporation, Qatar

BACKGROUND AND PURPOSE:
The clinical application of array comparative genomic hybridization (aCGH) has revolutionized the field of medical genetic diagnostics. The aCGH can analyze whole genome at a very high resolution to detect sub-microscopic copy number changes and overcomes the limitations of karyotyping or locus-specific molecular techniques. Multiple studies of hundreds of patients with idiopathic mental retardation and normal karyotype and/or subtelomeric testing using genome-wide microarray platforms have detected chromosome abnormalities in 17 to 29% of cases depending on ascertainment. In our laboratory aCGH has been offered as first line testing tool for all constitutional referrals, since 2010. The purpose of this talk is to review data and report our findings.
METHODS AND MATERIALS Genomic DNA extracted from peripheral blood was processed according to established protocol in laboratory. Briefly, samples were co-hybridised with commercially available control DNA. Agilent and CytoSure 4x44k ISCA design oligonucleotide arrays were used which included additional probes in regions of clinical interest, telomeric and pericentromeric regions. The analysis was performed by Cytogenomics and CytoSure software.
RESULTS: Referral indications ranged from preterm neonatal, IUGR, dysmorphic, congenital anomalies, autism, speech delay, developmental delay, generalized hypotonia etc. Out of a total of ~1600 patients tested with array CGH, ~10% of these patients had CNVs either in known pathogenic regions or in other regions where imbalances have not been reported in the normal population. Of these CNVs, 50% were deletions or nullisomy, 30 % were duplications or triplications. Majority (69%) of the abnormalities were were <5Mb and would likely not be detected by G-banded chromosome analysis. About 90% of the studied cases were de novo.
CONCLUSION: Array CGH is a robust and cost-effective technology alternative to traditional cytogenetic, it provides a higher diagnostic detection rate and adds to the sum of information and understanding of the role of genomic imbalance in disease.

Keywords: Microarray, aCGH, Mental retardation, Developmental delay, Genetics, Diagnosis, Dysmorphic

O 21

The Use of Whole Exome Sequencing (WES) to Unravel Disease Genes Causing Autosomal Recessive Disorders in the Population of Qatar

[1,2]Tawfeg Ben-Omran, [1]Mariam Almuriekhi, 1Rehab Ali, [3]Zafar Nawaz, [4]Somayyeh Fahiminiya

[1]Clinical and Metabolic Genetics, Department of Pediatrics, Hamad Medical Corporation, Doha, Qatar, [2]Weill Cornell Medical College in Qatar, Qatar, [3]Section of Cytogenetic, Department of Pathology and Laboratory Medicine, Hamad Medical Corporation, Doha, Qatar, [4]Department of Human Genetics, Faculty of medicine, McGill University and Genome Quebec Innovation Center, Montreal, Quebec, Canada

BACKGROUND AND PURPOSE: WES was applied as a molecular diagnostic tool to identify disease-causing mutations in autosomal recessive disorders (ARD) in Qatari population where alternative molecular diagnostic tools had failed to detect pathogenic variants in causal genes. The prevalence of consanguinity is high in Qatar (47%), results in a higher incidence of ARD. To reduce the overall socio-economic burden ARD, the development of diagnostic tools and prevention strategies is a priority. To achieve these goals, the genes causing human genetic diseases should be first discovered. METHODS AND MATERIALS: Whole exome capturing, sequencing and bioinformatics analyses were performed using our standard protocols. RESULTS: WES was performed on 26 consanguineous Qatari families. The mode of inheritance was assumed to be AR because of unaffected status of parents, their consanguinity and having equally affected male and female children. In families with one or only male affected child, de novo and X-linked inheritance were also considered. This led to the identification of definitive causal mutations in 12 families: Hypophosphatemic rickets; unknown syndrome; Glycogen storage disease; Noonan-Like syndrome; Seckel syndrome; Geleophysic dysplasia; Limb-girdle muscular dystrophy; Multiple Fractures; Metachromatic Leukodystrophy; Immunodeficiency and Juvenile onset cataract. For 6 other families, we identified several candidate (1-26) genes in which the validation or functional studies are in progress: mental retardation; CNS anomaly; eye anomalies; peripheral neuropathy; axonal peripheral neuropathy and Oro-facio-digital syndrome. The 8 remaining families are still inconclusive, but further bioinformatics analysis and comparisons with future samples may yet reveal pathogenic cause. CONCLUSION: Our study highlights that WES is a powerful molecular approach for discovery pathogenic gene mutations- especially when traditional molecular genetic screening has failed. Furthermore, with decreasing sequencing costs and improving analysis pipelines, we expect WES to be in widespread clinical use in the near future and to focus on appropriate treatment and supportive care.

Keywords: Autosomal recessive disorders, Qatar, Consanguinity, Whole exome sequencing, Whole genome sequencing

ORAL PRESENTATIONS

O 22

Identification of Known and Novel Variants Associated with Paediatric Disorders using Whole Exome Sequencing and Array-CGH

Arif Anwar
Sengenics Sdn Bhd, Malaysia

Here we present a novel pipeline for identification of clinically significant mutations using Array-Comparative Genomic Hybridization (a-CGH) combined with Whole Human Exome Sequencing. For the Exome Sequencing, variants in exons of more than 20,000 genes were screened in nearly 1000 samples. A proprietary methodology was developed to filter, optimize and categorize variants. Variants were filtered based on empirical rules including novelty, zygosity, effect on protein structure and pathway related attributes. A proprietary reference database specific to the Arab population was used to classify variants linked to more than 300 different diseases. Regions of loss of heterozygosity (LOH) were identified using a previously published method. Samples from parents and affected/unaffected siblings were sequenced for familial aggregation analysis to finalise diagnosis. Furthermore, structural variations such as genomic deletions and amplifications detected using a-CGH were verified using MLPA. Identification of clinically significant mutations using this comprehensive strategy resulted in a significant increase in diagnostic yield.

Keywords: Whole exome sequencing, Array comparative genomic hybridization, Loss of heterozygosity

O 23

Whole-Exome Sequencing (WES) Deciphers Rare Recessive Disorders Segregating in Consanguineous Families from the United Arab Emirates (UAE)

Nadia Akawi, Bassam Ali, Lihadh Al Gazali
United Arab Emirates University-College of Medicine and Health Sciences, United Arab Emirates

Background: Recessive disorders are highly prevalent in the United Arab Emirates (UAE) due to high rates of consanguinity among many of its subpopulations. However, the molecular causes underlying many of the rare recessive disorders present in the UAE are still unknown. Recent advances in Next-Generation Sequencing and bioinformatics have significantly expedited the discovery of the defective genes and mutations of many genetic conditions. We present our experience on the usage of whole-exome sequencing for the identification of genes and mutations of several rare recessive disorders. Methods: In two affected members of each family we captured and sequenced the whole-exome to a mean coverage of 30x and sufficient depth to call variants at approximately 97% of each targeted exome. All the called variants were annotated and filtered against public SNP and exome databases. Each candidate variant was assessed separately for novelty in ethnically matched controls. The impact of each variant on the protein function and/or structure was weighed using commonly used pathogenicity prediction programs such as SIFT, Polyphen and Mutation taster. Results: We have identified a novel mutation in LINS which is a WNT signaling pathway modulator in a consanguineous family with two affected children exhibiting autosomal recessive intellectual disability. In another family, we have identified a novel missense mutation in the Hedgehog pathway regulator KIF7, causing a unique autosomal recessive syndrome consisting of macrocephaly, multiple epiphyseal dysplasia and distinctive facial appearance. In addition, we have accurately diagnosed a heterogeneous case of Congenital Muscular Dystrophy with brain and eye anomalies in an extended family by detecting the causative mutation in POMGnT1, which is involved in glycosylation of α-dystroglycan. Furthermore, in several affected individuals from a family with Camptodactyly-arthropathy-coxa vara-pericarditis syndrome, Sanger sequencing failed to detect the causative mutation which was later detected by whole-exome sequencing in a highly repetitive sequence of PRG4, a boundary lubricant at the cartilage surfaces. Conclusion: Whole-exome sequencing is a highly powerful and efficient strategy for the diagnosis of single-gene disorders and is significantly accelerating the discovery of the molecular causes of numerous rare genetic disorders.

Keywords: Whole-exome sequencing, Rare recessive disorders, United Arab Emirates, Intellectual disability, Congenital muscular dystrophy, Multiple epiphyseal dysplasia, Hemorrhagic destruction of the brain, Camptodactyly-arthropathy-coxa vara-pericarditis syndrome

ORAL PRESENTATIONS

O 24

Identification of Genes Causing Monogenic Diabetes by Deep Sequencing of Accessible Coding Regions of the Human Genome

[1]Anette Gjesing, [2]Anders Albrechten, [3]Yukio Horikawa, [1,4]Oluf Pedersen, [1,5]Torben Hansen

[1]*The Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark,* [2]*Centre of Bioinformatics, Faculty of Science, University of Copenhagen, Copenhagen, Denmark,* [3]*Department of Diabetes and Endocrinology, Gifu University Graduate School of Medicine, Gifu, Japan,* [4]*Institute of Biomedical Science, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark,* [5]*Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark*

BACKGROUND AND PURPOSE: One class of monogenic (Mendelian) diabetes is Maturity-Onset Diabetes of the Young (MODY). MODY is characterized by an autosomal dominant inheritance, onset of diabetes before 25 yrs-of-age in at least one family-member and a partly preserved pancreatic beta-cell function. MODY accounts for 1-2% of all European diabetes cases. Mutations in at least seven genes (HNF4A, GCK, HNF1A, PDX1, HNF1B, NeuroD1 and INS) are known to cause MODY in both Asian and Caucasian populations. However, 30% of all MODY cases are still genetically uncharacterized. The overall aim of this study was to elucidate the genetic aetiologies and molecular mechanisms involved in unexplained MODY (MODYX) subtypes.

METHODS AND MATERIALS: Using deep whole-exome sequencing (WES), putative novel variants have been identified by comparison of variants identified by WES with SNP information in public and in-house databases, and metabo-chip genotyping and estimation of identity by descent (IBD) within Danish MODYX families. WES with an average depth above 100x was performed on triplets or quartets of individuals from 16 Danish MODYX families. The selected individuals included one offspring with MODY, both diabetic and healthy parents, and if available another more distantly related co-affected family member.

RESULTS: A minimum of 4 and a maximum of 29 novel variants present only among cases in each examined family have been identified. In order to further reduce the number of putative disease causing variants, we array-genotyped approximately 200.000 variants in each family member. This genotype-information was used to estimate the IBD sharing between cases and controls. Variants located in IBD regions shared by all cases in the families are prioritized for further studies which include resequencing of the putative MODYX gene(s) in additional MODYX probands and an examination of the functional impact of the mutation(s) in in vitro assays. Analyses are ongoing.

Keywords: Maturity-onset diabetes of the young, Monogenic diabetes, Deep sequencing

O 25

Association of APOA5 56C>G Gene Polymorphism with both Hypertriglyceridemia and Risk of Coronary Artery Disease (CAD) in Arterial Hypertensive Moroccan Patients

[1]Sanaa Ouatou, [1]Abdelhamid Barakat, [2]Houria Rhaissi, [3]Noreddine Ghalim, [1]Hassan Rouba

[1]*Laboratoire de Génétique Moléculaire et Humaine, Département de Recherche Scientifique, Institut Pasteur du Maroc, Casablanca, Morocco,* [2]*Laboratoire de Physiologie et Genetique Moléculaire, Faculté´ des sciences Ben M'Sik, Université´ Hassan II, Mohammedia, Morocco,* [3]*Laboratoire de Biochimie, Centre de Biologie Médical, Institut Pasteur du Maroc, Casablanca, Morocco*

BACKGROUND AND PURPOSE: Arterial Hypertension and hypertriglyceridemia are the important risk factors for development of coronary artery diseases. It has been reported that the APOA5 gene was associated to the metabolism of triglycerides in different ethnic groups. The goal of the present study was to investigate the association between the APOA5 56C>G polymorphism and arterial hypertension and risk of coronary artery disease in Moroccan patients.

METHODS AND MATERIALS: Our study was performed in 132 Moroccan patients with arterial hypertension and 134 controls. All subjects were genotyped for the APOA5 56C>G SNP by polymerase chain reaction, followed by enzymatic digestion with TaqI. Interactions between this variant and biochimical variables were analyzed, and the effect of lifestyle and sex, were also evaluated.

RESULTS: We found that the 56G allele is associated to increased TG (+43.24%, p=0.0003), increased CT/HDL ratio (+24.54%, p=0.005) and increased Sbp (+5.26%, p=0.01) in AHT patients compared with controls. In addition, the 56G allele frequency was significantly different between the hypertensive and control groups (21% vs.7%, respectively). However, no significant association was found between 56C>G polymorphism and HDL, LDL and glycemia. The frequencies of genotypes 56C>G differed significantly between the hypertensive and control groups (14.39% vs. 1.5%, respectively).

CONCLUSION: our data demonstrate for the first time that the 19W allele has confirmed a strong influence on triglyceride levels in a Moroccan population and that APOA5 polymorphism modulate Hypertention dyslipidemia. They clearly establish the association of APOA5 with elevated concentration level of TG in Hypertensive patients and risk of develop coronary artery disease CAD.

Keywords: APOA5 gene, 56C>G SNP, AHT, Risk of CAD, Morocco

ORAL PRESENTATIONS

O 26

Infantile Ascending Spastic Paralysis caused by a novel ALS2 mutation identified by Homozygosity Mapping

Salma Majid, Rula Abuthuraya, Khushnooda Ramzan, Samya Hagos, Haya Al Dossari
King Faisal Specilist Hospital & Research Center, Saudi Arabia

BACKGROUND AND PURPOSE:
Mutations in Alsin gene are causative for three clinically distinct motor neuron diseases, Infantile ascending spastic paralysis, juvenile primary lateral sclerosis and juvenile amyotrophic lateral sclerosis. A total of 23 different ALS2 mutations have been described for such disorders. Most of these mutations are predicted to result in frame shift leading to premature truncation of the alsin protein. The aim of this study was to identify the disease causing mutations.

METHODS AND MATERIALS:
Homozygosity Mapping was used for conducting whole genome scans with Axiom Mapping Array and direct sequencing was carried for the candidate genes.
RESULTS:
We report a novel ALS2 truncating mutation in two infants affected by infantile ascending spastic paralysis (IAHSP) with bulbar muscles involvement. This mutation resides in pleckstrin domain, a characteristic of GEFs for the Rho GTPase family involved in overall neuronal development or maintenance.

CONCLUSION:
This study highlights the importance of using homozygosity mapping combined with candidate gene analysis to identify the underlying genetic defect as in this small Saudi consanguineous family. This study would be helpful in genetic screening and consideration of preimplantation genetic diagnosis in such families. Our findings suggest that the novel R921X is the causative mutation underlying the disease in this family with IAHSP.

Keywords: Motoneuron, Alsin-2 gene, Homozygosity, Mutation, Amyotrophic lateral sclerosis, Hereditary spastic paraplegia

O 27

Homozygous Mutation in Fatty Acyl CoA Reductase 1 (FAR1) Causes Autosomal Recessive Intellectual Disability with Early Epilepsy and Constipation

[1]Rebecca Buchert, [1]Hasan Tawamie, [2]Bernd Schwarze, [1]André Reis, [1]Rami Abou Jamra, [1]Seffen Uebe, [3]Bassam Hallak, [1]Arif Bülent Ekici

[1]Institute of Human Genetics, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany, [2]Institue of Forensic Medicine, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany, [3]Practice for Pediatrics, Kefrenbel, Syria

We examined a consanguineous Syrian family with two children that presented with severe intellectual disability, muscular hypotonia, epileptic seizures since the age of 13 months, pronounced constipation, and bruxism. Pregnancy and birth were unremarkable. Chromosome analysis, tests for mitochondrial and metabolic disorders, brain CT scan, and ultrasound of heart and abdomen were unremarkable also we performed genome-wide genotyping using Affymetrix SNP-arrays 6.0 and excluded submicroscopic aberrations. Assuming an autosomal recessive inheritance model because of a familial specific founder mutation, we ran autozygosity mapping and identified 4 candidate regions. We conducted whole exome sequencing and identified over 40,000 variants. We filtered the data stringently based on mapping results, public variant data bases, in silico analyses, and genotyping in healthy controls, and we were left with a single candidate mutation; FAR1 NM_032228.5; c.639-651delAGTAGTCTATCCAinsT, p.EVVYP166-169D. FAR1 (fatty acyl CoA reductase 1) is essential for plasmalogen synthesis and catalyzes the reduction of fatty acids to their corresponding alcohols (e.g. palmitic acid to hexadecanol). Plasmalogen protects cells from damage through reactive oxygen species. Previous studies reported reduced levels of plasmalogen in brain to be associated with Alzheimer's disease, X-linked adrenolukodystrophy, and Down syndrome. To further explore the effect of our candidate mutation on protein function we transfected HEK293 cells with wild type and mutant FAR1, supplemented the cultures with palmitate and measured palmitate and hexadecanol concentration in lipid extracts with gas-chromatography. We found that wild type FAR1 metabolises almost all palmitate to hexadecanol, while with mutant FAR1 palmitate levels remain high and hexadecanol levels low. This proves a loss of function of the mutated gene and this is in line with the autosomal recessive inheritance model. We add FAR1 to the growing list of ARID genes. Further, our study underlines the importance of plasmalogen synthesis and fatty acid metabolism in brain development and function.

Keywords: Autosomal recessive intellectual disability, Homozygosity mapping, Next generation sequencing, Lipid metabolism, Plasmalogen synthesis

ORAL PRESENTATIONS

O 28

Ethical Issues in Genomic Research and Limits of the Informed Consent

Rachida Roky
Laboratory of Physiology and Molecular Genetics; University Hassan II Ain Chock, Casablanca, Morocco

BACKGROUND AND PURPOSE:
The advance of genomic research and its applications has raised new concerns among the public about ethical issues. Many institutions have developed guidelines and recommendations for the ethical framework of this development. The majority of these bodies have recommended a multidisciplinary and pluralistic dialogue between all stakeholders and the society. In this analysis we present an overview of the most relevant ethical issues in genomic research.

METHODS AND MATERIALS:
We performed a systematic search in the pubmed database followed by a manual search through original articles and reviews dealing with ethics in genomic studies. A total of 60 articles, published in the last ten years, was included in this analysis.

RESULTS:
Most ethical issues are related to confidentiality, privacy, autonomy, justice, stigma and discrimination. The first challenging aspect of genomics studies is the informed consent's scope and comprehension. In these studies, the information given to the participants and the patients is complex and needs to be addressed deeply. Secondly, because genomics provides information on susceptibility to diseases, it may affect the health insurance and healthcare policies and the notion of prevention which needs to be refined. This raises the limits of individual consent and the need of new process of ethical evaluation involving public debate. Finally, these new ethical considerations require that researchers and healthcare professionals have knowledge about complex genomic issues and provide appropriate information to healthy participants, patients, families, and communities.

CONCLUSION:
Genomic studies raise new and complex ethical issues requiring deep process for the obtention on the informed consent and public communication as an essential step in the transfer of knowledge from research to healthcare.

Keywords: Ethics, Informed consent, Genomic studies

O 29

Documentation of Inherited Disorders in the Moroccan Population in the Moroccan National Mutation Database

[1,2]Ilham Ratbi, [2]Siham Chafai Elalaoui, [2]Imane Cherkaoui Jaouad, [3]Petros Papadopoulos, [4]Alae-eddine Gati, [5]Emmanouil Viennas, [5,6]Giannis Tzimas, [1]Jaber Lyahyai, [7]George Patrinos, [1,2]Abdelaziz Sefiani

[1]Human Genomic Center, Faculty of Medicine and Pharmacy, University Mohammed V Souissi, Morocco, [2]Department of Medical Genetics, National Institute of Health, Morocco, [3]Leuven, KU Leuven, Belgium, [4]National Institute of Health, Morocco, [5]Department of Computer Engineering and Informatics, Faculty of Engineering, University of Patras, Greece, [6]Department of Applied Informatics in Management & Finance, Faculty of Management and Economics, Technological Educational Institute of Messolonghi, Greece, [7]Department of Pharmacy, School of Health Sciences, University of Patras, Greece

The exponential discovery rate of new genomic alterations, leading to inherited disorders, as well as the need for comparative studies of different populations mutation frequencies necessitates recording their population-wide spectrum, in online mutation databases. The National Mutation Databases are continuously updated mutation depositories, which contain extensive information over the described genetic heterogeneity of an ethnic group or population. We have previously developed the Moroccan Human Mutation database (http://www.sante.gov.ma/Departements/INH/MoHuMuDa/index.htm) to document the incidence of genetic disorders in the Moroccan population. Here, we report the upgrade of the Moroccan Human Mutation database using the upgraded version of the ETHNOS software, developed by the Golden Helix Institute of Biomedical Research. The upgraded version of the ETHNOS software expands the previous querying capacity and provides new visualization tools, based on PivotViewer and Microsoft Silverlight technology, to comprehensively query and retrieve the data documented in the database, namely 178 disease summaries and 318 mutation frequencies, where possible. In the latter case, mutation frequency data have been made available using bidirectional links from the Frequency of Inherited Disorders database (www.findbase.org; van Baal et al., 2007; Georgitsi et al., 2011). Furthermore, there are numerous links to the respective Online Mendelian Inheritance in Man (OMIM) entries and, when available, to the locus-specific databases fruitfully integrate the databases content into a single web site. The Moroccan Human Mutation database, especially in its present format, can serve as a valuable online tool for molecular genetic testing of inherited disorders in the Moroccan population and could potentially motivate further investigations of yet unknown genetic diseases in this population.

Keywords: Mutation database, Moroccan population, Genetic disorders

ORAL PRESENTATIONS

O 30

Lessons Learned from Whole Exome Sequencing Data Analysis of Rare Diseases: Non-Coding Variants and Copy Number Variations

[1]Somayyeh Fahiminiya, [2]Frank Rauch, [3]Loydie Jerome Majewska, [1]Jacek Majewski

[1]*Department of Human Genetics, Faculty of Medicine, McGill University and Genome Quebec Innovation Center, Montreal, Quebec, Canada,* [2]*Shriners Hospital for Children and McGill University, Montreal, Quebec, Canada,* [3]*Department of Pediatrics, McGill University, Montreal Children's Hospital, Montreal, Quebec, Canada*

BACKGROUND AND PURPOSE: Sequencing of protein coding regions of human genome (Whole Exome Sequencing; WES), has demonstrated a great success in the identification of causal mutations for several rare genetic disorders in human. Generally, most of WES studies have focused on rare variants in coding exons and splicing-sites where missense substitutions lead to the alternation of protein product. Although focusing on this category of variants has revealed the mystery behind many inherited genetic diseases in recent years, a subset of them remained still inconclusive. Here, we present the result of our WES studies where analyzing only rare variants in coding regions was not conclusive but further investigation revealed the involvement of non-coding variants and copy number variations (CNV) in etiology of the diseases. METHODS AND MATERIALS: Whole exome sequencing was performed using our standard protocols at Genome Quebec Innovation Center, Montreal, Canada. All bioinformatics analyses were done using in-house WES pipeline. RESULTS: To date, we successfully identified several disease causing mutations within gene coding regions (e.g. SCARF2: Van den Ende-Gupta syndrome and SNAP29: 22q11.2 deletion syndrome) by using WES. In addition, we showed that variants in non-coding regions and CNV have also important value and should not be ignored and/or filtered out along the way of bioinformatics analysis on WES data. For instance, in patients with osteogenesis imperfecta type V and in patients with glucocorticoid deficiency, we identified variants in 5'UTR, resulting in the production of longer or truncating non-functional proteins. Furthermore, CNVs were identified as the main cause of the diseases in patients with metaphyseal dysplasia with maxillary hypoplasia and brachydactyly and in patients with osteogenesis imperfecta type VII. CONCLUSION: Our study highlights the importance of considering non-coding variants and CNVs during interpretation of WES data, as they can be the only cause of disease under investigation.

Keywords: Rare genetic disorders, Whole Exome Sequencing, Non-coding variants, Copy-number variations

华大基因 BGI

华大健康 BGI health

The World's Leading Expert in Genetic Testing

Pre-Marriage, Pre-Pregnancy, Pre-Implantation

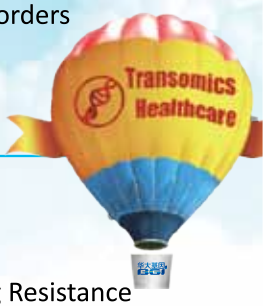
- Whole Exome Sequencing
- Genetic Testing for Monogenic Diseases
- Pre-implantation Genetic Diagnosis/Screening (PGD/PGS)
- Genetic Testing for Thalassemia
- Genetic Screening for Hearing Impairment

Pre-Natal

- Non-invasive Fetal Trisomy Test (NIFTY)
- Genetic Testing for Monogenic Diseases
- Genetic Testing for Chromosome-Abnormality-Induced Miscarriage
- Genetic Testing for Thalassemia
- Genetic Screening for Hearing Impairment

Newborn

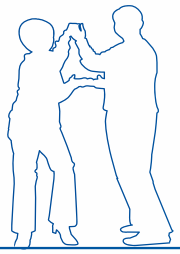
- Genetic Screening for Hearing Impairment
- Genetic Screening for Inherited Metabolic Disorders
- Genetic Testing for Monogenic Diseases
- HLA High Resolution Typing
- Genetic Testing for Thalassemia



Childhood

- Genetic Testing Panel for Hereditary Cancer
- Whole Exome Sequencing
- Genetic Testing for Monogenic Diseases
- Genotyping for Hepatitis B Virus (HBV) & Drug Resistance
- Genotyping for Hepatitis C Virus (HCV)

Adulthood



- Whole Exome Sequencing
- Genotyping for Hepatitis B Virus (HBV) & Drug Resistance
- Genotyping for Hepatitis C Virus (HCV)
- Genotyping for Human Papilloma Virus (HPV)
- Genetic Testing for Hereditary Breast Cancer/Ovarian Cancer
- Genetic Testing for Hereditary Colorectal Cancer
- Genetic Testing for Targeted Cancer Therapy
- Genetic Testing for Individualized Chemotherapy

BGI Asia-Pacific

Add: Building 11, Beishan Industrial Zone, Shenzhen 518083, China
Tel: +86 755 2527 3120
E-mail: P-Asia-Health@genomic.cn
Web: en.bgi-health.com

POSTERS

P1

Analysis of IFN-Gamma (+874 A/T) Gene Polymorphism with Risk of Schizophrenia

Dor Mohamad Kordi, Mahya Shariat Razavi
The University of Sistan & Baluchestan, Zahedan, Iran

BACKGROUND AND PURPOSE: Schizophrenia is a chronic, severe, and disabling brain disorder that has affected people throughout history. People with the disorder may hear voices other people don't hear. They may believe other people are reading their minds, controlling their thoughts, or plotting to harm them. This can terrify people with the illness and make them withdrawn or extremely agitated. Though the Schizophrenia is multifactorial disease, but Genetics plays an important role in the pathogenesis. The aim of this study was to assess the relationship between the +874T/A polymorphisms of interferon-gamma (IFN- gamma) genes and incidence of schizophrenia. METHODS AND MATERIALS: Total of 94 schizophrenic patients and 97 individuals as control samples were enrolled in this study. All samples were genotyped by ARMS PCR for candidate SNPs in IFN gamma. RESULTS: No significant association was found between various genotypes of IFN-gamma in selected SNPs with risk of Schizophrenia, As well as there was no significant variation in allelic frequency of IFN- gamma gene with risk of Schizophrenia. CONCLUSION: These data suggest that the +874T/A IFN-gamma genes are not involved in development of schizophrenia risk. To validate of this data suggesting more studies in various population with large sample size.

Keywords: Schizophrenia, IFN-gamma,IL-10, Gene, Polymorphism

P2

CRC- Risk Stratification Model

Moh'd Azzam Kayasseh
CEO, Dr. Kayasseh Medical Clinic, United Arab Emirates

CRC is one of the most preventable cancers in the world because we have already known lots of knowledge on the genetic pathogenesis of this disease and correlations with the surrounding food and environment to the degree that we can interfere with many useful precaution plans. The established pre-cancerous lesions of this disease like polyps, dysplasia, and IBD (especially chronic ulcerative colitis) also give us better opportunity for earlier discovery with subsequent resection. International and regional collaboration is highly recommended to reach the ideal public awareness campaign to protect us from this disease (such campaigns can reduce 70%–90% of the "CRC" incidence).

The genetic consideration for a family with features of the Lynch syndrome are microsatellite instability testing, consideration for immunohistochemistry evaluation, and the MMR mismatch repair gene testing, while, in contrast, a patient with FAP will require APC testing, and at last other germline mutations yet to be also identified when proved. Tests for high-penetrance mutations in appropriate populations have clinical utility, meaning that they -inform clinical decision making and -facilitate the prevention or -amelioration of adverse health outcomes. In my Program 'Dr. Kayasseh 'Care To Cure Program' 'in CRC, Healthy Colon 'Healthy Life' I am applying the new 'CRC -Risk- Stratification Model depending on.

Keywords: Genetotype, Clinicotype, Endotype, Imaginotype, Therapeutic response

P3

Diagnosing Hereditary Ataxias and Paraplegias Using a Next-Generation-Sequencing Panel

[1]Peter Bauer, [1]Marc Sturm, [2]Matthis Synofzik, [1]Olaf Riess, [2]Ludger Schöls
[1]*Institute of Medical Genetics and Applied Genomics,* [2]*Hertie Institute for Clinical Brain Research, German Center of Neurodegenerative Diseases, Eberhard-Karls-University, Tübingen, Germany*

BACKGROUND AND PURPOSE: Hereditary ataxias and paraplegias impose a relevant challenge when molecular diagnosis is sought. While more than 100 genes are involved in Mendelian diseases with ataxia, only a small proportion of these genes have been systematically tested in cohorts of patients with early onset progressive ataxia. A similar situation is true for hereditary paraplegias with slightly less candidate genes. With the advent of next-generation-sequencing (NGS) a massive sequencing approach can be implemented with relatively ease.

METHODS AND MATERIALS:We have established a selector-based enrichment method (HaloPlex, Agilent) targeting 57 ataxia genes, 43 metabolic ataxia genes, and 19 mitochondrial ataxia genes. A total of 310kb is specifically enriched and sequenced by Illumina MiSeq (2x 150 bp paired-end). For hereditary

paraplegias, 62 disease genes have been selected in a similar approach. A first batch analysis in 34 ataxia and 14 paraplegia patients showed that HaloPlex enrichment provided enrichment efficiency superior to standard whole exome procedures (>97% covered >20 reads; 90-95% of reads on target; mean coverage >500 reads per base).

RESULTS: Although massive parallel sequencing usually brings up a couple of variants (70-85 for the paraplegia panel, and 170-210 for the ataxia panel), filtering for rare variants (in our own NGS database and in 1000g, ESP) and for functional relevance (ns,ss,indel) reduced this count to 0 to 3. Several rare, disease causing mutations could be identified in genes like NIPA1, SPTBN2, KIAA0226, SYNE1, ANO10, NPC1, REEP1, GLB1 and others.

CONCLUSION: Therefore, this technology offers relevant advantages as compared to in-solution hybridization enrichment, because the workflow is more sensitive, much shorter and library production and sequencing is more cost-effective.

Keywords: Ataxia, Paraplegia, Next-generation sequencing, diagnosis panels

P4

CYP3A4 and CYP3A5 Expression and Genotype and Neuroblastoma Survival

[1]Hassan Dhaini, [1]Mohamad Darwish, [2]Rola Farah, [1]Ghada Farhat, [3]Paul-Henri Torbey, [4]Fatmeh Ghandour, [4]Noha Bejjani-Doueihy
[1]Faculty of Health Sciences, University of Balamand, [2]Pediatric Oncology, St George Hospital, [3]Pediatrics, Hotel Dieu de France Hosptial, [4]Pathology Department, Saint George Hospital University Medical Center, Lebanon

BACKGROUND AND PURPOSE: Although neuroblastoma is a rare pediatric disease in Lebanon, poor response to treatment remains a major challenge. Genetic polymorphism of drug-metabolizing enzymes may influence chemotherapy outcome. The purpose of this study is to investigate possible associations of CYP3A4 and CYP3A5 expression, and genotype, with survival in Lebanese neuroblastoma patients. METHODS AND MATERIALS: All patients with confirmed stage III and IV neuroblastoma diagnosed between 1995 and 2012 at three major hospitals in Beirut were included (N=27). After obtaining IRB approval, demographic information and survival time were collected from Archives. DNA and RNA were extracted from archival tumors. CYP3A4 and CYP3A5 genotypes and expression levels were determined by PCR-RFLP and qPCR, respectively. MYCN amplification was determined using TaqMan system. Hazard ratios (HR) and 95% confidence intervals (CIs) were determined using Cox regression to assess the association of gene expression, and genotypes, with the risk of death, adjusting for MYCN amplification. RESULTS: A statistically significant increased risk of death was found in patients with MYCN amplification (HR= 4.11, 95% CI 1.14-14.8). Patients with CYP3A5 expression levels above median had a lower death risk (HR= 0.61, 95% CI= 0.21-1.74), and patients with CYP3A4 expression levels above median had a higher death risk (HR= 2.0, 95% CI 0.67-5.9), compared to patients with expression levels below median. CYP3A5*3/*3 homozygote mutants had a 4.3-fold increased risk of death compared to homozygote wild type or heterozygote mutant genotypes (HR=4.30, 95% CI 0.56-33.3). Homozygote and heterozygote carriers of the CYP3A4*1B mutant allele had a 52% lower risk of death compared to non-carriers (HR= 0.48, 95% CI 0.06-3.76). CONCLUSION: Although our results do not show statistically significant associations, the magnitude of reported hazard ratios suggest a role for CYP3A4 and CYP3A5 in modulating clinical outcome in neuroblastoma. Further studies with larger sample sizes are warranted to confirm our results.

Keywords: Neuroblastoma, CYP3A4, CYP3A5

POSTERS

P5

Replication of GWAS identified Loci in the Tunisian Population: Susceptibility and Prognostic Implications in Breast Cancer

[1]Wijden Mahfoudh, [2]Jingxuan Shan, [1]Elham Hassen, [1]Noureddine Bouaouina, [2]Lotfi Chouchane
[1]*Laboratory of Immuno-Oncology, Faculty of Medicine of Monastir, University of Monastir, Tunisia,* [2]*Genetic Medicine and Immunology Laboratory, Weill Cornell Medical College, Doha, Qatar, Tunisia*

Recent genome-wide association studies (GWAS) have lead to the identification of multiple new genetic variants associated with breast cancer risk. Most of these breast cancer GWAS and replication studies have been conducted in European populations and to a lesser extent in Asians. Therefore, we designed a broad study to investigate the susceptibility and prognostic implications of the GWAS breast cancer loci in the Tunisian population. In a cohort of 640 unrelated patients with breast cancer and 371 healthy control subjects, we characterized the variation of 9 single nucleotide polymorphisms (SNPs) using the TaqMan® SNP genotyping assays. The chi-square test was used for statistical analysis.

Only 5 (rs1219648, rs2981582, rs8051542, rs889312, rs13281615) out of 9 GWAS breast cancer loci were found to be significantly associated with breast cancer in Tunisians. The strongest associations were found for rs2981582 in the FGFR2 gene and rs8051542 in the TNRC9 gene (OR = 1.55, P = 3 × 10(-6); OR = 1.40, P = 4 × 10(-4), respectively). Homozygous variant genotypes of rs2981582 were strongly related to lymph node negative breast cancer (OR = 3.33, P = 6 × 10(-7)) and the minor allele of rs2981582 was associated with increased risk of ER+ tumors (OR = 2.15, P = 0.001) and increased risk of distant metastasis development (OR = 3.57, P = 6 × 10(-5)). The association for rs8051542 was stronger for high-grade SBR tumors (OR = 2.54, P = 2 × 10(-4)). GG genotype of rs13387042 on 2q35 showed a significant association with the risk of developing distant metastasis (OR = 1.94, P = 0.02). In conclusion, GWAS breast cancer FGFR2, TNRC9, MAP3K1, and 8q24 loci are associated with an increased risk of breast cancer and genetic variation in FGFR2 gene may predict the aggressiveness of breast cancer in Tunisians.

Keywords: Breast cancer, SNPs, GWAS, FGFR2 gene

P6

Patterns of X Inactivation in Abnormal X Chromosome

[1]Peter Fahmy, [2]Mervat El Ansary, [2] Nesrine El Gharbawi, [1]Hassan Hussein, [1]Amal Mahmoud
[1]*Human Cytogenetics Department, National Research Center,* [2]*Clinical and Chemical pathology Department, Faculty of Medicine, Cairo University, Egypt*

BACKGROUND AND PURPOSE:
X inactivation is a mechanism of dose compensation which results in silencing the majority of genes on one of the two X chromosomes in every somatic cell of human females. Early in embryonic development, cells inactivate all their X chromosomes except one, regardless of the number of X chromosomes in the karyotype. Once an X is chosen, it is stably inherited through subsequent somatic mitotic divisions. The process of X inactivation is under the control of X inactivation center. AIM: The study of X inactivation patterns in cases with abnormal X chromosome and its correlation with the patients phenotype.

METHODS AND MATERIALS:
15 selected patients having abnormalities of the X chromosome were subjected to Clinical examination, GTG banding, FISH technique to detect origin of some structural X abnormalities and Detection of X chromosome replication pattern (Late Replicating Chromatin) technique.

RESULTS:
Cases were classified according to their karyotypes into three groups: Cases with numerical X abnormalities, Cases with iso X chromosome and Cases with other structural X abnormalities. In most of X aneuploidies, each cell has only one active early replicating X, while other extra or abnormal X chromosomes are inactivated late replicating. Regarding the balanced X;autosome translocation, there was a mosaic pattern; in majority of cells translocated X was late replicating inactive, while in few cells translocated X was early replicating active X chromosome.

CONCLUSION:
It has been found that at least 30 X-linked genes are expressed on the inactivated X chromosome. The varying degree of phenotypes within each syndrome occurs because the genes that escape X inactivation are expressed at varying degrees.

Keywords: X Inactivation, X chromosome abnormalities, gene expression

POSTERS

P7

Cytogenetic Biodosimetry for Clinical Estimation of Radiation Doses Received in Cases of Radiological Accidents

Ghazi Alsbeih, Khaled Al-Hadyan, Sara Elewisy, Sara Al-Qahtani, Belal Moftah, Najla Al-Harbi, Nikki Venturina
King Faisal Specialist Hospital & Research Centre, Saudi Arabia

BACKGROUND AND PURPOSE: The beneficial applications of radiation in medicine, agriculture, energy, industry and research greatly improve the quality of our daily life. In addition to nuclear radiation fears, the increase in various radiological applications in the Arab world will collaterally be associated with increased probability of instances in which one or more individuals will accidentally be overexposed to ionizing radiation. Therefore, it is important to build national capacity to provide suitable dose assessment, medical triage, diagnoses and treatment to victims.

METHODS: Cytogenetic bio-dosimetry, based on scoring of dicentric chromosomal aberrations, is a proven, ISO and IAEA standardized biotechnology technique for calculating medically relevant radiation doses received. Peripheral blood lymphocytes were collected from four healthy Saudi volunteers and irradiated with radiation doses (between 0 and 5 Gy) of 250 KeV X-Rays. Stained cytogenetic slides were prepared from cultivated lymphocytes. The Metafer system was used for automatic metaphase finding and assisted scoring of dicentric chromosomes. Data points were fit to the linear-quadratic dose-response model (Y=C+alphaD+betaD^2).

RESULTS: In this study, we have established a cytogenetic biodosimetry laboratory and produced the 1st dose-response calibration curve, pre-required to estimate doses in cases of accidental radiation overexposure. Results generated the following values (C= 0.0144, alpha= 0.0013, beta= 3.4526E-6).

CONCLUSION: The dose-response calibration curve was comparable to those described in other populations. This is the first Biodosimetry Laboratory in the Arabic world and member of the 'Global Biodosimetry Laboratories' network for radiation emergencies (BioDosNet). This biotechnology approach adds depth to information for decision-makers and public health officials who assess the magnitude of public, medical, occupational and accidental radiation exposures, in addition to providing a platform for advanced education, research and development in the Kingdom of Saudi Arabia and neighbouring countries. Supported by KACST 'National Comprehensive Plan for Science and Technology' (Project# 9-MED749-20; RAC#2110-005).

Keywords: Chromosomal aberrations; Cytogenetics; Dicentric chromosomes; Biodosimetry, Radiation exposure

P8

Using Exome Sequencing in Genetic Diagnosis and Counselling for Congenital Myopathy

Pratima Dash, Sunita Bijarnia, Ratna Puri, Renu Saxena, Ishwar Verma
Center of Medical Genetics, Sir Ganga Ram Hospital, India

BACKGROUND AND PURPOSE: Congenital myopathies are heterogeneous group of inherited disorders. Precise molecular diagnosis is essential for therapy and for prenatal diagnosis.

MATERIALS: A 6-years-old girl with congenital myopathy, born to a non-consanguineous couple, was evaluated. Weakness of muscles appeared in infancy, first in the legs and then in the arms. She was unable to rise from the floor or sit up. At 6 years she was thinly built with a long face, ptosis, external opthalmoplegia, masseter weakness, hypotonia with areflexia of all limb muscles. There were no sucking or swallowing difficulty.

METHODS: Serum creatine kinase was normal Nerve conduction studies showed reduced CMAP amplitude in all nerves tested with normal sensory studies. Electromyography showed myopathic pattern. Muscle biopsy was suggestive of centronuclear myopathy. This is known to be caused by mutations in four genes - MTM1, DNM2, BIN1 and RYR1. As cost of sequencing these genes sequentially would be prohibitive exome sequencing was carried out using Nimbelgene SeqCap EZ human exome V3 kit. The libraries were sequenced to 150x on Illumina platform.

RESULTS: No clinically significant variations were detected in BIN1, MTM1 and DNM2 genes. Three heterozygous mutations in RYR1 gene were observed. Of these, heterozygous change of C>T at codon 4709 (p.T4709M) on chromosome 19 has been reported to be associated with the phenotype of central core disease. This missense mutation was inherited from the asymptomatic mother. The other two variations p.R1100C and c.G2060C have not been reported for any clinical relevance, however computational prediction shows that these variations could have damaging effects on protein function. These were inherited from the father, who had inherited the same from his father (grandfather of child). CONCLUSION: Based on this knowledge the couple can be offered prenatal diagnosis. Exome sequencing has facilitated clinical genetic practice to a remarkable degree.

Keywords: Congenital Myopathy, Exome Sequencing, RYR1 gene

POSTERS

P9

Evaluation of SNP Calling Using Single and Multiple-Sample Calling Algorithms by Validation Against Array Based Genotyping and Mendelian Inheritance

Pankaj Kumar, Alice Aleem, Wadha Al Muftah, Mashael Al-Shafai, Karsten Suhre
Weil Cornell Medical College in Qatar, Qatar

BACKGROUND AND PURPOSE: With diminishing costs of NGS, whole genome analysis becomes a standard tool for identifying genetic causes of inherited diseases. Commercial NGS service providers in general not only provide raw genomic reads, but further deliver SNP calls to their clients. However, the question arises whether to use the SNP data as-is, or process the raw sequencing data further through more sophisticated SNP calling pipelines with more advanced algorithms. Here we report a detailed comparison SNPs called using popular GATK multiple-sample calling protocol to SNPs delivered as part of a 40x sequencing project by Illumina Inc of 222 human genomes from families of Arab descent.

METHODS AND MATERIALS: As benchmarks we use independent array-based SNP calls using Illumina Omni 2.5 platform and consistency with Mendelian inheritance. Illumina SNP calls were based on Cassava pipeline while we implemented GATK pipeline following best practice guidelines, including base and variant recalibration.

RESULTS: We observed significant differences in SNP discovery between both algorithms. On average Illumina SNPs calls (~3.8 million) were fewer than calls made by GATK (~4.5 million). We found high concordance (~99%) in genotype for SNPs that were called by both algorithms and generally have higher genotype quality. Also these high quality SNPs calls matched with Omni array genotype calls. We also found that major fraction of low quality discordant SNPs did not follow Mendelian inheritance based on pedigree information. In addition, we note that many high quality SNPs called only by GATK were annotated as deleterious and could therefore represent potentially missed candidate variants for some of the genetic disorders we seek to explain.

CONCLUSION: Although high quality SNP calls delivered by commercial NGS sequencing projects in general show concordance with array genotypes and Mendelian inheritance, application of more sophisticated SNP calling platforms, i.e. using multiple-sample calling, may provide additional candidates for monogenic disorders.

Keywords: Next Gen Sequencing, Calling Algorithms, Array-based Genotyping

P10

Association of MTHFR 1793 G>A and VEGF- 1154 G>A Polymorphisms with Multiple Consecutive Failing IVF Cycles in Women

[1]Saeede Soleimanian, [2]Mohammadhasan Sheikhha, [1]Pooneh Nikuei, [1]Tasnim Eqbal Eftekhaari, [3]Mohammadhadi Tamaddon
[1]Molecular Medicine Research Center of Hormozgan University, [2]Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Science, Yazd, [3]Department of Managment, Science and Research Branch, Islamic Azad University, Hormozgan, Iran

BACKGROUND AND PURPOSE: Successful embryo implantation depends on trophoblast propagation, migration and, finally, invasion of the endometrium. So, vascular endothelial growth factor (VEGF) is the best described regulator of angiogenesis. Another one of suggested reason of IVFfailure is hyperhomocysteinemia. Polymorphic genes involved in homocysteine and folate metabolism,(MTHFR) are regarded as an important risk factors for homocysteine accumulation and modulator of IVF failure susceptibility. Thus the aim of this study was to evaluate the frequency of MTHFR polymorphism 1793G>A and VEGF-1154 G>A genotype in women undergoing in vitro fertilization (IVF) program.

MATERIAL AND METHODS: We have examined 132 Iranian women with a history of 3 or more IVF failure in the first pregnancy trimester. The control group consisted of 60 women without obstetrical complication, any history of miscarriage and with at least one live birth in anamnesis. The investigated polymorphisms were determined by PCR/RFLP method for MTHFR polymorphism 1793G>A and for VEGF-1154 G>A genotype, we used ARMS/PCR. Finally all data were compared using the Student t-test. Final analysis was carried out using the Fisher chi-square test.

RESULT: For MTHFR 1793G>A polymorphism we have observed significant overrepresentation of heterozygotic GA genotypes in IVF failure group (66.4% vs6.7% in the controls, OR=4.48, p=0.001). We have detected significant association, in IVF failure for VEGF -1154 group AA genotype (43.9% vs0.0% in the controls, OR=3.48, p=0.001).

CONCLUSIONS: Our research indicate the possible role of MTHFR 1793G>A and VEGF-1154G>A polymorphism in pathogenesis of IVF failure. A panel of tests MTHFR 1793AG and VEGF -1154A/A may be useful to identify women at risk for implantation failure after IVF.

Keywords: IVF failure, MTHFR, VEGF, Polymorphism

POSTERS

P11

Personalized Genomic Implication in a Case of Neurofibromatosis Type 1-Associated with Advanced Gastrointestinal Stromal Tumour: Case Report

Samer Sawalhi
Dubai Hospital, United Arab Emirates

BACKGROUND AND PURPOSE: There are several differences between gastrointestinal stromal tumors (GISTs) in a neurofibromatosis type 1 (NF1) patient and sporadic GISTs with regard to the tumor site, tumor behavior, targeted therapeutic approach, survival, prognosis, and recurrence based on genomic mutations. Wild type GISTs, those that do not have mutations in KIT or platelet-derived growth factor receptor-alpha (PDGFR-?), are typically resistant to imatanib therapy. Mutational analysis is critical in predicting tumor behavior and might individualize targeted therapy. We show that sequencing for KIT and PDGFR-? provide a useful tool in predicting tumor behavior of GIST in a NF1 patient.Our aim was to analyze the behavior of gastrointestinal stromal tumor (GIST) in a type-1 neurofibromatosis (NF1) Von Recklinghausen patient.

METHODS: We report a 27-year old woman with NF1, who presented with a lower abdominal mass, symptomatic anemia, and significant weight loss. Computed tomography (CT) scan, surgical tumor resection, histological diagnosis, immunohistochemical analysis (CD117, CD24, Bcl-2) .Genomic DNA analysis of the GIST sample was prepared from formalin-fixed tumor tissue (Qiagen). Direct sequencing of exon and intron-exon boundaries of the c-KIT and PDGF-a genes was performed (Applied Biosystems 3130 XL Genetic analyzer). Imatinib mesylate (Gleevec) was given as adjuvant therapy.

RESULTS: CT scan delineated a large thick wall cavity lesion connecting to the small bowel segment. Resection of the tumor yielded a mass of 17cm x 13cm with achievement of safety margins. The histological diagnosis was GIST, confirmed by immunohistochemical expression of CD117, CD34, and Bcl-2 Oncoprotein antibody. There were no mutations in exons 9, 11, 13 or 17 in the c-KIT gene or in exons 12, 14, or 18 in the PDGFR-a gene. There was no evidence of recurrence, metastasis or metachronous GIST for over three years.

CONCLUSION: Selective genotyping is advisable for high risk patients to predict tumor behavior.

Keywords: KIT, Gastrointestinal stromal tumor, Imatinib, Neurofibromatosis type-1, Platelet-derived growth factor receptor-alpha

P12

Identification of a Causative Gene for Oral-Facial-Digital Syndromes Type II or Mohr Syndrome

[1]Mohammad Al-shboul, [2]Hanan Hamamy, [1]Bruno Reversade
[1]*nstitute of Medical Biology/A*STAR, Singapore,* [2]*Department of Genetic Medicine and Development, Geneva University Hospital, Geneva, Switzerland*

Mohr syndrome belongs to a multisystemic and heterogeneous group of disorders called oral-facial-digital syndromes (OFDS). OFDS comprises of 13 clinical subtypes that are characterized by congenital defects in the oral cavity, facial structure, and digits. Until now, only two OFDS genes (responsible for types I and IV) have been identified. Mohr syndrome is an autosomal recessive disease characterized by bilateral preaxial polydactyly, brachydactyly, syndactyly, hypertelorism, broad nasal root, absence of medial incisors, cleft lip and cleft palate.

We performed homozygosity mapping followed by massive parallel sequencing in 2 Jordanian probands diagnosed with Mohr syndrome. We found a frameshift mutation in the ASUN (MIM 615079) gene that segregated with the disease. This mutation results in the production of a truncated protein in patients' cells. ASUN is localized to the cytoplasm and in the nuclear and peri-nuclear space in human cells and marks the axoneme of primary cilia. Loss of ASUN in human cells caused loss of primary cilia and severe mitotic cell cycle defects. In addition, patient nasal epithelial cells are disrupted in motile cilia formation. Depletion of asun using morpholino antisense oligos (MOs) in both Xenopus and zebrafish caused severe developmental delay accompanied with motility defects and specific ciliary phenotype.Overall, ASUN plays a pivotal role in both primary and motile cilia function and formation. The identification of ASUN as a causative gene for OFDS type II may now provide insights into the identification of other OFDS causative genes.

POSTERS

P13

Deep Coverage Next-generation Sequencing Enables Detection of Ancestral Genomic Fragments in Qataris of Bedouin Ancestry and Demographic Inference of Ancestral Out-of-Africa Populations

[1,2]Juan Rodriguez-Flores, [3]Khalid Fakhro, [2]Francisco Agosto-Perez, [3]Amal Robay, [1]Ronald Crystal, [1,2]Jason Mezey
[1]*Weill Cornell Medical College, Department of Genetic Medicine, New York,* [2]*Cornell University, Department of Biostatistics and Computational Biology, Ithaca, NY, USA,* [3]*Weill Cornell Medical College in Qatar, Department of Genetic Medicine, Doha, Qatar*

BACKGROUND AND PURPOSE: As early as 125 thousand years ago, anatomically modern humans migrated out of Africa, across the Red Sea into the Arabian Peninsula, and subsequently onwards into Asia, Europe, and America. Little is known about the demographic history of the original out-of-Africa population, however next-generation sequencing enables high-resolution detection and analysis of ancestral genomic fragments in contemporary humans. Given its close proximity to the original out-of-Africa bottleneck, Qatar is an ideal location for such analysis.MATERIALS AND METHODS: In order to infer the demographic history of the ancestral out-of-Africa population, we selected 60 Qataris with over 95% Bedouin ancestry and at least 3 generations of ancestry in Qatar for 30x deep coverage genome sequencing and comparison to 2500 low-coverage genomes from 26 populations spanning Africa, Asia, Europe and America that were sampled by the 1000 Genomes Project Consortium. Single nucleotide polymorphisms in these genomes were identified and stringent quality filters were applied. Three major methods for demographic inference were applied to the data, including coalescent inference of the effective population size of the ancestral population, phylogenetic clustering of chromosomes and identification of genomic segments of shared ancestry between individuals.RESULTS: Using the pairwise-sequential Markov coalescent inference method, we determined that Bedouins experienced the same out-of-Africa bottleneck over 30 thousand years ago as other non-African populations. Neighbor-Joining tree cluster analysis of pairwise identity-by-state between genomes placed Bedouins near Mediterranean European and South Asian populations. Ancestral deconvolution analysis using SUPPORTMIX detected up to 15% Bedouin ancestry in both European and South Asian populations, while little or no Bedouin ancestry was detected in East Asians.
CONCLUSION: These results in combination suggest migration of anatomically modern humans from Africa to Arabia, then splitting into three groups: Bedouins who remained in Arabia, migrants to South Asia, and migrants to Mediterranean Europe.

Keywords: Population migration, Bedouin, Arab, Next generation sequencing, Deep coverage

P14

Homozygous Mutations in GRID2 Cause a Novel Recessive Syndrome of Cerebellar Ataxia and Tonic Upgaze

[1]Ganeshwaran Mochida, [1]L. Benjamin Hills, [2]Amira Masri, [3]Elizabeth Lim-Melia, [4]Michisuke Yuzaki, [5]Kotaro Konno, [4]Wataru Kakegawa, [1]Anh-Thu N. Lam [3]Nandini Chandy, [1]R. Sean Hill. [1]Jennifer N. Partlow, [6]Muna Al-Saffar, [1]Ramzi Nasir, [1]Joan M. Stoler, [7]A. James Barkovich, [5]Masahiko Watanabe

[1]*Boston Children's Hospital, USA,* [2]*Jordan University Hospital, Jordan,* [3]*New York Medical College, USA,* [4]*Keio University, Japan,* [5]*Hokkaido University, Japan,* [6]*United Arab Emirates University, UAE,* [7]*University of California, San Francisco, USA*

BACKGROUND AND PURPOSE: There are numerous genetic disorders that have cerebellar ataxia as a prominent feature, but few have an identified genetic cause. We performed a genetic study to identify the cause of a unique syndrome characterized by cerebellar ataxia and eye movement abnormalities. METHODS AND MATERIALS: We ascertained a family from Jordan and another from the U.S., both with cerebellar ataxia, tonic upgaze and global developmental delay. Genetic studies conducted included SNP genotyping, linkage analysis, array comparative genomic hybridization, quantitative PCR and Sanger sequencing. Eye movement recordings of mutant mice deficient for the ortholog of the identified candidate gene were obtained, and immunohistochemistry using human and mouse brain specimens were performed. RESULTS: Homozygosity mapping identified the disease locus on chromosome 4q. Within this region, we found a homozygous deletion of GRID2 exon 4 in the Jordanian family and compound heterozygous deletions involving GRID2 exon 2 in the U.S. family. Grid2-deficient mice showed larger spontaneous and random eye movements compared to wild-type mice. In developing mouse and human cerebella, GRID2 localized to the Purkinje cell dendritic spines. Brain MRI of two affected children showed progressive cerebellar atrophy, which was more severe than that observed in Grid2-deficient mice. CONCLUSION: Our study shows that homozygous deletions of GRID2 cause a novel syndrome of cerebellar ataxia and tonic upgaze. The phenotypic resemblance and similarity in protein expression pattern between humans and mice suggest a conserved role for GRID2 in the synapse organization between parallel fibers and Purkinje cells. GRID2 is genomically located in a common fragile site, which shows a high rate of genomic rearrangements. Thus, GRID2 mutations might be a more common cause of genetic cerebellar ataxia than expected.

Keywords: Cerebellar ataxia and tonic upgaze, GRID2, Homozygosity mapping

POSTERS

P15

Comprehensive Map of Copy Number Variants in the Qatari Population

[1]Khalid Fakhro, [2]Noha Yousri, [3,4]Juan Rodriguez-Flores, [1]Amal Robay, [2]Karsten Suhre, [1]Jason Mezey, [1]Ronald Crystal

[1]Department of Genetic Medicine, and [2]Department of Physiology and Biophysics, Weill Cornell Medical College - Qatar, Qatar, [3]Department of Genetic Medicine, Weill Cornell Medical College, New York, USA [4]Department of Biostatistics and Computational Biology Cornell University, Ithaca, USA

BBACKGROUND AND PURPOSE: Genetic variation in Arab populations has been largely uncharacterized at high resolution, leading to difficulties interpreting clinical findings in disease research studies. In this study, we identify high resolution copy number variants (CNVs) in native Qataris and present the first analysis of genomic structural variation within this small but diverse population. Generating a high resolution CNV map could provide valuable information on demographic history, evolutionary pressures and disease burden in this population. METHODS AND MATERIALS: We studied 108 unrelated individuals from the 3 major native Qatari subpopulations (Q1-Bedouin, Q2-Persian and Q3-African) using both high density (2M) genotyping arrays and whole-genome sequencing (WGS). We devised a hybrid strategy in which we first assembled a set of high confidence CNVs derived from the union of 2 algorithms applied to array data, followed by using WGS CNVs from these same individuals to map CNV breakpoints accurately and analyzed their distribution and functional impact in this population.

RESULTS: We used WGS CNVs to define breakpoints in 108 individuals for 1551 CNV Regions (CNVRs) comprising 1129 deletions and 422 duplications; 446 of 1551 CNVs (~24%) overlapped 2011 unique genes, suggesting functional impact in the population. Interestingly, 448 of 1551 (~24%) were novel to Qataris; 89 affected 237 genes, including 14 known to cause severe Mendelian disease. These rare alleles could contain signs of recent selection pressures on the population. We also found >45,000 WGS-derived CNVRs in the same individuals, overlapping >5000 unique genes, with an enrichment of pathways relevant to Qatari public health (e.g., diabetes and cardiovascular health). CONCLUSION: We present the first high-resolution CNV resource of Gulf Arabs using 2 platforms and 4 algorithms and find that a large fraction of CNVs is highly specific to either platform, supporting use of hybrid strategies in future study design in this and other new populations.

Keywords: CNVs, Qatari, Gulf Arabs, Hybrid strategies

P16

The Functional Relevance of Polymorphisms in Chemokines and Chemokine Receptor Genes in the Pathophysiology of Asthma (Scotch and Saudi Family-Based Study)

Saleh Al-Abdulhadi

Salman Bin Abdulaziz University, Saudi Arabia

BACKGROUND AND PURPOSE:
Several molecular genetic studies has been made during the past few years in developing a better understanding of pathophysiology of asthma, which has led to the identification of several chromosomal regions and loci showing linkage and association with asthma and asthma-related phenotypes. Chemokines contribute to the asthmatic airway inflammation by acting on endothelial cells, eosinophils, basophils, and monocytes.

METHODS AND MATERIALS:
Nuclear families (n=154, 453 unrelated individuals) including 303 unrelated parents, and 150 unrelated children. Asthma was defined as physician diagnosed asthma (PDA). Atopy defined as skin prick test (SPT > 3 mm) to common inhaled allergen. In order to gain further insights into the biological function of the chemokines and their receptors and candidate genetic variants were modeled using the bioinformatic databases BLAST, and MatInspector. Suggested polymorphism and mutation were genotyped using TaqMan assay, Pyrosequencing and PCR method.

RESULTS:
many statistical analysis including PDT, case control, haplotype and linkage analyses suggested the SNP-64I within CCR2 gene was functional as it was recognized as having a common protein binding site. Likely functional binding sites in the CCR3 gene were also identified for the SNPs -17Y, -21G, and 5'UTR. The -403A and -28C SNP's in the RANTES promoter were identified as belonging to common functional binding sites. No such functional relevance were suggested for any of the SNP's so far identified in the genes coding for MCP-1, and eotaxin-3.

Conclusions:
Taking into account these results suggested novel mechanisms relevant to asthma and the possible functional effects of the studied polymorphisms that clearly need verification in model biological systems. Confirming this novel mechanism will develop new clinical pathways and better pharmacogenetic industrial research and development.

Keywords: Asthma, Haplotype analysis, Linkage analysis, Chemokine, Chemokine receptor

POSTERS

P17

Molecular Genetics and Genetic Counseling in Myopathy About 30 Families

[1]Laila Bouguenouch, [1]Imane Samri, [2]Sana Chaouki, [2]Mostapha Hida, [1]Karim Ouldim
[1]*Medical Genetics and Oncogenetics Unit, and* [2]*Pediatrics Department, Hassan II University Hospital, Morocco*

BACKGROUND AND PURPOSE:
Myopathy is a muscular disease caused by many different pathways. We will talk about Inherited forms that can be autosomal-dominant or –recessive. These diseases are distinguished by the severity of their symptoms and their patterns of inheritance.

METHODS AND RESULTS:
We report the case of 30 Moroccans families with myopathi compiled between October 2009 and Marsh 2013. The average age of our patients ranged from 1 month to 12 years. An electromyogram was realized for all patients wile 3 underwent a muscular biopsy. The molecular study was performed for 10 patients.

CONCLUSION:
Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are X-linked recessive disorders caused by mutations of the DMD gene located at Xp21. In DMD patients, dystrophin is virtually absent; whereas BMD patients have 10% to 40% of the normal amount. Deletions in the dystrophin gene represent 65% of mutations in DMD/BMD patients Childhood-onset proximal. Spinal muscular atrophy (SMA) is an autosomal recessive disorder caused by degeneration of the anterior horn cells of the spinal cord, leading to progressive paralysis with muscular atrophy. In more than 95% of the cases, it results from deletion of exon 7 of the SMN gene localized on 5q13, easily identified by molecular biology The clinical and molecular diagnosis of the myopathy allowed us to provide an appropriate management to the patients and to make a genetic counselling to their families.

Keywords: Myopathy, Duchenne muscular dystrophy, Becker muscular dystrophy, Dystrophin, Spinal muscular atrophy

P18

Management of Sex Differentiation Disorders at Hassan II University Hospital, Fez, Morocco

[1]Laila Bouguenouch, [1]Imane Samri, [2]Sana Abourazzak, [2]Mostapha Hida, [1]Karim Ouldim
[1]*Medical Genetics and Oncogenetics Unit*
[2]*Pediatrics Department, Hassan II University Hospital, Morocco*

BACKGROUND AND PURPOSE:
Sex differentiation disorders represent all the abnormalities in development of the gonads, the genital tracts, and the external genitalia. Disorders of sexual differentiation are due to genetic defects or endocrine imbalance. Sex-determining genes (SRY gene) dictate the gonadal sex whereas the fetal testicular hormones determine the somatic sex during sex differenciation. Abnormal sexual development causes unconformity between gender identity and gender role. The aim of this study was to evaluate the frequency, the genital anatomy appearance, the diagnostic and the surgical management of disorders of sex development (DSD) discovered during the neonatal period and the enfance.

METHODS AND RESULTS:
Between September 2009 and Marsh 2013, 30 patients with abnormal sexual development were identified in our unit. First-line testing included biology measurement and imaging. A surgical management was offered for some patients. Sexual dismorphic with genital ambiguity was the first reason of consultation. One patient had male breast development. All clinical evaluation suggested genital ambiguity.

CONCLUSION:
This presentation points out the need of an accurate diagnosis of sexual differentiation disorder during the neonatal period. The intervention of a multidisciplinary team is essential as well for assignment of sex as for therapeutic guidelines.

Keywords: Sex differentiation disorders, Genital ambiguity, Diagnosis, Sex assignment

POSTERS

P19

Identification of 3 Novel Mutations in LCA5 (Lebercilin) in Leber's Congenital Amaurosis Families

[1]Musallam Al-Araimi, [2]James Poulter, [2]Jennifer Mason, [3]Martin McKibbin, [2]Carmel Toomes

[1]Ministry of Health, Sultanate of Oman, [2]Leeds Institute of Molecular Medicine, and [3]Department of Ophthalmology, St James's University Hospital, Leeds, United Kingdom

BACKGROUND AND PURPOSE:
Leber's congenital amaurosis (LCA) is considered as a group of hereditary retinal disorders, which causes severe and early visual loss. It is a rare form of retinal dystrophy that present in the first year of life. Studies commenced into the molecular genetics of LCA revealed fourteen different LCA genes correlated to 70% of LCA cases. Determining the molecular defect underlying the disease in patients is becoming increasingly important with the recent gene therapy clinical trials performed in LCA patients.

METHOD AND MATERIALS:
homozygosity mapping analysis was done on three Pakistani LCA families using affymetrix 5.0 SNP chip analysis. A shared region of homozygosity was identified among all the affected individuals. Homozygosity at LCA5 locus was confirmed and LCA5 gene was sequenced in all affected patients.

RESULTS:
Three novel mutations were identified. Two nonsense mutations (238 C>T - R80X and 629delCT - p S210X) in exon2 and one frameshift mutations (c.1550delGA - R517fsx519) in exon7.

CONCLUSION:
To date, eight mutations in LCA5 gene were published. Here we introduce three novel mutations in the same gene identified in three LCA families. This achievement will elaborate the knowledge and enhances the understanding of LCA5 gene (lebercilin) as a cause of Leber's congenital amaurosis disorder.

Keywords: Leber's congenital amaurosis, LCA5, Homozygosity mapping, mutation

P20

Genotypic Diversity of Pseudomonas Aeruginosa in Cystic Fibrosis Siblings Using AFLP Fingerprinting

[1]Atqah Abdul Wahab, [2]Saad J Tajaldeen, [3]Ferry Hagen, [1]Ammar Sadoon, [1]Sanjay Diophode

[1]Department of Pediatric Pulomonology, Hamad Medical Corporation, Qatar, [2]Microbiology Division, Department of Laboratory Medicine and Pathology, Qatar, [3]Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands

BACKGROUND AND PURPOSE:
P. aeruginosa is one of the primary pathogens in patients with cystic fibrosis (CF) and a major cause of morbidity and mortality. Reports of the spread of epidemic or transmissible strains of P. aeruginosa within and across CF centers raised the possibility of clonal spread among siblings with CF. Aim: To genotype P. aeruginosa in CF patients with the CFTR I1234V mutation belonging to a large kindred family, and to determine whether the genotypes are identical among CF siblings and among different families with the same CFTR mutation.

METHODS AND MATERIALS:
Sixty six P. aeruginosa isolates were obtained from sputa/deep-pharyngeal swabs from 27 CF patients belong to 17 families. Genotypic relatedness was assessed using amplified fragment-length polymorphism (AFLP) fingerprinting.

RESULTS:
The results demonstrated the presence of the same genotypes of P. aeruginosa between CF siblings within one family and closely related families.Twenty three distinct genotypes of P. aeruginosa were identified. Ten families each had one distinct genotype of P. aeruginosa. In the other 7 families more than one genotype was observed; four families each showed 2 genotypes, two families each had 3 genotypes and one family had 4 genotypes of P. aeruginosa. CONCLUSION: The similar genotypes within the same and closely related CF families suggesting cross-transmission of P. aeruginosa.

CONCLUSIONS:
Taking into account these results suggested novel mechanisms relevant to asthma and the possible functional effects of the studied polymorphisms that clearly need verification in model biological systems. Confirming this novel mechanism will develop new clinical pathways and better pharmacogenetic industrial research and development.

Keywords: Cystic fibrosis, Cystic fibrosis siblings, Pseudomonas aeruginosa, AFLP fingerprinting

POSTERS

P21

Recovery of the Cystic Fibrosis Deletion Mutation in the CFTR Channel

[1]Wael Rabeh, [2]Gergely Lukacs
[1]*New York University Abu Dhabi, UAE,* [2]*McGill University, Canada*

Cystic Fibrosis (CF) is a genetic disorder that is caused by mutations in the gene for the CF Transmembrane Conductance Regulator (CFTR). CFTR is an ABC transporter chloride channel containing five domains: two membrane-spanning domains (MSD1 & 2) connected by two nucleotide-binding domains (NBD1 & 2) and linked by a regulatory domain. The most common CF causing mutation is the deletion of phenylalanine 508 (del508) in NBD1. It was shown that delF508 thermodynamically destabilizes NBD1, as a result, misfold and degrade CFTR channel in the endoplasmic reticulum and prevents its processing and translocation to the plasma membrane. An effective drug that rescue the channel enhance its folding will increase its concentration on the plasma membrane.

Here, we show stabilization of del508-NBD1 with second site mutations was not sufficient to increase the del508-CFTR folding efficiency and membrane concentration to that of the wild-type level. However, the introduction of additional mutations that stabilizes the interaction between NBD1 and MSD2 of CFTR in the presence of del508-NBD1 stabilization mutations increased the del508-CFTR folding efficiency and biogenesis from ~2% to 80% of the wild-type. As a result, a two-component drug that energetically stabilizes del508-NBD1 and maintain the NBD1-MSD2 interface interactions are required for wild-type like folding, processing, and transport function, suggesting a two step correction process.

Keywords: Cystic Fibrosis, CFTR gene, Protein rescue

P23

Experience with Cardiogenetic Research at Princess Al-Jawhara Al Brahim Center of Excellence in Research of Hereditary Disorders

[1]Jumana Al-Aama, [2]Zahir Bhuiyan, [1]Amnah Bdier, [1]Khadija Bakur, [3]Arthur Wilde
[1]*King Abdulaziz University, Jeddah, Saudi Arabia,* [2]*CHUV, Lausanne, Switzerland,* [3]*Academic Medical Center, Amsterdam, The Netherlands*

Princess Al-Jawhara Al brahim Center of Excellence in Research of Hereditary Disorders (PACER-HD) was established in August 2008 at King Abdulaziz University(KAU) Jeddah, Saudi Arabia. It is a comprehensive genetic center that provides clinical, diagnostic, research, training and public education services related to genetics. It is linked to the department of Genetic Medicine at KAU. It receives around 400 patients per year and both undergraduate and postgraduate medical and applied medical science students.

In 2010, PACER-HD established a cardiogenetic unit which consists of the cardiogenetic clinic, the genetic counseling unit and the molecular laboratory; the members of the cardiogenetic unit are: adult and pediatric cardiologists, an electrophisiologist, a clinical geneticist, a genetic counselor, a molecular geneticist and lab technologists. So far several patients from various parts of the Kingdom and neighboring countries have been assessed. We provide molecular genetic testing for the following disorders:Brugada syndrome (SCN5A - Jervell-Lange Nielsen syndrome (KCNQ1, KCNE1) - Long QT Syndrome (KCNQ1, KCNH2, KCNE1, and KCNE2) - Catecholaminergic Polymorphic Ventricular Tachycardia (CASQ2, RYR2) - Arrhythmogenic right ventricular dysplasia (PKP2). In this talk I will give an introduction about this service, present some examples and the phenotype genotype correlation for some interesting cases.

Keywords: Molecular genetic testing, Diagnotic service, Phenotype genotype correlation

POSTERS

P24

Inheritance of Quantitative Dermatoglyphic Traits with Asymmetry and Diversity in Muzeina Bedouin Tribe: A Small Isolated and Consanguineous Population from South Sinai

[1]Bibha Karmakar, [2]Ida Malkin, [2]Eugene Kobyliansky
[1]*Indian Statistical Institute, India,* [2]*Tel Aviv University, Israel*

BACKGROUND AND PURPOSE:
The genetic factors contribute significantly to the determination of dermatoglyphic traits is well established. However, the controversies in views and findings of this issue are still inconclusive. The present study is an attempt to evaluate the inheritance of diverse quantitative dermatoglyphic traits with asymmetry (DA and FA) and diversity (Div) through sibling correlations.

METHODS AND MATERIALS:
Data include 218 individual from (88 families) in a small isolate, the nomadic tribe Muzeina with a high degree of consanguinity (0.09) from South Sinai. Statistical analyses include sibling correlations, cross-correlations and genetic correlation (GC) - a ratio of sibling cross-correlation between traits divided on square root of the both traits sibling correlation product.

RESULTS:
The familial correlation coefficients for diverse dermatoglyphic traits are perhaps expected lower in such a small isolated and consanguineous population than our previous studied in Indian populations and Chuvashian populations from Russia. These results indicate a simpler genetic basis due to high degree (0.09 inbreeding coefficient) of consanguinity in Muzeina Bedouin tribe. There is no evidence of major gene involvement, although a little genetic effect obtained from familial correlations on asymmetry (DA and FA) and diversity (Div) traits through sibling correlations. The significant interaction between sexes was found, which contradicts with the other populations perhaps due to high level of consanguinity.

CONCLUSION:
Lower correlation coefficients than in other non- consanguineous populations for quantitative dermatoglyphic traits indicate a simpler genetic basis due to high degree of inbreeding coefficient (0.09) in Muzeina. Dermatoglyphic asymmetry and diversity traits may be due to environmental factors rather than dominance in Bedouins, although a little genetic effect was found suggests a measure of developmental instability in human (FA).

Keywords: Muzeina tribe, familial correlation coefficients, Inbreeding, Dermatoglyphic asymmetry, Diversity traits

P25

The Impact of Molecular Genetics on the Diagnosis and Outcome of Leukemia Patients

Salem Khalil
King Faisal Specialist Hospital and Research Centre, Saudi Arabia

BACKGROUND AND PURPOSE:
The Molecular Hematology Laboratory, Department of Pathology and Laboratory Medicine (DPLM) at King Faisal Specialist Hospital and Research Centre (KFSH&RC) were established in 1994. Since then the Laboratory is providing Molecular diagnostic services for thousands of patients (more than 30,000 samples) at KFSH&RC and other Saudi Health Institutions through Reference Laboratory and outreach activities.

METHODS AND MATERIALS:
Testing has included different molecular assays for Leukemia and Lymphoma .The menu of molecular hematology testing have been expanded over the last few years to include more than 25 different tests.

RESULTS:
The heterogeneity of acute leukemia is reflected by differences in molecular abnormalities that have been recently discovered as potential diagnostic and prognostic factors. In this review, a variety of leukemia specific mutations and translocations will be evaluated, i.e. FLT3, NPM1, IDH1, IDH2, CEPBA, DNMT3A, RUNX-1, c-KI, WT, BCR-ABL, PML-RARA and MLL gene. CONCLUSION: A genetic-based classification of leukemia is essential for accurate diagnosis, prognostic stratification, monitoring of minimal residual disease and developing targeted therapies.

Keywords: Leukemia, Molecular heterogeneity

POSTERS

P26

The Impact of Consanguinity on Birth Defects in a Saudi Population: A Case/Control Study

[1]Mohammed Majeed Saidan, [1]Amer Ammari, [1]Amal Al hashem, [2]Mohammed Shoukri, [1]Ahmad Kurdi
[1]*Prince Sultan Military and Medical City in Riyadh,* [2]*King Faisal Specialist Hospital and Research Center, Saudi Arabia*

BACKGROUND AND PURPOSE:
The role of consanguinity on birth defects outside the chromosomal and inherited disorders has always been debatable. To study the independent role of consanguinity on birth defect in a population with high rate of consanguineous marriage.

METHODS AND MATERIALS:
A case and control study nested within a 3 years cohort study for pattern of fetus and neonatal malformation in a Saudi population at Prince Sultan Military Medical City, Riyadh region, Saudi Arabia. Associations between potential risk facotrs and the outcome of interest (fetal anomalies) are tested using Chi-Square tests. Variables measured on the continuous scale are reported as means +/- standard deviations. A parsimonous multivariable logistic regression model is built to evaluate the joint effect of the potential risk factors and possible confounders. The statistical analyses were done with the SPSS version-20 program.

RESULTS:
During the 1st two years of the study period there were 19165 births, 785 babies with birth defects and 745 babies were selected as Controls. The prevalence rate of birth defects is 41/1000 total birth. The consanguinity has a statistically significant contributions in cases of genetic syndrome, isolated renal defect and isolated others, with a P value of <0.05. It has no statistically significant contribution in cases of chromosomal aberration, NTD, Isolated Congenital Heart Disease and multiple malformations. The Multi variant logistic regression analysis showed that consanguinity is an independent risk factor for this high rate of birth defects in the study population (P. value 0.0002).

CONCLUSION:
The prevalence rate of birth defects in the study population is higher than what was reported from the European countries. Consanguinity has an independent role in the high rate of birth defects..

Keywords: Consanguinity, Birth defects, Multi variant logistic regression analysis

P27

Molecular Study of the Retinoblastoma in Western Algerian Population: Research of gene Rb mutations at the constitutional level

[1]Lotfi Louhibi, [1]Amina Mama Boubekeur, [2]Khadidja Mahmoudi, [1]Rym Khadidja Abderrahmanne, [1]Nadhira Saidi Mehtar
[1]*University of Science and Technology Mohamed Boudiaf USTO, Algeria,* [2]*Pediatric Hospital of Cancastel, Algeria*

The study included 61 unrelated patients with unilateral or bilateral sporadic retinoblastoma, recruited at the clinic ophthalmology of 'front de mer' in Oran and pediatric ophthalmology department of the EHS Canastel. Oran. The DNA of patients were designated by Ru or Rb letters, respectively, for unilateral and bilateral forms followed by a number Extraction of genomic DNA was performed from whole blood using the NaCl technique (5). The 27 exons of the RB gene were amplified by PCR (6). Twenty-seven primer pairs were used for amplification of the promoter and 27 exons Rb gene components. Exons 15 and 16 were amplified together. The choice of primers (7) was done in intronic parts flanking each exon to cover with all primers, most of the RB gene. Analysis of the Rb gene at the constitutional level was performed by DGGE (Denaturant Gradient Gel Electrophoresis) (8) for 15 exons and SSCP (Single Strand Conformation Polymorphism) (9) for the remaining 12 exons. Both techniques enable screening of the index case to sequence (ABI 3130 appliedbiosystems) (10). The sequencing results were analyzed by two software 'Seqscanner' and 'Multalin'

Keywords: Retinoblastoma, Rb gene, Mutation analysis

POSTERS

P28

Non-Alcoholic Fatty Liver Disease: A Complex Disease Involving Multiple Gene Interactions

[1]Zahurin Mohamed, [1]Shamsul Zain, [2]Rosmawati Mohamed
[1]*Pharmacogenomics Laboratory, Department of Pharmacology, and* [2]*Department of Medicine, Faculty of Medicine, University of Malaya, Malaysia*

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of a liver disorder ranging from benign simple steatosis to severe steatohepatitis (non-alcoholic steatohepatitis or NASH) and then to cirrhosis which can progress to liver failure and liver-related mortality. Other than environmental factors, NAFLD appears to develop from a complex network of interactions among different causative gene pathways. Our aims are to investigate the association of genetic polymorphisms of candidate genes with NAFLD, and to assess the gene-gene interaction between these genes with the highly studied adiponutrin gene (PNPLA3). We genotyped 35 single nucleotide polymorphisms (SNPs) of candidate genes from various pathways including PNPLA3 in a total of 144 biopy-proven NAFLD patients and 198 controls that were free from fatty liver using Sequenom MassARRAY. Four genes (PNPLA3, AGTR1, GCKR, and LEPR) were found to be significantly associated with NAFLD ($P < 0.05$). Each of the genes (GCKR, AGTR1 and LEPR) showed significant interaction with PNPLA3 (empirical $P < 0.05$). The gene-gene interaction results were further confirmed by logistic regression. Interestingly, these interactions did not necessarily involve the same pathway as the lipid-related pathway of PNPLA3, suggesting that there are involvement of various pathways from different genes to result in the wide spectrum of NAFLD. In conclusion, our study provided evidence of the complex nature of the interaction between genes in NAFLD.

Keywords: Non-alcoholic fatty liver disease, PNPLA3, SNPs

P29

Results of Massive Parallel Sequencing of 60 Families with Autosomal Recessive Intellectual Disability in Arabic Families: from Research to Clinical Application

[1]Rami Abou Jamra, [1]Rebecca Buchert, [1]Hasan Tawamie, [2]Muhammad Ayman Al Khateeb, [1]André Reis, [1]Seffen Uebe, [6]Heinrich Sticht, [6]Arif Bulent Ekici, [5]Tim Strom, [4]Johannes Schumacher, [2]Ahmad Haj Ahmad, [2]Ayman Zyada, [2]Saber Hamdan, [2]Amina Ismael, [2]Safia Muhammad, [2]Bassam Hallak, [4]F.F.Brockschmidt, [4]M.M.Nöthen.
[2]*Amina Ismael,* [2]*Safia Muhammad,* [2]*Bassam Hallak,* [4]*F.F.Brockschmidt,* [4]*M.M.Nöthen,* [1]*Institute of Human Genetics, Germany,* [2]*Praxis for Pediatrics, Syria,* [3]*Neuherberg Institute of Human Genetics, Helmholtz Centre Munich, German Research Center for Environmental Health, Germany,* [4]*Institute of Human Genetics, University of Bonn, Germany,* [5]*Institute of Human Genetics, Helmholtz Centre Munich, German Research Center for Environmental Health, Germany,* [6]*Institute of Biochemistry, Friedrich-Alexander-Universität, Erlangen-Nürnberg, Germany*

Intellectual disability is an unsolved health and socioeconomic problem. Most of the causes are autosomal point mutations and are still insufficiently studied. We ran systematic autozygosity mapping in 133 Arabic consanguineous families with autosomal recessive intellectual disability (ARID). We then enriched the exomes of the index patients of 60 families using Agilent SureSelect 37 Mb or 50 MB and massively parallel sequenced those using Solexa or SOLiD platforms. We then stringently filtered the identified variants by excluding variants that are out of candidate regions, that are reported in public databases, that are found in internal database (over 300 exomes), and that do not influence the protein sequence. We prioritized the remaining variants based on in silico prediction, molecular modelling, and function of the affected protein. The identified candidate mutations were then validated by Sanger sequencing, tested for segregation, and genotyped in a control cohort. We could clarify the aetiology in ten families by identifying an obvious pathogenic mutation in one of the following known intellectual disability genes AlH1, ALDH5A1, CC2D1A, CRBN, C12orf65, GCDH, GPR56, HGSNAT, and SPG20. In further 8 families we identified one convincing candidate mutation in each of the novel ARID genes AP4S1, CCDC23, EDC3, EZR, FAR1, HMG20A, PGAP1, PGAP2, and TMTC3 and proved pathogenicity. In further 25 families we identified candidate genes that are still under further analyses. Our results show that in 18 of 60 (30%) families, exome sequencing was able to identify the causing mutation in a known gene or to identify a novel ARID gene. Our results contribute to the elucidation of the genetics of intellectual disability and of brain functions. Our results also show that the sequencing strategy can be used as a diagnostic tool, especially in consanguineous families.

Keywords: Intellectual disability, Autosomal recessive, Homozygosity mapping, Next generation sequencing, Syria

POSTERS

P30

CFC1 Gene Mutation in Tetralogy of Fallot and Dextro-Transposition of Great Arteries in Pakistani Population

Afsheen Arif, Sitwat Zehra, Abid Azhar
The Karachi Institute of Biotechnology and Genetic Engineering, University of Karachi, Pakistan

BACKGROUND AND PURPOSE:
Congenital heart diseases (CHDs) are the most common of all birth defects and one of the leading causes of mortality in the first year of life. It can be broadly classified as cyanotic and acyanotic. Cyanotic Cardiac malformation accounts 25% of all CHDs; however, no data is available from Pakistan. CFC1 gene is a cell signaling protein is a co receptor in nodal signaling pathway and involve in right and left axis determination during gastrulation.

METHODS AND MATERIALS:
This is a case-control study, recruited 225 non syndromic patients and 140 controls, healthy unrelated individuals. The study, after formal approval includes patients from various pediatric cardiology centers in 3 years. A detailed family history was taken to elucidate the genetic and environmental factors. Pediatric cardiologist confirmed the diagnosis on the basis of all standard testing like chest X-ray, CBC, ECG, ECHO, cardiac catherization reports etc. DNA extraction and sequencing was done and data was interpreted by multiple sequence alignment software. Statistical data was done by SPSS 17.0.

RESULTS:
The mean age for controls was 3.14±1.82 years, for TOF; 2.97±1.21and for DTGA patients 1.84±2.26 years, respectively. TOF and DTGA were frequent in males. The study demonstrates frequency of this disease; with its variation in Pakistani population. Consanguinity affects the rate of CHDs, as it is 62% in patients and 25% in controls. Two novel mutations were found in CFC 1 gene.

CONCLUSION:
The study demonstrates frequency and prevalence for TOF and DTGA there variation and association with other cardiac defects. Environmental factors are taken into consideration and consanguinity proves to be an element for the increasing number of disease. CFC1 plays a key role in cardiac malformation and its mutations.

Keywords: Congenital heart diseases, Cell signaling protein, Crypto, Cryptic, Tetralogy of fallot, Dextro transposition of great arteries

P31

A First Look at Arabic Genome Data from a New Clinical NGS Diagnostics (C-NGS-D) Tools: How the Gulf Regions is Empowering the Genomic Revolution.

[1]Darrol Baker, [2]Fahd Al-Mulla
[1]GoldenHelix, United Kingdom, [2]GenaTak Ltd, United Kingdom

This talk will address our experience in offering genomic sequencing services, including data analysis and clinical interpretation and reporting. It will address innovative solutions to increase the efficiency of genomic reporting through software solutions and widespread data sharing and real time connection of ICD10 data to physician based diagnostic client reporting. We have taken a selected number of Arabian genomes from private individuals to pilot a new Arab based NGS diagnostics tool, which we will showcase at this meeting.

Keywords: Next generation sequencing, Diagnostics, Arabian genom.

P32

Molecular Mechanisms Associated with Malignancy: Array CGH, Comparative Transcriptome and Exome Sequencing Identifies Cmet, SPP1 and SUZ12 Genes Involved in the Development of Neurofibromatosis Type 1 (NF1)-Associated Malignant Peripheral Nerve Sheath Tumours

Meena Upadhyaya, Laura Thomas, Jincy Winston, Kevin Ashelford, Ellie Reed
Institute of Cancer and Genetics, UK

Neurofibromatosis type 1 (NF1) is a familial tumour predisposition syndrome caused by inactivating germline mutations of the NF1 gene. NF1 is associated with the growth of peripheral nerve sheath derived benign and malignant tumours. About 10-15% of NF1 patients develop malignant peripheral nerve sheath tumours (MPNSTs) which are highly aggressive and therapeutically resistant. Half of all MPNSTs diagnosed occur in association with NF1. The current diagnosis and clinical management of NF1-MPNSTs is unsatisfactory and the molecular mechanisms underlying transformation to malignancy is not fully defined. Surgery and radiotherapy are the mainstay of treatment, but the local recurrence risk is high. In order to find diagnostic and prognostic biomarkers for MPNST, we have employed array CGH, comparative transcriptome and exome sequencing.

We have identified a number of therapeutic targets including cMET, SPP1 and SUZ12. All of these genes were found to be significantly differentially expressed in MPNSTs in comparison to benign neurofibromas. Suppression of these genes either by shRNA or pharmacological inhibition reduced the tumorigenic properties of MPNSTs (invasion and migration) in culture. As a part of an international collaboration (UK, Belgium, USA and France) we have demonstrated that SUZ12 is somatically mutated in a number of MPNSTs. SUZ12 is an epigenetic regulator and functions by silencing a variety of other genes by histone modification. SUZ12 is a component of polycomb repressive complex 2 (PRC2) which together with EZH2 and EED, mediates gene silencing through methylation of lysine 27 of histone H3 (H3K27). SUZ12 is aberrantly expressed in human primary tumours. Animal studies and SUZ12 inactivation in NF1 microdeletion patients also provide evidence for a role of SUZ12 in NF1 malignancy. Specific signalling pathways involved with NF1 malignancy will be presented.

Our study indicates a role of cMET, SPP1 and SUZ12 in the development of NF1 MPNST and identifies therapeutic targets.

Keywords: Neurofibromatosis type 1, Benign tumours, Malignant peripheral nerve sheath tumours (MPNSTs), SPP1, SUZ12, Therapeutic targets

P33

Association of MTHFR C677T and A1298C Polymorphisms with Breast Cancer and Male Infertility in Jordan

[1]May Sadiq, [1]Doa'a Mfadi, [2]Nadia Abu Issa
[1]*Yarmouk University,* [2]*Jordan University of Science and Technology, Jordan*

BACKGROUND AND PURPOSE:
Methylenetetrahydrofolate Reductase (MTHFR) is one of the key enzymes in the folate metabolic pathway. The polymorphisms MTHFR C677T and MTHFR A1298C lead to the reduction in the enzyme activities, which affect DNA synthesis, methylation, repair and gene expression. These polymorphisms were reported in different populations to be associated with different disorders related to the regulation of cellular functions such as gene expression and development. The purpose of this study is to examine the association between these two polymorphisms with male infertility and female breast cancer.

METHODS AND MATERIALS:
For infertility study, a group of 150 cases of infertile men (45 with oligozoospermia; 71 with severe oligozoospermia; 34 with azoospermia) along with 150 age matched fertile controls were recruited from different Jordanian infertility clinics. As for breast cancer study, 200 breast cancer patients and 200 age-matched unaffected control females were recruited from two major Jordanian Hospitals. Informed consent was obtained from each subject. DNA was isolated from blood withdrawn in EDTA vacutainers from all subjects. Genotyping of both MTHFR A677T and MTHFR A1298C polymorphisms was performed using PCR-RFLP technique followed by regression analysis.

RESULTS:
The results showed an association between MTHFR 677TT genotype and male infertility ($P < 0.05$), while the distribution of MTHFR A1298C was not different between the fertile and infertile groups ($P > 0.05$). Both MTHFR A677T and MTHFR A1298C polymorphisms showed no significant differences in their distribution between the cases and the controls.

CONCLUSION:
This study showed that MTHFR A677T but not MTHFR A1298C polymorphism is a risk factor of male infertility, while neither MTHFR A677T nor MTHFR A1298C polymorphism are risk factors of female breast cancer in Jordanians.

Keywords: Breast cancer, Male infertility, MTHFR, Jordanian

POSTERS

P34

Pharmacogenomics: the genetic basis for variability in drug response- Indian Study

Kalpana Joshi
University of Pune, India

BACKGROUND AND PURPOSE:
The study of association between genetics and drug response is called pharmacogenomics. Inter-individual variability in drug response can be attributed to polymorphism in genes encoding different drug metabolizing enzymes, drug transporters and enzymes involved in DNA biosynthesis and repair. Genetic polymorphism in Drug Metabolizing Enzymes (DMEs) gives rise to 3 distinct subgroups of people who have measurable differences in their ability to metabolize drugs to either inactive or active metabolites. Individuals capable of efficient drug metabolism are called extensive metabolizers (EMs). Individuals with deficiencies in metabolism, which typically require mutation or deletion of both alleles of a gene, are termed poor metabolizers (PMs). Conversely, overexpression due to gene amplification results in ultra-rapid metabolizers (UMs). Standard doses of drugs with a steep dose-response curve or a narrow therapeutic range may produce adverse drug reactions, toxicity, or decreased efficacy in PMs. When taken by UMs, the standard dose may be inadequate to produce the desired effect.

RESULTS:
Major genetic polymorphisms affecting DME activity are related to drug oxidation by cytochrome P450 enzymes (CYP) 2C19, 2C9 and 2D6. Such polymorphism gives rise to important inter-individual and inter-ethnic variability in the metabolism and disposition of several therapeutic agents resulting in differences in clinical response to these drugs. Ayurveda, India's traditional system of medicine has a unique way of classifying human population based on individual constitution types or Prakriti or constitution. We observed interesting correlations between CYP2C19 genotypes and Prakriti with fast and slow metabolism being one of the major distinguishing and differentiating characteristics.

CONCLUSION:
We analyzed Single nucleotide polymorphisms (SNP) in genes coding for Methotrexate (MTX) metabolism in Indian Rheumatoid Arthritis (RA) patients and reported some newer risk associations. Classification methods based on traditional medicine Ayurveda has genetic connotation.

Keywords: Pharamacogenomics, Cytochrome P450, Ayurveda, CYP2C19, Methotrexate metabolism

P35

An Association between Olfactory Receptor Gene Polymorphism and Diabetic Complication: A Significant Trend of the C-(ORG)-C in Nephropathy Patients

Mohamed Jahrami
Salmaniya Medical Complex, Bahrain

Long-term complications of diabetes develop gradually. Eventually, diabetes complications may be disabling or even life-threatening. Recently we have reported a significant association among a polymorphism in olfactory receptor gene (ORG) and type 1 diabetes. As there are reports about involvement of olfactory receptor in diabetic complication we have genotyped our patients with diabetic complications for the same gene polymorphism. We used 25 patient with neuropathy, 27 patients with nephropathy, 29 patients with retinopathy and 30 patients and we used 32 diabetic complication controls.

Patients with 20 years long history with no complication effects were considered as diabetes complication control. Samples were genotyped for ORG using Taqman SNP Genotyping Assay Protocol (C-2519386-10), Applied Biosystems. Results matched Hardy-Weinberg rules. The Fisher's 2-sided exact test was used to compare allele frequencies of the genotype and allelic frequencies of A(ORG)C. The genotype C(ORG)C was significantly associated with nephropathy, p=0.00009, compared to diabetic control group. There was no significant difference among diabetic neuropathy, retinopathy compared with diabetic control. This critical association emphasizes on the importance of ORG in the nephropathy pathogenesis and might have a future therapeutic value. However, ORG should be investigated further in large studies.

Keywords: Olfactory receptor gene, HLA-F, Diabetic complication, Hypertension, Nephropathy

POSTERS

P36

Investigating the Potential Effect of Consanguinity on Type 2 Diabetes Susceptibility in a Saudi Population

[1]IM Gosadi, [2]MD Teare, [2]EC Goyder
[1]King Saud University, Saudi Arabia, [2]Sheffield University, Saudi Arabia

BACKGROUND AND PURPOSE:
Several studies suggested association between consanguinity and risk of developing type 2 diabetes (T2D). Aim: To examine mechanisms by which inbreeding might increase the risk of T2D in a Saudi population. Study Design: Family-based cross-sectional study.

METHODS AND MATERIALS:
362 adult male participants were recruited, 179 were T2D patients and 183 healthy participants were siblings of recruited patients. Severity was assessed in patients by recording age at diagnosis. Risk in healthy subjects was inspected by assessing their body mass index (BMI), fasting blood glucose (FBG), and waist circumference (WC). Extended pedigrees were constructed to calculate inbreeding coefficients (IC). 23 Single SNPs incurring higher risk of T2D were genotyped. All subjects were interviewed to answer food frequency and physical activity questionnaires to account for environmental variation between participants.

RESULTS:
Significant inverse association was detected between IC and age at diagnosis accounting for environmental covariates (B: -0.572 P-value: 0.012). In 42 families, we were able to recruit 2 healthy siblings from each. Pearson's correlation coefficient of FBG between siblings was 0.317 (P= 0.04). Correlations between siblings' FBG increased with increased range of consanguinity suggesting a stronger genetic influence leading to lower variation of FBG between siblings. The effect of consanguinity on variation of FBG was further assessed by fitting a regression line and controlling for difference in age, caloric intake, and level of physical activity (B: -0.118 P-value: 0.024). No significant associations were detected between number of loci identical for risk alleles and age at diagnosis, BMI, WC, or FBG. An association of marginal significant was detected between age at diagnosis and total number of risk alleles when accounting for parental history of diabetes and IC (B:-0.399 P: 0.052).

CONCLUSION: Study's findings suggest consanguinity might increase risk of T2D by earlier development of the disease, and by strengthening possible genetic effect on FBG.

Keywords: Diabetes mellitus type 2, Consanguinity, Inbreeding

P37

Rheumatoid Arthritis: Role of IL-1 Gene Polymorphism, Mycoplasmal Infection, and CD4+CD25+ Regulatory T-Lymphocytes

[1]Faten Bayoumi, [2]Tagreed Gaafar, [2]Mai Sheif, [1]Waleed Elsenousy, [1]Botos Morcos
[1]National Research Centre, Egypt, [2]Faculty of Medicine, Cairo University,

BACKGROUND AND PURPOSE:
Rheumatoid arthritis (RA) is a systemic disease of unknown etiology, often considered as an autoimmune disease. Although the exact mechanisms that are responsible for the disease remain unclear, it is accepted that different factors contribute to the etiology and pathogenesis of RA. Among these factors are infectious agents like bacteria and viruses, pro-inflammatory cytokines and regulatory T cells. The aim of the study was to differentiate effectiveness of Mycoplasma infection role as a triggering agent of the autoimmune process in RA., the association of IL-1 gene polymorphism in RA patients and the role of CD4+CD25+ Regulatory T cells counts in RA.

METHODS AND MATERIALS:
This study was conducted on adult patients suffering from rheumatoid arthritis (8 males and 42 females with age range from 18-78 years). They were divided into three groups according to Disease Activity Score (DAS) of RA. They were compared with 50 healthy individuals as controls. CD4+CD25+ T-cell were determined by flow-cytometry and IL-1 genes polymorphism was detected through conventional PCR and RFLP, conventional nested PCR was used for Mycoplasma fermentans detection.

RESULTS:
Indicated that there were no significant differences concerning the allele type of both IL-1B and IL-1RN genes between different patient groups and control group. Also, comparing with the control group, results showed no significant difference concerning CD4+,CD25+ T-cell count in relation to patients of group I (low DAS) but was significant with patients of other groups. Mycoplasma fermentans DNA was not detected in any case of the patient or control groups.

CONCLUSION:
The increase in circulating CD4+CD25+ (Treg) cells number in RA was directly related to the severity of the disease, therefore, it was supposed to be the prognostic factor for RA more than the effect of infection with Mycoplasma fermentans and/or IL-1B and IL-1RN gene expression.

Keywords: Rheumatoid arthritis, CD4+CD25+ T-cell, IL-1 gene, Mycoplasma fermentans

POSTERS

P38

Evaluation of Hypermethylation and Expression Pattern of Glutamate and Dopamine Receptors Genes in Patients with Schizophrenia

Dor Mohammad Kordi-Tamandani
Univertsity of Sistan and Baluchestan, Iran

BACKGROUND AND PURPOSE:
Schizophrenia (SCZ) is type of psychotic disorders that affect 1% of population. Dopamine and glutamate are the major neurotransmitters in brain and their receptors are associated with number of psychotic disorders such as schizophrenia. The aims of the present study were to analyze methylation and expression profile of dopamine and glutamate receptors genes in patients with SCZ.

METHODS AND MATERIALS:
Methylation-specific polymerase chain reaction (MS-PCR) was used to estimate promoter hypermethylation of dopamine and glutamate receptors genes on 81 isolated genomic DNA, from peripheral blood of individuals with schizophrenia and 71 healthy control subjects. In addition, real-time reverse transcription- PCR was used to estimate mRNA levels in 34 blood samples of healthy controls and cases.

RESULTS:
Methylation of GRM2 and GRM5, highly increased the risk of schizophrenia in comparison to reference unmethylated pattern [OR= 2.82, (1.05-7.75), p=0.038], [OR= 12.09, (1.84-79.57), p= 0.0001] respectively. Regarding the dopamine receptors genes, Promoter methylation of DRD4 and DRD5 genes were statistically different ($p< 0.05$) in cases when compared to healthy controls in blood samples. Outcomes of expression analysis revealed statically, significant difference between cases (n=17) and health controls (n=17) regarding relative genes expression of GRM2, GRM5 and GRIA3, DRD2, DRD4 and DRD5 ($p<0.0001$).

CONCLUSION:
To the best of our Knowledge, this is the first report which indicates the methylation status and expression profile of GRs and DRs genes with the risk of SCZ. These outcomes, suggesting more attention on effect of epigenetic variations in development of SCZ in further investigations.

Keywords: Schizophrenia, Promoter hypermethylation, Dopamine receptor, Glutamate receptor

P39

Characterization of Cytokine Profiles and Signaling Pathways of the Immune System-Released Activating Agent (ISRAA) During Cellular Interactions

Sahar Elhannan, Moiz Bakhiet, Safa Taha
Arabian Gulf University, Bahrain

ISRAA is an immune mediator produced as a result of a nerve stimulus initiated by immune challenge. The active site of ISRAA was demonstrated to represent an interspecies conserved motif sharing 72% homology with TNFR1, a receptor connected to intracellular domains inducing dose-dependent signals for survival or death, since potential proliferative effects of the mouse ISRAA on human cells were recorded. In this work, a broad spectrum of proinflammatory and anti-inflammatory cytokines were measured in response to ISRAA stimulation of human PBMCs.

Furthermore, the signaling pathways used by ISRAA to induce cytokine production was studied by examining phosphorylation of signaling proteins and nuclear translocation of transcription factors involved in this process. The results demonstrated high levels of IL-6, IL-8, IL-10 and TNF-gamma production by human PBMCs stimulated with ISRAA, but no production of the cytokines IL-2, IL-4, IL-17 or TGF-beta was noted. Among the produced cytokines, IL-6 showed the highest measurable levels. Studies on signaling pathways revealed that Erk1/2 as a downstream signals in the MAP kinase pathway were activated due to ISRAA stimulation.

In conclusion, mechanisms used by ISRAA to induce cellular activity on human peripheral mononuclear cells demonstrated preferential expression of the cytokine IL-6 and that the MAP kinase pathway and its downstream Erk1/2 signals were critically involved during this process. Understanding these pathways of cellular activity induced by ISRAA is essential while studying pharmacodynamics and pharmacokinetics of ISRAA effects in future therapeutic approaches to treat immunosuppressed patients.

Keywords: PIAS (Protein Inhibitor of Activated Signal Transducer and Activator of Transcription), TRAFs (TNF Receptor-Associated Factors). MAPKs (Mitogen-Activated Protein Kinases), ERK (Extracellular signal Regulated Kinase), STAT (Signal Transducer and Activator of Transcription)

POSTERS

P40

A Strategic Plan to Control Sickle Cell Disease in the Kingdom of Bahrain

Mohamed Jahrami
Salmaniya Medical Complex, Bahrain

Sickle Cell Anemia Disease (SCD) is a genetic disease that is only contracted when both parents pass the defective gene to their child. The Kingdom of Bahrain along with kingdom Saudi Arabia, Kuwait, Oman suffers from the same syndrome. Although this syndrome has been under control for several years, unfortunately, there is not adequate published statistics about SCD in Bahrain. Annually there are a number morbidity and mortality because of this disease. Which has attracted the attention of the Supreme Ruling leaders represented by HE the Prince Khalifa Bin Salman Al-Khalifa to specify his time in order to discuss the issue of sickle cell anemia in Bahrain. To improve the quality of life for individuals with sick(SCD, and the reduction of morbidity and mortality from this disease a fifteen year strategic plan is designed hoping to eradicate and control SCD in the Kingdom by year 2023.

Although there have been a great effort made to control the SCD situation in Bahrain this plan is based on the recent findings of UK as well as USA sickle cell organizations. In this plan responsibilities of controlling SCD is logically distributed among ministries of health, education, information, work and justice, in addition to Bahrain Society for Sickle Cell Patient-care as well as communal societies who can play a critical role. Raising awareness in the community and distributing responsibilities as well as well-planned restrictions on marriage of sickle cell trait carrier will indeed solve this population threatening disease.

Keywords: Genetic counseling, Sickle Cell anemia, Strategic plan, Patient education, Social awarness

P41

Antileishmanial Antibody Response in Cutaneous Leishmaniasis

[1]Hind Abushama, [1]Maathr Abdelwahab, [2]Hiba Mohamed, [1]Omran Osman, [2]Ahmed Elhassan
[1]*Faculty of Science, and* [2]*Institute of Endemic Diseases, University of Khartoum, Sudan*

The role of antibody levels in protective immunity against cutaneous leishmaniasis (CL) is largely unknown. The aim of this study is to investigate the role of antibody response against CL among Sudanese population. Fifty six clinically diagnosed CL subjects were enrolled in this study. Forty eight of them had healed scar and eight have active lesions. The leishmanin skin test (LST) was 54.7% positive. The frequency of human IL4RP2 alleles was investigated in this study. The results showed 83.9% (183 bp) and 16.1% (253 bp) and the heterozygosity was 39%. The mean antibody levels using direct agglutination test (DAT) has found to be higher against Leishmania major (L. major) antigen than Leishmania donovani (L. donovani) antigen and the difference was found to be significant ($P = 0.01 < 0.05$).

The anti L. major IgG was quantified in this study using enzyme linked immunosorbent assay (ELISA). The mean of antibody levels measured by ELISA and DAT was significantly higher in study participants with scars more than those with skin lesions. Overall this outcome would be supportive to indicate a possible role of antibody-mediated protection in CL and would signify the importance of identification of antigens that may elicit protective antibodies.

Keywords: Cutaneous leishmaniasis, L.major, L.donovani, Antibody response, IgG

POSTERS

P42

Application of Whole Exome Sequencing in the Diagnoses of Monogenic Diseases

Cao Wenjing, Gao Ya, Huang Hui, Chen Yanhua, Wang Wei
BGI-Shenzen, China

OBJECTIVES: To investigate the whole exome sequencing technology used in diagnoses of monogenic diseases with clinical application values.

METHODS: Peripheral blood from a young male with suspected Charcot-Marie-Tooth disease was collected, and DNA was extracted for whole exome sequencing(WES). The exome sequencing result was aligned to standard reference sequences and filtered using genetic databases in order to identify possible causative variations, and positive results were varified for mutated loci. Main Symptoms: Lower extremity weakness, gait abnormalities for 13 years; feet deformities and decreased visual acuity for 10 years. Distal muscle of lower limbs weakness and atrophy while muscle stiffness; feet deformities in shape of 'horseshoe'; early-onset glaucoma.

Electromyography: The current NCV and EMG finding is consistent with a primary demyelination velocities and absent of SNAPS; the clinical diagnosis is compatible with Charcot-Marie-Tooth Disease type 1.

Urinary metabolites: The concentration level of 3- hydroxyl propionic acid, oxalic acid, glycerol acid,and 3- hydroxyl glutaric acid increased; prompti ng nutrition disorders.Mutation in SMN1 gene was not detected.

RESULTS: WES was performed on patient's DNA. We identified a homozygous deletion in the patient's SBF2 gene, resulting in autosomal recessive Charcot-Marie-Tooth disease type 4B2, which, as observed on the patient, is a demyelinating hereditary motor and sensory neuropathy characterized by abnormal folding of myelin sheaths with early-onset glaucoma.

CONCLUSION: Comparing to regular genetic testing methods, such as Sanger sequencing, MLPA, karyotype analysis, WES tests and analyzes most coding region of the genome, and can simultaneously study multiple genes related to Charcot-Marie-Tooth disease. It can be applied to the test of hereditary diseases with complex pathology and monogenic diseases, which requires effective diagnostic evidence that can be hardly obtained via routine approaches.

Keywords: Charcot-Marie-Tooth disease, Whole exome sequencing, SBF2 gene

P43

3' Tetranucleotide Microsatellite Polymorphism of Leptin Gene in Patients of Metabolic Syndrome

[1]Naglaa AbdRaboh, [1]Neveen Hemimi, [2]Samira Hemedi
[1]Dubai Medical College, [2]Department of Clinic and Community Medicine of Dubai Municipality

BACKGROUND AND PURPOSE:
Metabolic syndrome is a cluster of metabolic disorders that predispose to increased risk of developing diabetes mellitus and cardiovascular disease. Despite its growing prevalence worldwide, there is a great debate regarding its pathogenesis. Objective: to evaluate the association of 3'tetranucleotide microsatellite polymorphism of Leptin (LEP-tet) gene with metabolic syndrome and related disorders.

METHODS AND MATERIALS:
The present study has included 240 subjects (106 cases of metabolic syndrome (MS cases), and 134 normal individuals as control group) with matched age and gender. LEP-tet polymorphic region was amplified by polymerase chain reaction of DNA extracted from peripheral blood samples. The produced fragments were visualized by agarose gel electrophoresis separating two genetic groups of alleles separated as short group which was considered class I and long group as class II. Metabolic parameters were estimated in blood serum including lipid profile and fasting blood sugar.

RESULTS:
our data indicated the higher frequency of class I containing genotypes [I/I, I/II] 81% (86/106) in MS cases as compared to 73% (98/134) in control group (OR = 1.6, CI 0.85-2.93, p>0.05). when analyzing the association of (LEP-tet) metabolic syndrome related abnormalities as obesity, dyslipidemia, hypertension, and high blood glucose level, there only significant association was related to body weight as we detected class I containing genotypes [I/I, I/II] in 83% of obese MS cases, while it was in 50% of ms cases with normal body weight (OR = 4.9, CI 1.4-17.1, p<0.05).

CONCLUSION:
wider scale of work is needed to confirm our suggestion that 3'tetranucleotide microsatellite polymorphism of LEP genes may be linked to pathogenesis of metabolic syndrome through effect on body weight.

Keywords: Leptin gene, Metabolic syndrome, Polymorphism, Phenotype, Tetranucleotide microsatellite

POSTERS

P44

Antisense Transcripts and R-Loops are Formed by Topoisomerase I Inhibition at Divergent CpG-Island Promoters

[1]Giovanni Capranico, [1]Jessica Marinello, [2]Giovanni Chillemi, [2]Susana Bueno, [1]Stefano Manzo
[1]*University of Bologna, Bologna, Italy,* [2]*Caspur, Rome, Italy*

BACKGROUND & PURPOSE: DNA Topoisomerase I (Top1) is required to relax DNA supercoils generated by RNA polymerases (RNAP). Top1 is inhibited with high specificity by camptothecin, an effective anticancer agent, and by oxidative base damage and ribonucleotides in DNA strands, resulting into Top1-DNA cleavage complexes (Top1ccs). Top1ccs are repaired primarily by Tdp1 in living cells. Tdp1 is a Tyrosyl-DNA phosphodiesterase enzyme, a mutation (H493R) of which causes an autosomal recessive disorder known as SCAN1, Spinocerebellar ataxia with axonal neuropathy (OMIM 607250).

METHODS: To understand how Top1ccs affect genome functions, we have therefore investigated the global transcriptional response to CPT-induced Top1ccs by Illumina NGS and bisulfite-treatment of RNAs. Chromatin-immunoprecipitation and qrtPCR techniques were also used.

RESULTS: Top1ccs trigger an accumulation of antisense RNAPII transcripts specifically at active divergent CpG-island promoters in a replication-independent and Top1-dependent manner. As CPT increases antisense transcript levels in the presence of DRB, a transcription inhibitor, Top1ccs likely impair antisense RNA degradation. Time-course data showed a burst of Top1ccs increased by CPT at promoter sites and along transcribed regions, causing a transient block of RNAPII at the promoter. Moreover, cell immunofluorescence and biochemical assays showed that Top1ccs induce transient increases of R-loops specifically at highly transcribed regions such as nucleoli and CGI promoters. In addition, preliminary data show that a TDP1 gene deletion can increase antisense transcripts at divergent CGI promoters.

CONCLUSION: Thus, a specific and highly dynamic transcriptional response to Top1ccs occurs at divergent active CpG-island promoters including a transient stabilization of R-loops. The results clarify molecular features of a response pathway leading to transcription-dependent genome instability and altered transcription regulation. Moreover, TDP1 gene mutations may alter the molecular response to Top1ccs likely affecting the regulation of transcription of tissue-specific genes..

Keywords: DNA topoisomerase I, Top1-DNA cleavage complexes, CpG-island promoters

P45

Impact of FMR1 Gene CGG Repeat Polymorphism and Anti-Mullarian Hormone (AMH) Levels in the Susceptibility to Premature Ovarian Failure in South Indian Women

[1]Prasanna Latha Komaravalli, [2]Anupama Deenadayal, [3]Usha Rani V, [1]Parveen Jahan
[1]*Department of Genetics, Osmania Unversity, Hyderabad* [2]*Infertility Institute and Resesrch Centre, Hyderabad,* [3]*Government Maternity Hospital, Hyderabad, India*

BACKGROUND AND PURPOSE: Fragile X syndrome is characterised by the loss-of-function mutation of the fragile X mental retardation gene (FMR1) due to expansion of the 5 UTR CGG repeat (> 200) at Xq 27.3. Alleles with 6 to ~45 repeats transmit in stable manner, whereas, premutation alleles (~55-200) are unstable, may expand to full mutation alleles (>200 repeats) upon maternal transmission. It was reported that ~21% of FMR1 premutation female carriers confer a significantly increased risk for premature ovarian failure (POF). POF is the cessation of ovarian function before 40 years of age, affects 1% of women worldwide, characterised by elevated gonadotrophins, anovulation, hypo-estrogenism, and low anti-mullarian hormone (AMH) levels that lead to secondary amenorrhoea and infertility. AMH, produced by developing antral follicles, is currently thought to be a reliable prognostic marker of ovarian reserve. The purpose of the study which is first from South India was to investigate whether AMH serum levels and FMR1 gene premutation alleles are associated with POF susceptibility.

METHODS AND MATERIALS: After informed consents were obtained, 5ml of venous blood was collected from 35 patients and 35 age matched controls; serum was separated and genomic DNA was extracted. AMH levels were quantified and FMR1 gene amplification was performed to screen the CGG repeat polymorphism. Data was analysed by student t-test and p-value <0.05 was considered significant.

RESULTS: We have identified the mean age at marriage and the AMH levels differed significantly between patients and controls ($p<0.01$). Though women from both the groups were found to have CGG repeats in normal range it was the patient group who showed elevated frequency of higher CGG repeats.

CONCLUSION: The highly significant low serum levels of AMH among the patients seem to be a promising prognostic marker in the assessment of ovarian reserve, in the management and counseling of infertility..

Keywords: Fragile X syndrome, Premature ovarian failure, Anti-mullarian hormone, FMR1

POSTERS

P46

A Novel Ensemble Selection Algorithm for Cancer Diagnosis Using Micro-array Datasets

[1]Mohammed Gaafar, [1,2] Noha A. Yousri, [1]Mohamed A Ismail
[1]Computer Science and System Engineering Department, Alexandria University, Alexandria, Egypt, [2]Department of Physiology and Biophysics, Weill Cornell Medical College in Qatar, Doha, Qatar

Micro-array technology has played an important role in cancer diagnosis by classifying Micro-array samples. The accuracy of the classification is subject to two main challenges, the gene selection and the design of the classifier. The gene selection process should be integrated within the classification process. Ensembles of the classifiers have shown to enhance the accuracy compared to traditional single classifiers. However, diversity among classifiers is a challenging issue when designing ensembles.

METHODS AND MATERIALS:
A novel ensemble selection algorithm is proposed for classifying Micro-array samples. The proposed algorithm addresses the aforementioned challenges. It generates subsets of relevant genes with minimum redundancy between them in each gene subset. A genetic algorithm is then used to search the space of ensembles for the most accurate and diverse ensemble. This is done by using a fitness function that introduces a trade-off between accuracy and diversity. In order to enhance the robustness of the classification, the proposed algorithm introduces diversity between the ensemble members at the classifiers level by using k-NN classifiers with different values of k, and at the features level by training each ensemble member using a different gene subset. In order to study robustness, a measure for robustness is proposed as well.

RESULTS:
The performed experiments present a comparison between the different diversity methods used in ensembles. The experiments were performed on six standard Micro-array datasets. This comparison shows that the diversity method used by the proposed algorithm outperforms the other diversity methods in terms of accuracy and robustness.

CONCLUSION:
A novel algorithm is proposed to address the challenges of gene selection and ensemble selection. This algorithm uses a diversity method that was proven to outperform other diversity methods in terms of accuracy and robustness. The future work includes considering the robustness in the selection process.

Keywords: Micro-array datasets, algorithm, Ensemble selection

P47

Identifying Inherited Autism Mutations from Consanguineous Families

Tim Yu, Maria Chahrour, K Schmitz-Abe, C.A Walsh
Boston Children's Hospital, USA

Despite significant heritability, autism spectrum disorders (ASDs) have proven one of the most challenging disorders to understand from a genetic perspective, likely due to extreme genetic heterogeneity. To penetrate this heterogeneity, we analyzed a large cohort of ASD pedigrees enriched for a parental consanguinity and/or multiplicity, bringing to bear linkage, homozygosity mapping, CNV analyses, and whole exome sequencing.

METHODS AND MATERIALS:
We performed SNP genotyping on over 200 families (>90% consanguineous, >25% multiplex), linkage analysis, and homozygosity mapping. CNV analyses were performed using multiple algorithms (Birdsuite, PennCNV, Nexus, Affymetrix Genotyping Console). Whole exome sequencing was performed and integrated with linkage and CNV data to identify causative mutations.

RESULTS:
We demonstrate that consanguineous and multiplex families with ASD have an underlying genetic architecture different from that of nonconsanguineous families due to increased recessive contributions, as evidenced by altered male:female ratios, a lower burden of de novo CNVs, and an excess of homozygous deletions. In several cases, linkage and whole exome sequencing pinpoint specific, causative mutations (AMT, PEX7, MTRR, PAH, COH1, CEP152, HIST3H3, SYNE1). In several cases (AMT, PEX7, MTRR, COH1) we demonstrate that the specific mutations found in these families are hypomorphic, ie retain residual enzymatic activity, resulting in milder presentations of generally more severe Mendelian diseases.

CONCLUSION:
Consanguineous families with autistic children have a significantly different genetic architecture than nonconsanguineous families, with fewer de novo events and an enrichment of recessive point mutations and deletions. Recessive cases also demonstrate that ASD can be an unexpected manifestation of partial loss-of-function mutations in genes with more classical syndromic associations, and illustrate how further study of consanguineous ASD families will be important in dissecting a complex and heterogeneous disorder.

Keywords: Autism, Intellectual disability, Metabolic disease, Exome sequencing, Genomics

POSTERS

P48

DNA Diagnostics: Identifying HLA B27 in patients of Acute Anterior Uveitis

[1]PK Menon, [2]P Lamba, [2]Salwal
[1]*CABRI, Gulf Medical University, UAE,* [2]*GMCHRC Ajman, UAE*

OBJECTIVE:
The human leukocyte antigens (HLA) are a group of cell surface molecules encoded for by the major histocompatability locus on the short arm of human chromosome six. Individuals carrying the HLA-B27 gene, have been shown to have a higher incidence of isolated acute anterior uveitis (AAU). This study aims to examine the incidence of the HLAB27 gene in individuals presenting with AAU at GMCHRC.

MATERIALS AND METHODS:
This pilot study was carried out for a period from May 2013 to July 2013 at GMCHRC Ajman UAE. Four patients of clinically diagnosed AAU were examined for the presence of the HLA B27 gene. Genomic DNA was amplified using primers and cycling parameters were as described by Bunce et al using exon-2, B-locus- specific primers. The PCR products were run in a 1% agarose gel stained with ethidium bromide (0.5 µg/ml) and visualized under U.V. light.

RESULTS:
Four cases of AAU were subjects in this study. Of the four cases examined two (50%) were positive for the HLAB27 gene. The M:F ratio of the cases 3:1. All the HLA B27 positive cases were males. The average age of the positive cases was 37.5 years as compared to 53.5 years in the negative cases. There was no racial predisposition seen. Using the above set of primers, DNA from HLA B27 positive individuals gave a 150 bp band.

CONCLUSION:
AAU is the most common form of uveitis. Of the cases reported in literature half of all cases of AAU are HLA-B27 positive and this is similar to the results displayed in our series of four cases. Cases positive for HLAB27 in AAU require active treatment using immunomodulators for early resolution and topical cycloplegic agents and steroids are the cornerstones of treatment. Methotrexate, Salazopyrine, anti-TNF and anti-CD20 therapy may be used to prevent recurrent attacks. This study exemplifies the use of PCR and DNA diagnostics in the identification of HLAB27 gene in cases of AAU. Further studies using the Dideoxy Sequencing are proposed to be carried out.

Keywords: HLA B-27, Acute anterior uveitis, DNA diagnostics

P49

Role of S100A8/A9 in the Cross-Talk between Cancer Cells and Stroma-Associated Cells

[1]Taoufik Nedjadi, [2] Eithne Costello, [2]John Neoptolemos
[1]*King Fahd Medical Reseach Centre, King Abdulaziz University, Saudi Arabia,* [2]*Department of Molecular and Clinical Cancer Medicine, Liverpool University, United Kingdom*

BACKGROUND AND PURPOSE:
Pancreatic cancer is characterized by the presence of a highly reactive stroma. The latter harbors a variety of cellular compartments which includes stellate cells, fibroblasts, endothelial cells and a variety of inflammatory cells such as macrophages and monocytes. Interaction between tumour cells and surrounding stromal cells (tumour micro-environment) plays an important role in pancreatic cancer progression. We have previously shown that stroma-associated monocytes express low molecular weight proteins: s100A8 and S100A9. The aim of this study is to investigate at the involvement of S100A8 and S100A9 proteins in the tumour-stroma crosstalk and to decipher the potential signaling mechanism.

METHODS AND MATERIALS:
Cell culture of pancreatic cancer cells and monocytic cells, HL-60 and primary isolated human monocytes. Isolation of Conditioned medias. Cytokines multiplexing assay (27-plex, BioRad). Cell signaling assay. Luciferase assay.

RESULTS:
1. The expression of S100A8 and S100A9 in monocytes is increased factors secreted from pancreatic cancer cells.
2. Cytokine profiling of cell supernatants, using Luminex assay, showed that PCC secrete a number of cytokines and growth factors including IL-8, FGF and TNF-a.
3. S100A8 and S100A9 increased phosphorylation of MAPK, erk1/2 and p38 and SAPK/JNL in a RAGE dependent manner.

CONCLUSION:
S100A8 and S100A9 promote specific cytokine secretion from pancreatic cancer cells. Interestingly, a number of these cytokines, in turn, induce the secretion of S100A8 and S100A9 from monocytic cells, creating a paracrine loop. These events may create a favourable environment for tumour development and metastases.

Keywords: Pancreatic cancer, S100A8, S100A9, Cytokines

POSTERS

P50

Simple Tandem Repeat (TTTA)N Polymorphism in CYP19 (Aromatase) Gene and PCOS Risk in South Indian Women

Ranjith Reddy, Deepika M.L.N., Lakshmana Rao S.S., Usha Rani V., Parveen Jahan
Department of Genetics, Osmania University, Hyderabad, India

BACKGROUND AND PURPOSE: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder characterized by clinical features such as hyperandrogensim, chronic anovulation, and polycystic ovary. It is affecting 5-12% of women worldwide and a leading cause of infertility. Overproduction of ovarian androgen is the key patho-physiologic feature of PCOS. A number of genes encoding major enzymes of the androgen metabolic pathways have been examined and associations reported. However, these associations have not been unanimous. The CYP19 gene encodes aromatase (P450 arom), a key steroidogenic enzyme that catalyzes the final step of estrogen biosynthesis by converting testosterone and androstenedione to estradiol and estrone separately. The present study was designed to evaluate the role of a simple tandem repeat (STR) polymorphism (TTTA)n of CYP19 gene in the susceptibility to PCOS in South Indian women.

METHODS AND MATERIALS: A total of 360 subjects comprising of 181 patients and 179 healthy age matched, ultrasound scanned controls are included in the present study. Five micro liters of venous blood was collected from all the study subjects and genomic DNA was isolated by salting out method. Genotyping for CYP19 (TTTA) n repeat polymorphism was performed by PCR using specific primers followed by 12% polyacrylamide gel electrophoresis.

RESULTS: The percentage distribution of SS, SL and LL genotypes were 69%, 2%, 29% in patients while 86%, 8%, and 6% in controls respectively. Chi-square analysis revealed a statistically significant difference between patients and controls with respect to genotypes and alleles ($p<0.05$). Individuals with LL genotype was significantly predominated in patient group compared to controls (OR= 6.99, 95% CI=3.42-14.28, $p<0.05$).

CONCLUSION: The homozygous long allele, LL genotype exhibited nearly a seven fold risk of developing PCOS compared to other genotypes. Therefore, we conclude that CYP19 gene STR (TTTA) n polymorphism may be functional and plays a critical role in the susceptibility to PCOS.

Keywords: Aromatase, LL genotype, PCOS, STR(TTTA)n polymorphism, South India

P51

Diagnoses of the Prevalent Mutation of XPC Gene Using Sizing in Fragment Analysis

[1]Salima Bensenouci, [1]Lotfi Louhibi, [2]Khadidja Mahmoudi, [3]Cécile G.E.D., [1]Nadhira Saidi-Mehtar
[1]Université des Sciences et de La Technologie d'Oran, [2]Ophthalmology Department, Children's Hospital of Oran Canastel, [3]Université Bordeaux Segalen, INSERM U1035, Algeria

Xeroderma Pigmentosum (XP) is a rare autosomal recessive disorder characterized by an inability to repair DNA damages caused by UV light. XP patients have a highly excessive risk of developing skin cancer. Seven genes which have been described as defective in XP, are involved in the nucleotide excision repair (NER) pathway, defining the complementation groups XP A to G. An additional XP variant form is included and caused by mutations in POLH gene. The XP complementation group C (XPC) is the frequent disease causing gene in North Africa with a unique frame shift mutation (c.1643_1644delTG or p.Val548Ala fsX23) responsible for an important proportion of cases. From a collection of 20 unrelated XP families, we obtained 58 DNA samples (19 index cases, 31 parents and 8 siblings suffering from XP) to validate a routine analysis which includes a specific amplification of a short region surrounding the 2 bp deletion using a fluorescent primer and fragment sizing (GeneScan Size) on a sequencing gel.

Unambiguous determination was obtained in all the samples tested and three possible genotypes were identified (wild-type, heterozygous and homozygous for the deletion) Among the19 index cases, 17 were homoallelic for the 2bp deletion, their siblings were checked for the same mutation and we found that they were also homoallelic for the 2bp deletion. Biallelism was confirmed by the analysis of both parents in most cases. Finally the use of fragment sizing is the simplest method to analysis this 2 bp deletion for the DNA samples coming from countries where the mutation c.1643_1644delTG of XPC gene is the prevalent.

Keywords: Xeroderma pigmentosum, XPC gene, Mutation analysis

POSTERS

P52

Mutation Detection of Breast Cancer Gene (BRCA1) Using Fluorescence Uni-probes and Melting Curve Analyses

[1]Safa Fitouri, [2]Nouri Ermeli, [2]Salah Bensaber, [3]Anton Hermann, [1'2]Abdul Gbaj, [2]Mousa Jaeda, [2]Ibrahim Mrema

[1]National Medical Research Centre, Libya, [2]Faculty of Pharmacy, University of Tripoli, Libya, [3]Department of Cell Biology, University of Salzburg, Austria

BACKGROUND AND PURPOSE:
Recently there is increasing in number of breast cancer cases around the world, this is due to several factors, including genetic defects. BRCA1 breast cancer early onset gene, which called as Breast Cancer Anti-estrogen resistance-1 gene is one of the human caretaker genes that plays crucial role in repairing DNA damage. Mutated BRCA1 gene produces altered protein can lead to breast cancer.

METHODS AND MATERIALS:
Using fluorescence uni-probes to detect wild type and SNPs (single nucleotide polymorphism) of BRCA1 gene [(170-190, Gât'T) and (290-310, Gât'T)] were performed. The probe system was used by attaching of Cy5 dye and TAMRA dye to (10-mer) oligonucleotide, both separately. The target sequences used were synthetic oligonucleotides and genomic DNA extracted from blood samples.

RESULTS:
Once the probe and target hybridized, changes in fluorescence intensity and Tm melting curves are seen. These changes showed significant differences between WT and SNPs allele targets.

CONCLUSION:
The results showed that, this technique may help in high throughput applications in molecular diagnostics and genetic testing.

Keywords: Breast cancer, BRCA1, Fluorescence uni-probes, SNPs

P53

Accurate, Fast, and Comprehensive Ion Semiconductor Based Test for BRCA1 and BRCA2 Mutation Analysis

[1]Hicham Ouchene, [1]Marcel Nelen, [1]Arjen Mensenkamp, [2]José Luis Costa, [2]José Carlos Machado, [1]Marjolijn Ligtenberg

[1]Radboud University Medical Centre, The Netherlands, [2]IPATIMUP Diagnostics, Portugal

BACKGROUND AND PURPOSE:
To develop an accurate and fast test for the detection of BRCA1 and BRCA2 mutations making use of highly multiplex PCR technology combined with ion semiconductor sequencing.

METHODS AND MATERIALS:
The design of 3 multiplex sets of about 55 primer pairs each assures full coverage of all coding exons without allelic drop out due to SNPs at primer sites. To test and optimize the methodology and the appropriate settings in the mutation analysis software, 20 mutations were selected based on the presence of mutations in or within close proximity of homopolymeric regions. Using the optimized workflow an additional 25 cases, representing the most common point mutations in Portugal and the Netherlands, and a set of 10 consecutive clinical samples were tested.

RESULTS:
All SNPs and mutations including missense, nonsense and indel mutations that were identified by Sanger sequencing were detected with our multiplex PCR-based ion semiconductor sequencing approach. False positive calls, at most 5 per sample, were recurrent within a run and thus recognizable.

CONCLUSION:
Mutation screening of BRCA1 and BRCA2 using novel next generation sequencing technology is accurate and fast, as it gives results within days. Both these qualities are essential for optimal use in clinical decision making.

Keywords: BRCA genes, Ion Torrent PGM, Diagnostics, NGS, Massive parallel sequencing

POSTERS

P54

PLEKHG5 Deficiency Leads to an Intermediate Form of Autosomal Recessive Charcot-Marie-Tooth Disease

[1]Hamid Azzedine, [1]Petra Zavadakova, [2]Violaine Plante-Bordeneuve, [3]Maria Vaz Pato, [1]Jennifer Zenker, [1]Luca Bartesaghi, [1]Olivier Poirot, [1]Nathalie Bernard-Marissal, [1]Estelle Arnaud Gouttenoire, 1Giulia Venturini, [4]Edward Makowski, [5]Ludger Schöls, [6,7]Kristl G. Claeys, 8Gérard Said, [4]Jay Baraban, [1]Eric LeGuern, [10]Jan Senderek, [1]Carlo Rivolta, [1]Roman Chrast, [3]Nuno Pinto

[1]Department of Medical Genetics, University of Lausanne, Lausanne, Switzerland, [2]ServicedeNeurologie, CHU Henri Mondor, Créteil, France, [3]CICS-Health Science Research Centre, Universidade da Beira Interior, Portugal, [4]Solomon H. Snyder Department of Neuroscience, John Hopkins University, Baltimore, USA, [5]Department of Neurodegenerative Disease, Hertie-Institute for Clinical Brain Research and Center for Neurology, Tübingen, Germany, [6]Institute of Neuropathology, University Hospital RWTH Aachen, Germany, [7]Department of Neurology, University Hospital RWTH Aachen, Germany, [8]Department of Neurology, Pitié-Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris, University Pierre et Marie Curie, Paris, France, [9]Centre de Recherche de l'Institut du Cerveau et de la Moelle épinière, France, [10]Department of Neurology, Friedrich-Baur-Institute, Ludwig-Maximilian - University, Munich, Germany

Charcot-Marie-Tooth disease (CMT) comprises a clinically and genetically heterogeneous group of peripheral neuropathies characterized by progressive distal muscle weakness and atrophy, foot deformities, and distal sensory loss. Following the analysis of two consanguineous families affected by a medium to late-onset recessive form of intermediate CMT, we identified overlapping regions of homozygosity on chromosome 1p36 with a combined maximum LOD score of 5.4. Molecular investigation of the genes from this region allowed identification of two homozygous mutations in PLEKHG5 that produce premature stop codons and are predicted to result in functional null alleles.
Analysis of Plekhg5 in the mouse revealed that this gene is expressed in neurons and glial cells of the peripheral nervous system, and that knockout mice display reduced nerve conduction velocities that are comparable to those of affected individuals from both families. Interestingly, a homozygous PLEKHG5 missense mutation was previously reported in a recessive form of severe childhood onset lower motor neuron disease (LMND) leading to loss of the ability to walk and need for respiratory assistance. Together, these observations indicate that different mutations in PLEKHG5 lead to clinically diverse outcomes (intermediate CMT or LMND) affecting the function of neurons and glial cells.

Keywords: Charcot-Marie-Tooth disease, PLEKHG5, Homozygosity mapping

P55

Molecular-Genetic Analysis of Tunisian Patients with Retinoblastoma: Benefits Ffor Disease Management

[1]Hajer Ayari Jeridi, [2]Hedi Bouguila, [1]Olfa Baroudi, [1]Imen Mdimegh, [1]Ines Omrane, [1]Khaoula Charradi, [1]Hassan Bouzayene, [3]Dietmar Lohmann, [1]Amel Benammar-Elgaaïed

[1]Laboratoire de Génétique Immunologie et Pathologies Humaines, Faculté des Sciences de Tunis, Université de Tunis El Manar, Campus universitaire, Tunisia, [2]Institut Hédi Rais d'Ophtalmologie de Tunis, Tunisia, [3]Eye Cancer Research Group, Institut für Humangenetik, Universitätsklinikum Essen, Germany

BACKGROUND AND PURPOSE: Retinoblastoma, an aggressive eye cancer of infancy and childhood, represents the prototypic model for inherited cancers. It is associated to loss of function of both alleles at the RB1 tumor suppressor gene on chromosome 13. This simultaneous loss of function happens usually through two mutational or epigenetic events: the first at germ line and the second at somatic level. Identification of these mutations in patients is crucial for genetic counseling and clinical management of relatives at risk and can reduce mortality. Unfortunately, mortality from retinoblastoma is relatively high in countries of low and middle income because of several factors including poor management on the genetic level. While genome technologies could make genetic testing a reality for every family affected by retinoblastoma. METHODS AND MATERIALS: Our work addresses the ongoing debate on the efficiency of RB1 mutation analysis in retinoblastoma patients from countries outside Western Europe and Northern America. We show that highly efficient mutation testing is possible if a rational methodic approach is taken. We present here, a methodological strategy for identification of RB1 gene mutations using direct sequencing and MLPA. RESULTS: Our results include all types of germinal mutations including large deletions, nonsense and splice-mutations. These results were completed by analysis on the functional consequences on the mRNA-level. Furthermore, we were surprised to find an unexpected high rate of non-penetrance among parents carrying deleterious germ line mutation. In previous studies on other ethnic groups non-penetrance among parents is rare by comparison. CONCLUSION: In order to enhance care for families with retinoblastoma, molecular genetic studies of the RB1 gene must be proposed to all patients with familial or sporadic unilateral or bilateral retinoblastoma in our countries. Genetic testing must be performed in the context of a genetics consultation in collaboration with the ophthalmology, pediatric oncology and radiotherapy teams managing the child. decision making.

Keywords: Retinoblastoma, RB1, Mutation analsyis

POSTERS

P56

Does Genetic Testing for Cardiovascular Risk Promote Better Control Over Existed Risk Factors?

[1]Valentina V. Markova, [1,2]Oksana A. Makeeva
[1]*Research Institute of Medical Genetics SB RAMS, Russia,* [2]*Research Institute for Complex Issues of Cardiovascular Diseases SB RAMS, Russia*

PURPOSE: To examine how genetic testing for disease predisposition can influence the control of existing controlled risk factors in relatively healthy young adults.

METHODS AND MATERIALS: Two groups of volunteers were recruited during routine annual medical examination. Group A(N=95), 70% males, mean age 31±6 years, mean body mass index(BMI) 28.3 ±2.9, undergo medical consultation in respect their body mass reduction as the obesity is a risk factor for a number of diseases, including cardiovascular disease(CVD). Group B(N=103), 71% males, mean age 31±6, mean BMI 29.3±3.5 undergo similar recommendation on body mass lowering and were offered to undergo genetic testing in respect to cardiovascular risk assessment. Blood samples were collected and genotyped for several well-know risk alleles. In a month period subjects were invited for genetic consultation and their genetic risk for CVD communicated. In one-year period all subjects were contacted for a follow up visit. Information about their weight and BMI was collected.

RESULTS: Weight difference after one-year period was analyzed and compared for two groups. Both groups reduced their weight. Mean weight difference between groups was not significantly different. When men and women were analyzed separately, it was revealed that in women weight reduction was significantly higher in the subgroup underwent genetic testing (Group B): -4.22±0.80 vs -0.82±0.55 kg, p=0.0006, while in men it did not differ: -1.50±0.53 vs -1.81±0.43 kg. In subjects who were genetically tested this association did not depend on a risk score (high, low or average risk of CVD).

CONCLUSION: Women tend to pay more attention for doctor's recommendation in respect to body mass control when this was followed by genetic risk assessment, but risk estimate itself was not the factor, which had influence. Men generally tend to respond to doctor's recommendation for BMI reduction and genetic testing for the future health problems had no impact.

Keywords: Genetic testing, Predictive diagnostics, Genetic risk assessment, Preventable health condition

P57

Nano-Particle of Genistein Could Effectively Modulate Methylation Status and Expression of Several Genes in ALL

[1]Kianoosh MalekZadeh, [2]Mohsen Nikbakht, Mohammad Shekari
[1]*Molecular Medicine Research Center (MMRC), Hormozgan University for Medical Science (HUMS), Iran,* [2]*Hematology-Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Iran*

BACKGROUND AND PURPOSE: Acute Lymphoblastic Leukemia (ALL) is a malignant neoplasm of hematopoietic stem cells. Antimutagens and anticarcinogens can intervene at multiple points of the carcinogenic process and have been reported to alter the epigenetic and subsequent gene expression status cancer relevant genes. In our previous studies deduced that one of mechanisms that genistein can modulate gene methylation, e.g, genistein alters DNA methylation patterns in anonymous novel CpG islands in mouse prostate DNA.

METHODS AND MATERIALS: Two ALL cell-lines, blastocytes of aspirated-bone marrow of ALL childhood patients as well as stem cells as non-cancer immortal cells, cultured and treated with a low, nontoxic concentration of genistein (3.0 lM, resupplemented every 48hr for 1week). Two other groups as same to above-defined cells - one was treated with same above-dosage of synthesized nano-particles of genistein and another was untreated- considered in this investigation. The status of methylation as well as expression of TMS-I as a key-gene in apoptosis - has been studied by MS-PCR, MS-Seq, RT-PCR and ELISA. Apoptosis has been measured by flowcytometry.

RESULTS: It has been observed that genistein has the capacity to modulate DNA methylation for several genes relevant to ALL in cancer cells, as well as in immortalized but noncancer cells. We found that nontoxic dosage partially demethylates the promoter of the tumor suppressor gene in cells. RT-PCR studies confirm a lack of GSTP1& expression in untreated cells, with restoration of GSTP1 expression after genistein treatment.

CONCLUSION: These data show for the first time that genistein at very low concentrations particularly in nano-forms has direct DNA demethylating activity of pro-apoptotic genes, promote their expression and, can be consider a candidate as chemopreventive agent against of ALL.

Keywords: Acute lymphoblastic leukemia, Genistein, Epigenetic status, Nanoparticles

POSTERS

P58

Partial Silencing of MTS2 and MTS1 in Effect of Aberrant Promoter Hypermethylation in Childhood ALL: Candidate Biomarkers

[1]Kianoosh MalekZadeh, [2]Mohsen Nikbakht
[1]*Molecular Medicine Research Center (MMRC), Hormozgan University for Medical Science (HUMS), Iran,* [2]*Hematology-Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Iran*

BACKGROUND AND PURPOSE:
Acute Lymphoblastic Leukemia (ALL) is a malignant neoplasm of hematopoietic stem cells. The tumor suppressor genes MTS1 and MTS2 are cycline dependent kinas inhibitors inactivated in some human neoplasms via several mechanisms such as hypermethylation.

METHODS AND MATERIALS:
We have investigated the methylation status of MTS1 and MTS2 in its effect on transcriptional down-regulation in 125 bone marrow aspirate (7 cases T-cell and 118 cases B-cell phenotypes) from childhood ALL patient and 100 healthy control in north Indian population by using MSP-PCR ,bisulfite sequencing, SQRT-PCR and QRT-PCR.

RESULTS:
There were significant differences in pattern of hypermethylation between patients and healthy controls of MTS2 (p=0.000) and MTS1 (p=0.001) and also when both genes methylated. Patients with hypermethylated of both genes showed an increasing risk for 2.33 fold (95%CI=2.33(1.97-2.77), p=0.03). Significant association of MTS1 hypermethylation was observed only among the male patients (p=0.004) in contrast to hypermethylation of MTS2.

CONCLUSION:
In conclusion our data also indicate the impact of hypermethylation mediated inactivation of these genes which is associated with risk of childhood ALL. This abnormality occurs in leukemogenesis and it may use as a biomarker in population of study and frequently reported to be associated with poor prognosis in acute lymphoblastic leukemia (ALL).

Keywords: Acute lymphoblastic leukemia, MST1, MST2, hypermethylation

P59

Assesment of Abortion Causes in Women Referred to Bandar Abbas Welfare Organization

[1]Pooneh Nikuei, [1]Tasnim Eghbal Eftekhaari, [2]Minoo Rajaei, [1]Saeedeh Soleimanian, 3Fouzieh Hajizadeh
[1]*Molecular Medicine Research Center, and* [2]*Fertility and Infertility Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran,* [3]*Bandar Abbas Welfare Organization, Iran*

BACKGROUND AND PURPOSE: Repeated pregnancy loss (RPL) is critical problem affecting about 0.5-2% of women.Assumed aetiological factors are chromosomal aberrations, uterine abnormalities, infectious and endocrine dysfunctions. These factors are present in about 50% of all women with RPL, but in the majority of cases the cause is unknown or idiopathic

METHODS AND MATERIALS: A two year prospective study was carried out on women with 3 or more consecutive abortions from 2009-2011. History of abortions and live births were recorded. Positive histories of abortion in paternal and maternal grandmothers were also noted. Positive history of abortion in siblings were also recorded. The diagnostic procedure included, uterine sonography,TORCH infection study ,assessment of hormonal status, andIgM/IgG anticardiolipin, antiphospholipid tests and paternal and maternal karyotype . Data were analysed by SPSS 20 with descriptive analytics, t test and p value <0.0001 was considered significant.

RESULTS: A total of 40 couples entered our study. Mean age was 40 years in mothers and was 36 in fathers (p<0.0001). Four maternal siblings had history of abortion while only one paternal sibling suffered from abortion (p>0.0001). Only 25% of couples had a live birth. 12.5% of maternal grandmothers had abortion while paternal grandmothers had no abortion.10% of maternal siblings suffered from abortion while only 2.5% of paternal siblings had abortion. 45% of couples were first cousins and 7.5% were second cousins while 27.5% were not cousins and the rest were double cousins. 97.5% of women had normal karyotype, and 2.5% had abnormal karyotype. 95% of men had normal karyotype and about 5% had abnormal karyotype.

CONCLUSION: It seems that maternal age and a positive history of abortion in maternal grandmothers has more effect on abortions. The molecular genetic background for spontaneous abortion should be considered in couples suffering from abortion.

Keywords: Repeated pregnancy loss, Abortion, Maternal, Genetic

POSTERS

P61

Identification and Characterization of a Novel Centromere Protein

[1]Mohammed Alhousani, [2]Damien Hudson, [2]Paul Kalitsis, [2]K.H. Andy Choo
[1]*Ministry of Health, UAE,* [2]*Murdoch Childrens Research Institute - Royal Children's Hospital - Melbourne, Australia*

Problems of chromosome missegregation can result in aneuploid cells with gained or lost chromosomes. In humans, aneuploidy is often associated with cancer due to the loss of tumour-suppressor genes or gain of oncogenes. As the centromere is a key structure that underpins chromosome stability and faithful segregation, a sound knowledge on the organisational and functional properties of this structure would lead to a better understanding and management of the associated conditions. In this study we pre-screened patient sera for the presence of additional non CENP-A, B and C bands using immunoblotting, which were subsequently used to probe a HeLa cDNA phage expression library. Two novel centromere autoantigens have been identified, one included the recently characterized SCAN-zinc finger protein, ZNF397, and the other, FAM44A, a large protein, approximately 330 kD, containing domains with hallmarks of chromatin regulation. Using RNAi knockdown in human cells we show that this protein plays an important role in the correct segregation of chromosomes during mitosis. Mitotic defects include, poor chromosome alignment during metaphase, lagging anaphases and chromatin bridges. These results suggest that FAM44A may have a role in the regulation of other chromosome segregation protein/s.

Keywords: Repeated pregnancy loss, Abortion, Maternal, Genetic

P62

Over Expression of the Glycoprotein P and Reversion of the Phenotype MDR

Seddiki Sonia, El Kebir Fatima Zohra
University of Oran, Algeria

The 'Multidrug resistance' (MDR) is an important obstacle to the success of the chemotherapy of many human cancers. The cellular multi chemoresistance is due to the over expression of the glycoprotein P, which confers the phenotype MDR to the cells. The aim of these researches if the localization of the fixation site of the steroid chemosensitizing in order to prepare efficacious modulating molecules of the MDR 'phenotype'. The first object has consisted in increasing the expression level of the Pgp in the R7 cells born of (descended from) a patient attacked by an erthroleuchaemis expressing concentrations of doxorubicin. The characterization of the Pgp presence has been realized by affinity photomarking with azidopine tritiée. An augmentation of the Pgp concentration is observed in the membranous fractions of the R7 cells treated by the doxorubicin. The second aim has consisted in preparing different radio active chemomarkers by peptidic coupling of bromo acetic [14C] the terminal amine of the progesterone derivatives substituted on the carbon 11 but the introduction of different hydrophobic chains, and in testing these chemomarkers with the membranous fractions of the R7 cells treated with the doxorubicin.

Key words: Glycoprotein P, Progesterone, Chemomarkers, Doxorubicin, Azidopine tritiée.

P63

Molecular Classification of Myeloproliferative Neoplasms (MPNS) Patients in the State Of Qatar According to World Health Organization (WHO) 2008 Criteria

[1,2]Nader Al-Dewik, [3]Bruno Cassinat, [3]Jean-Jacques Kiladjian, [1]Hanadi El Ayoubi, [1]Mohammed Yassin
[1]*NCCCR, Hamad Medical Corporation, Qatar,* [2]*QMGC, Hamad Medical Corporation, Qatar,* [3]*Hôpital Saint-Louis, Paris, France*

BACKGROUND AND PURPOSE: MPNs are clonal haemopoietic disorders that are characterized by excessive proliferation of one or more of blood lineages. MPNs include PV, ET and PMF which are associated by presence of JAK2 V617F mutation in about 90% of PV and 50% of ET and PMF. The molecular workup of JAK2 and related gene mutations were included in WHO 2008 as one major criterion for the diagnosis of Ph- MPNs. Genetic characterization of Qatar MPNs patients according to WHO criteria using molecular studies.MATERIALS AND METHODS: DNA was extracted from suspected MPN cases. RQ-PCR was used to evaluate the JAK2 and sequencing RESULTS: 300 patients were classified into PV, ET and PM. Out of 119 PV, 97 % of cases were positive for the JAK2 V617F mutation and 3% of cases were negative for other mutations. Out of 165 ET, 48% of cases were positive for JAK2 V617F, one had MPL S505N mutation and 50% of cases were negative for other mutations. Out of 15 PMF, 33% of cases were positive for JAK2 V617F and one unclassified case was characterized by DVT had JAK2 exon 13 mutation (R564L). CONCLUSION: This study used novel molecular approaches to confirm the diagnosis of MPNs cases in Qatar. The observed patterns of mutations were found to be similar to the international data. In our cohorts of patients, JAK2 V617F mutation was found to be present in almost every patient with PV, nearly 50% of ET patients and less than 50% of PMF patients due to the low number of PMF patients in this study. Our original finding is the presence of MPL S505N mutation in one ET patient which was reported both as an inherited or acquired mutation in very rare cases of ET and R564L mutation in one unclassified MPNs case.

Keywords: MPNs, Jak2V617F mutation, JAK2 exon 12 mutations, MPL mutation, RQ-PCR, HRM

POSTERS

P64

Mutational Spectrum of KRAS Gene in Chronic Myeloid Leukemia, Colorectal and Bladder Cancers and its Correlation with Clinical Parameters

[1]Slah Ouerhani, [2]Karim Bougatef, [1]Ismail Soltani, [1]Salem Abbes, [1]Samia Menif
[1]*Pasteur Institute of Tunis, Tunisia,* [2]*Faculty of Sciences of Tunis, Tunisia*

BACKGROUND AND PURPOSE:
Mutations in the KRAS gene have been shown to play a key role in the pathogenesis of a variety of human tumours. However the mutational spectrum of KRAS gene differs by organ site. In this study, we have analysed the mutational spectrum of KRAS exon 1 in bladder tumours, colorectal cancers (CRC) and chronic myeloid leukemia (CML).

METHODS AND MATERIALS:
A total of 366 patients were included in the present study (234 bladder tumours, 48 CRC and 84 CML). Mutations in exon 1 of KRAS gene were screened by PCR and direct sequencing.

RESULTS:
The frequency of KRAS mutations in bladder cancer was estimated at 4.27%. All of them were found in codon 12. 90% of KRAS mutations were found in advanced bladder tumours. However the correlation between KRAS mutations and tumour stage and grade does not report a statistical significant association. The frequency of KRAS mutations in CRC was estimated at 35.41%. The most frequent mutations were G12C, G12D and G13D. These mutation were significantly correlated with histologic differentiation of CRC (p=0.024). Although the high frequency of KRAS in CRC in comparison to bladder cancer (p=0.00), these two cancers appear to have the same mutational spectrum (p>0.05). However we have not found any mutation in CML groups. This result suggests that KRAS gene could not be implicated in the leukemogenesis of CML.

CONCLUSION:
In conclusion we retain that KRAS could not be implicated in the leukemogenis of CML. Moreover CRC and bladder cancer appear to have the same mutational spectrum (p>0.05). This mutational spectrum can be linked to tobacco smoking.

Keywords: Bladder tumours, Colorectal cancers, Chronic myeloid leukemia, KRAS gene, Mutational spectrum

P65

Novel Mutations in ADAMTSL2 Gene Underlying Geleophysic Dysplasia in Families from UAE

[1]Salma Ben-Salem, [1]Jozef Hertecant, [2]Aisha M. Al-Shamsi, [1]Bassam R. Ali, [1]Lihadh Al-Gazali
[1]*CMHS, UAE University, United Arab Emirates,* [2]*Tawam Hospital, United Arab Emirates*

Geleophysic dysplasia (GD) is an autosomal recessive disorder characterized by short stature, brachydactyly, stiff joints, thick skin and cardiac valvular abnormalities that are often responsible for early death. Mutations in ADAMTSL2 and FBN1 genes have been shown to cause GD due to the dysregulation of TGF-beta signaling pathways. Small numbers of mutations in ADAMTSL2 have been reported so far in patients with GD type 1 (GD1).

METHODS:
In this study, we clinically evaluated two children from two consanguineous Arab families living in the United Arab Emirates with GD1. In addition we have sequenced all the coding exons of ADAMTSL2 gene using Sanger sequencing.

RESULTS:
The two patients exhibited most of the typical features of this rare bone dysplasia. Molecular analysis of the ADAMTSL2 gene revealed two novel homozygous missense mutations (c.938T>C, p.M313T and c.499G>A, p.D167N). The mutations segregated well in the studied families with the parents being heterozygous. In addition, bioinformatics analyses showed that these mutations are affecting conserved amino acids residues and thus strongly support their pathogenicity.

CONCLUSION:
We describe the clinical phenotypes of two patients with GD type 1 (GD1) that are caused by two novel homozygous missense mutations in the ADAMTSL2 gene.

Keywords: Short stature, ADAMTSL2, Geleophysic Dysplasia, mutations, TGF-β signaling pathways

POSTERS

P66

The rs198389 Single-Nucleotide Polymorphism in the Brain Natriuretic Peptide Gene may be Modestly Associated with Type 2 Diabetes in the Algerian ISOR Study, Search for Functional Variants

[1]Djabaria Naïma Meroufel, [1,2]Hadjira Ouhaïbi-Djellouli, [1,2]Sounnia Médiène Benchekor, [3]Xavier Hermant, [3]Benjamin Grenier-Boley, [1]Sarah Aïcha Lardjam Hetraf, [1]Houssam Boulenouar, [1,4]Imane Hamani Medjaoui, [1]Nadhira Saïdi Mehtar, [3]Philippe Amouyel, [1,5,6] Leïla Houti, Louisa Goumidi, [3]Aline Meirhaeghe

[1]Laboratoire de Génétique Moléculaire et Cellulaire, Université des Sciences et, Algeria, [2]Département de Biotechnologie, Faculté des Sciences de la Nature et de la Vie, Université d'Oran, Oran, Algeria, [3]Institut Pasteur de Lille, Université Lille Nord de France, Lille, France, [4]Caisse Nationale des Assurances Sociales des travailleurs salariés, Clinique Spécialisée en Orthopédie et Rééducation des Victimes des Accidents de Travail, Oran, Algeria, [5]Faculté de Médecine de Sidi Bel Abbès, Sidi Bel Abbès, Algeria, [6]Laboratoire des Systèmes d'Information en Santé, Université d'Oran, Algeria

BACKGROUND AND PURPOSE:
The rs198389 is a single-nucleotide polymorphism (SNP) located into the promoter of the natriuretic peptide precursor B (NPPB) gene. A previous study showed association between this SNP and the risk of type 2 diabetes mellitus (T2DM). However, considering the relatively large discrepancy in frequency and impact of this variant between ethnic groups and populations, our purpose was to evaluate the association between this SNP and the risk of T2DM and quantitative metabolic traits in an Algerian population sample, the ISOR study. We also conducted in vitro functional studies for this SNP and 7 other SNPs in strong linkage disequilibrium with rs198389.
METHODS AND MATERIALS:
The association study was performed in a T2DM case-control study (with 78 cases and 645 controls) nested into the ISOR population-based study. Statistical analyses were performed with SAS software. To determine the potential functionality of the rs198389 SNP and seven other SNPs in strong linkage disequilibrium with rs198389, we performed luciferase reporter-gene assays in HepG2 and MIN6 cell lines. RESULTS: The minor C allele of the NPPB rs198389 SNP protected against T2DM (odds ratio [95% confidence interval]=0.72 [0.50-1.03], one-sided p=0.04) and we showed that it was also associated with lower fasting plasma insulin levels (p=0.05) and a lower homeostatic model assessment insulin resistance index (p=0.05). Three polymorphisms in strong LD with the NPPB rs198389 SNP (rs632739, rs2981953 and rs35458601) presented significant allele differences in luciferase activity.
CONCLUSION:
As observed in European populations, the NPPB rs198389 SNP appears to modulate the T2DM risk in an Algerian population - perhaps via its effect on insulin levels and insulin sensitivity. Functional polymorphsms affecting the transcriptional regulation of NPPB may contribute to explain these associations.

Keywords: Type 2 diabetes, Insulin, BNP gene, Polymorphisms, Ouest Algerien population

P67

Genetic Variation in the TCF7L2 Gene qnd Diet Predict the Development of Type 2 Diabetes in an Algerian Population; The ISOR Study

[1,2]Hadjira Ouhaibi-Djellouli, [1,2]Sounnia Mediene Benchekor, [1]Sarah Aicha Lardjam Hetraf, [3]Imane Hamani Medjaoui, [4]Aline Meirhaeghe

[1]Laboratoire de Génétique Moléculaire et Cellulaire, Université des Sciences et de Technologie d'Oran Mohamed Boudiaf, Oran, Algeria, [2]Département de Biotechnologie, Faculté des Ssciences de la Nature et de la Vie, Université d'Oran, Oran, Algeria, [3]Caisse Nationale des Assurances Sociales des travailleurs salariés, Clinique Spécialisée en Orthopédie et Rééducation des Victimes des Accidents de Travail, Oran, Algeria, [4]Institut Pasteur de Lille, Université Lille Nord de France, Lill, France

INTRODUCTION: Type 2 diabetes (T2D) is characterized by hyperglycemia that can occur through mechanisms such as impaired insulin secretion, insulin resistance in peripheral tissues and increased glucose output by liver [American Diabetes Association., 2004]. T2D with the exception of rare monogenic forms of the disease [American Diabetes Association., 2004], arises from interactions between the genetic background of the patient and the environment. A SNP (rs7903146) within intron 3 of the transcription factor 7-like 2 (TCF7L2) gene is associated with a higher of risk T2DM in population of European descent (Grant & al., 2006). AIM: This study investigated the relationships between the TCF7L2 rs7903146 polymorphism and T2D risk and glucose-related phenotypes, and evaluated potential interactions with diet intake in an Algerian population sample. SUBJECTS AND METHODS: The association study was performed in a T2D case-control study consisting of 76 cases and 644 controls nested into the ISOR population-based study. Food intake was assessed with

POSTERS

a weekly food frequency questionnaire. RESULTS: The rs7903146 T risk allele was associated with a significant higher risk of T2D (OR [95%CI]=1.55 [1.09-2.20], p=0.01), independently of BMI. Significant interactions were observed between desert or milk intakes and the rs7603146 SNP on the risk of T2D (p=0.05 and p=0.01, respectively). The risk of T2D was greater in T allele carriers eating a high quantity of desert and milk (OR≥2.5). Moreover, in the group of high consumers of desert, the T allele was associated with higher fasting plasma glucose levels (4.78±0.51 in CC vs 4.72±0.48 in CT vs 4.89±0.46 mmol/L in TT subjects, p=0.03). CONCLUSION: We confirmed that the risk allele of the TCF7L2 rs7903146 SNP was associated with a higher T2D risk in an Algerian population sample. This association was exacerbated by a high desert intake, suggesting that deleterious gene-diet interactions increase T2D risk..

Keywords: TCF7L2, Type 2 diabetes, Gene-diet interaction, Polymorphism, ISOR study

P68

Oocyte Competency Prediction with the use of Mitochondrial Gene Expression Profiling

Senan Baqir, Noura Al-Zeheimi, Khalsa Al Husseini
Department of Biology, College of Sciences, Sultan Qaboos University, Oman

Oocyte selection with superior quality and relatively high developmental competence that support in vitro embryo production is a challenging task. The current morphological assessment methods used to select the oocyte for ART applications are neither accurate nor conclusive. Thus, this study was conducted to evaluate camel oocyte competency using molecular markers in cumulus cells (CC) responsible for energy metabolism as predictive measure for oocyte maturation. Oocytes were recovered from camel ovaries (n= 4) collected from local slaughterhouse in Sinaw-Oman. Following oocyte retrieval by aspiration and slicing, BCB staining was carried out. Oocytes were denuded from cumulus cells (CC) by hyaluronidase treatment. Three groups of CCs were obtained; control, BCB- and BCB+. The cells were centrifuged at 2000 rpm for 2 min and the resulting pellets were subjected to RNA extraction. Total RNA was extracted from CCs using the RNeasy® Mini Kit (Qiagen, US) according to the manufacturer's recommendations. The RNA was quantified using a Nanodrop. Reverse transcription was performed to obtain cDNA using Omniscript® Revers Trascription kit (Qiagen). qPCR was achieved using a conventional PCR kit (Taq PCR Core Kit- Qiagen), the resulting fragments were quantified using Genetool software (version 4.03.00). Marker genes used in this study were; ND5, ATP6, COX3, COX2 and CYTB. A total of 55 oocyte were recovered from 4 ovaries, 42 were BCB+ and 13 were BCB-. Our data shows that all mitochondrial genes studied in CCs of BCB+ were over-expressed compared to BCB- CC. While COX3 and CYTB genes displayed similar expression levels in CCs of BCB+ (1.5X), ATP6, ND5 and COX2 illustrate a 5X over-expression in CCs of BCB-. These results indicate that BCB+ oocytes were characterized by high mitochondrial activity thereby exhibiting higher levels of oocyte competency. Therefore, mitochondrial gene expression evaluation of CCs would provide an accurate mean of high quality oocyte selection.

Keywords: Oocyte, Brilliant cresyl blue, Cumulus cells, Gene expression, Mitochondrial marker

P69

Prevalence of Intron 1 and 22 Inversions of Factor 8 Gene in West Algeria

[1]Abdi Meriem, [1]Fodil Mostefa, [1]Boudjema Abdallah, [2]Touhami Hadj, [1]Zemani Fodil Faouzia
[1]Laboratoire de Génétique Moléculaire et Cellulaire, Université des Sciences et Technologie Oran -Mohamed Boudiaf-, Algeria, [2]Service d'hématologie, Centre Hospitalo-universitaire d'Oran, Algeria

Hemophilia A is an X-linked recessive bleeding disorder caused by mutations widespread in the factor 8 gene (F8) encoding coagulation factor VIII (FVIII). Molecular genetic testing of HA can lead to accurate diagnosis and contribute to patient care decisions. However, this testing is still complicated by the large size of F8 gene and the heterogeneity of mutations. The disease is frequently caused by intron 22 and intron 1 inversion which occur in respectively 50% and 2% to 5% of cases with severe form of the disease. Our objective was to determine, for the first time in Algeria, the prevalence of intron 1 and 22 inversions in a group of 24 severe hemophilia A patients belonging to 19 unrelated families from west Algeria. We initially detected the presence of the intron 22 inversion by Long Rang Polymerase Chain Reaction (LR PCR). Then, negative patients for this inversion were analyzed for the intron 1 inversion by Multiplex PCR. Our results revealed that the frequencies of intron 1 and 22 inversions in our Algerian patients were 5.25% and 57.8% respectively. These frequencies are higher in our patients than data from other Arab countries. This result shows that our patients have a specific genetic profile which could be confirmed by a larger number of patients studied. Further molecular analysis is required in order to determine genetic alterations in patient without these two inversions.

Keywords: Hemophilia A, F8, Intron 1 inversion, Intron 22 inversion, PCR Long Range, PCR Multiplex

POSTERS

P70

Cellular Mechanisms Underlying Mutations in the Bone Morphogenetic Protein Type II (BMPR2) receptor causing Familial Pulmonary Arterial Hypertension (FPAH)

[1]Anne John, [1]Rachelle El-Helou, [1]Nadia A Akawi, [2]Lihadh Al-Gazali, [1]Bassam Ali

[1]Pathology Dept, and [2]Department of Pediatrics, College of Medicine & Heath Sciences, UAEU, UAE

Background: FPAH is a relatively rare but could be fatal disorder with reduced penetrance. It is characterized by elevated arterial pressure due to lesions in the proliferating endothelial cells of the arteries which leads to heart failure and death. FPAH is inherited as an autosomal dominant trait and is caused by heterozygous mutations in the BMPR2 gene, which encodes for the bone morphogenic protein type II receptor (BMPR2). The latter, belongs to the TGF beta/BMP superfamily of receptors (BMPR2) that initiates signal transduction cascade via SMAD signaling pathway. The 1038 amino acid BMPR2 peptide consists of ligand binding, a kinase domain and a cytoplasmic tail.

Methodology: To investigate the cellular and functional consequence of BMPR2 mutations, we generated 18 C-terminal Flag-tagged BMPR2 disease-causing mutants using site directed mutagenesis. The generated plasmids were transiently co-transfected along with GFP-Hras into HeLa cells. The wild-type GFP-hRAS has been used as marker for plasma membrane (PM). The subcellular localizations of the mutant proteins have been investigated using immunoifluorescence confocal microscopy.

Result: Amongst the 18 mutants, ten were retained in the Endoplasmic Reticulum (ER) as evidenced by their co-localization with the ER marker calnexin suggesting the involvement of the ER-Associate protein Degradation (ERAD) in their pathology. Of note, subcellular localizations of all generated mutants that affect cysteine residue are retained in ER. All studied mutants in the ligand binding domain affecting highly conserved residues were also ER retained. Mutations within the kinase domain show both ER and PM distributions, while variations within the cytoplasmic tail localized exclusively to the PM.

Conclusion: The ER-Associate protein Degradation (ERAD) is involved in the mechanism of several morphogenic protein type II receptor missense mutants causing Familial Pulmonary Arterial Hypertension.

Keywords: BMPR2 (Bone Morphogenetic Protein Receptor Type 2), FPAH (Familial pulmonary arterial Hypertension), Mutagenesis, ERAD(Endoplasmic Reticulum Associated Degradation), Autosomal dominant

P71

TP53 Codon 72 Polymorphism as a Biomarker of Basal Cell Carcinoma, but not of Colorectal Cancer: An Algerian Population Study

[1]Rym Khadidja Abderrahmane, [1]Lotfi Louhibi, [2]Khedidja Benseddik, 1Amina Boubekeur, [1]Fatima Mogthit

[1]University of Science and Technology of Oran, Algeria, [2]CRCM-IPC, France

TP53 gene is named 'guardian of the genome', as it plays major roles in genomic stability. The polymorphic variants at codon 72 of TP53 (Arg72Pro) is associated to BCC and CRC diseases. In the present work, we undertook a case/control study to analyze TP53 Arg72Pro polymorphism for BCC and CRC in northwest Algerian population. TP53 Arg72Pro polymorphism was investigated by PCR/RFLP then confirmed by DNA sequencing of 121 controls versus 116 CRC cases and 50 BCC cases. The analysis of Arg72Pro polymorphism distribution in the control population showed Arg allele predominance (90.90%) compared to Pro allele (9.09%).

Unexpectedly no significant association was found between this potential marker and CRC (CRC group: Pro= 9.91% vs Ctrl: Pro=9.09 %, p= 0.7). BCC group showed a significant increase of frequency of Pro variant, with a strong association between this variant and BCC (BCC group : Pro=54%, vs Control: Pro=9.09 %, $p<10-6$ - OR 11.48 (6.40-20.60). This study allow us to characterize BCC subgroups regarding age, tumor location, and relapse, with no correlation between any of these criteria and one of the two variants. Finally, as expected, sun-exposure was confirmed as a risk factor for BCC.

Keywords: Basal cell carcinoma, TP53 variants, Coloractal cancer

POSTERS

P72

Cytogenetic and Molecular Detection of Y-Chromosome Material in Turner Syndrome Egyptian Patients

Ghada Elhady, Mervat Moustafa Hashishe, Sahar Ahmed Soliman Elshafei, Amal Kotb Behery, Ebtesam Mohamed AbdAllah Nassr
Medical Research Institute, Alexandria University, Egypt

BACKGROUND AND PURPOSE:
Turner syndrome is the most common chromosomal abnormality in females, affecting 1:2,500 live female birth.About 50% of the patients have a 45, X karyotype, while the remainder have structurally abnormal sex chromosomes or mosaicism including 45,X/46,XY. Cytogenetic technique detects Y chromosome mosaicism in about 5.5% of TS. PCR revealed hidden Y-chromosome material not detected by cytogenetic examination. Those with Y chromosomal material are at increased risk for developing gonadoblastoma with considerable malignant potential. The aim of this study was to detect the presence of Y chromosome material in TS patients to allow early and accurate detection of patients at high risk of gonadal tumor development and consequently their proper management.

METHODS AND MATERIALS:
This study was carried out on twenty patients with TS, diagnosed by karyotype. All cases were subjected to careful history taking, complete clinical examination, abdominal and pelvic songraphy, hormonal assays, cytogenetic examination, molecular studies for identification of Y-chromosome material by PCR amplification using DYZ3 and SRY specific primers. Results: Cytogenetic examination of all cases revealed 45% of patients have classical 45, X karyotype, 10% of patients have structurally abnormal X and 45% of patients have mosaic karyotype. PCR screening for Y-chromosome material using DYZ3 and SRY specific primers was done in all cases and revealed Y chromosome material in 4 patients. Three of these patients had 45, X karyotype that did not suggest the presence of Y-chromosome material, whereas the remaining patient had a marker chromosome (45, X/ 45, X+mar) which suggest the presence of Y chromosome material.

CONCLUSION:
The introduction of PCR technique has revealed the existence of hidden Y-chromosome material not detected by cytogenetic examination.

Keywords: Cytogenetic, Molecular, PCR, Y chromosome, Turner

P73

Genetic Polymorphisms and Cardiovascular Risk Factors of Alzheimer's Disease in an Algerian Population

[1]Ouldjaoui Ahmed, [2]Abadi Noureddine, [2]Sifi Karima, [3]Sifi Yamina, [3]Benlatreche Cherifa, [2]Hamri Abdelmadjid
[1]Laboratory of Biology and Molecular Genetics, Medicine Faculty, Constantine, Algeria, [2]Laboratory of Biology and Molecular Genetics, Medicine faculty, Biochemistry Service, Ibn Badis Hospital, Constantine, Algeria, [3]Laboratory of Biology and Molecular Genetics, Medicine Faculty, Neurology Service, Ibn Badis Hospital, Constantine, Algeria

BACKGROUND AND PURPOSE: Alzheimer's disease is a complex neurodegenerative disorder of unknown aetiology, and an important number of cases are sporadic. It is very important to understand the role of genetic and cardiovascular risk factors in AD in order to develop therapeutic strategies. We review some studies of these risk factors in an Algerian population to identify a few directives for future studies.

METHODS AND MATERIALS: Genotyping was carried out in 63 patients with clinically defined Alzheimer's disease (NINCDS-ADRDA criteria) and 124 non-demented controls in a cross-sectional study of people aged 85 years or over.

RESULTS: ApoE allele frequencies of AD cases and controls were 5.5% vs. 7.2% for E2, 63.5% vs. 83.9% for E3 and 31% vs. 8.9% for E4. AD patients compared with controls subjects had significantly higher mean total Cholesterol (191 ± 37mg/dl vs. 175 ± 37mg/dl, $p<0.05$), LDL-C (122 ± 29 mg/dl vs. 110 ± 32 mg/dl, $p<0.05$) levels in men and lower HDL cholesterol with mean values of (37 ± 08 mg/dl vs. 44 ± 07 mg/dl, $p<0.05$) in men and (42 ± 08 mg/dl vs. 47 ± 08 mg/dl, $p<0.05$) in women respectively. Carriers of allele E4 and E3/E4 subjects compared with E3/E3 are associated with an increased incidence of AD with odds ratio of 5.01[95%CI, 2.36 to 10.71] $p<0.001$ and 3.86 [95%CI, 1.72 to 8.72] $p<0.001$, respectively.

CONCLUSION: AD patients with APOE-E4 allele have a distinct plasma lipid profile and carrier of this allele with high (TC), LDL-C and low levels of HDL-C may be more susceptible to AD. We did not find significant associations between the polymorphisms of MTHFR C677T and AD. A statistically significant relation was observed between AD risk and high blood pressure, depression, head trauma, diabetes, or smoking.

Keywords: Alzheimer's disease, Genetic risk factor, Cardiovascular risk factors, Cholesterol, Age, Algerian population.

POSTERS

P74

Apolipoprotein E Gene Polymorphism and Lipids Profile in General Population and in Patients with Cardiovascular Diseases in Algeria

Khodja Djamel, Boumendjel Sabrina, Sifi Karima, Abadi Nordine, Benlatrech Cherifa
University of Constantine, Algeria

BACKGROUND AND PURPOSE: The present investigation is aimed at examining the Apolipoprotein E (APOE) genotypic influence on cardiovascular disease risk in east Algerian

MATERIALS AND METHODS: Lipids profiles, as well as genetic of apolipoprotein E (apoE) were determined in control (509), cerebrovascular disease CVD (205), myocardial infarctus (MI) (218) and in 30 peripheral artery disease (PAD) subjects. Polymorphisms of the ApoE gene was amplified by polymerase chain reaction (PCR) using the oligonucleotide primers. The dosage of cholesterol and triglycerides have been done by an auto analyzer, HDL-Cholesterol was measured after precipitation of apolipoprotein B containing lipoproteins by the phosphotungstate associated with magnesium chloride and the calculation of LDL-cholesterol was performed by using Friedewald formula

RESULTS: The apoE allele frequencies in our population were epsilon 3 (84.3%), epsilon 4 (10.7%) and epsilon 2 (5%), the genotype epsilon 3/epsilon 3 are the most frequent (70.9%) followed by epsilon3/epsilon4 (18.8%).The patients with CVD compared with control subjects have statistically significantly higher mean cholesterol (1.96+0.47 mg/dl vs. 1.82 +0.40 mg/dl p< 0.05) and LDL-C (1.28 ± 0.43mg/dl), vs. (1.09 ± 0.27 mg/dl , p< 0.01), The patients with MI have statistically significantly higher mean triglycerides (155 ± 75 mg/dl vs. 117 ± 7 mg/dl, p< 0.001) and lower HDL cholesterol (41±25mg/dl), vs. (45±15 mg/dl), p< 0.05. Compared with epsilon3/epsilon3 the carriers of allele epsilon4 and epsilon3/epsilon4 are associated with an increased incidence of ICVD with odds ratio 1.56 p< 0.05 and 1.72 p< 0.05 respectively, And increased incidence of (MI) with odds ratio of 1.77 p<0.01 and 1.95 p<0.01, respectively.

CONCLUSION: These results put in evidence an influence of genotypes of the apoE on lipids profile indicating the protective effect of the allele epsilon2, the deleterious effect of the allele epsilon4 and its contribution as factor of risk in cardiovascular disease. Keywords: ApoE, polymorphism, cardiovascular diseases .

Keywords: ApoE, Polymorphism, Cardiovascular diseases, Cerebrovascular disease, Lipoprotein

P75

Comparative Study of Three APOE Gene Polymorphisms on Lipid Profile on Population from Algeria and France

[1]Houssam Boulenouar, [1,2]Sounnia Mediene Benchekor, [1]Djabaria Naïma FEL, Naïma Meroufel, [3]Aline Meirhaeghe, [3]Louisa Goumidi, [3]Dominique Cottel, [1]Sarah Aicha Lardjam Hetraf, [1,2]Hadjira Ouhaibi Djellouli, [3]Xavier Hermant, [3]Benjamin Grenier-Boley, [4]Imane Hamani Medjaoui, Jean Dallongeville, [1]Nadhira, Saidi Mehtar, [3]Philippe Amouyel, [1,5,6]Leila Houti
[1]*Laboratoire de Génétique Moléculaire et Cellulaire, Université des Sciences et de Technologie d'Oran Mohamed Boudiaf, Oran, Algeria,* [2]*Département de Biotechnologie, Faculté des Sciences de la Nature et de la Vie, Université d'Oran, Oran, Algeria,* [3]*Institut Pasteur de Lille, Université Lille Nord de France, Lille, France,* [4]*Caisse Nationale des Assurances Sociales des travailleurs salariés, Clinique Spécialisée en Orthopédie et Rééducation des Victimes des Accidents de Travail, Oran, Algeria,* [5]*Faculté de Médecine de Sidi Bel Abbès, Sidi Bel Abbès, Algeria,* [6]*LABoratoire des Systèmes d'Information en Santé, Université d'Oran, Oran, Algeria*

The three Apolipoprotein E (APOE) isoforms (E2, E3 and E4), coded by the APOE  polymorphism, interact differently with specific lipoprotein receptors and thus influence plasma cholesterol concentrations. The 4 allele is associated with higher total cholesterol and LDL-cholesterol levels whereas the 2 allele presents the opposite effects. Furthermore, the APOE rs439401 SNP is associated with higher plasma triglyceride and lower plasma HDL-cholesterol concentrations whereas the APOE rs4420638 SNP is associated with lower plasma HDL-cholesterol levels and higher total cholesterol and LDL-cholesterol levels. To our knowledge, the relationship between APOE SNPs and plasma lipid and lipoprotein concentrations in an Algerian population has never previously been studied. We then assessed the relationships between APOE polymorphisms and plasma lipid concentrations in an Algerian population sample (ISOR study, 787 subjects aged 30-64 yrs, recruited in Oran), and compared the results with those obtained for a French population sample (MONA LISA Lille study, 1578 subjects aged 35-74 yrs, recruited in the Lille area) with contrasting environmental factors and genetic backgrounds. In the French study, total and LDL-cholesterol levels were higher in 4 allele carriers (p=1.4x10-3 and p=4.0x10-4, respectively) and lower in 2 allele carriers (p=5.8x10-7 and p=5.9x10-12, respectively), relative to 3 allele carriers. In the Algerian sample, 4 allele carriers had higher plasma triglyceride (p=0.0004) and LDL-cholesterol (p=0.006) levels than 3 allele carriers. Linkage disequilibrium and haplotype analyses showed that the A allele of the rs4420638 SNP may exert a protective effect on LDL-cholesterol levels (independently of the APOE epsilon

POSTERS

polymorphism) in the ISOR study only. In conclusion, even though the populations presented differences (baseline lipid parameters, genotype distributions and linkage disequilibrium), our results showed that the epsilon polymorphism has the expected impact on the plasma lipid profile and suggested that another APOE SNP may have an independent effect only in the Algerian population .

Keywords: APOE polymorphisms, Algerian population, French population, Lipid parameters, Cardiovascular risk

P76

Investigation of the Major HCV Genotype in Asymptomatic Patients in Iraq by the Use of Reverse- Transcription PCR

[1]Ghanim A. Al-mola, [2]Hashim R. Tarish, [3]Abdulkareem Abdullah Al Radhi, [2]Karar M. Abdulsada
[1]Department of Biology College of Science for Women, Babylon University, Babylon, [2]Department of Microbiology College of Medicine-University of Kufa, 3Department of Community Medicine ;Kufa College of Medicine, Iraq

BACKGROUND AND PURPOSE: Globally, asymptomatic patients represent approximately 80% of total hepatitis C virus patients as indicated by Reverse-Transcription Polymerase Chain Reaction (RT-PCR) based viral genotyping. OBJECTIVES: The present study was conducted to detect HCV genotypes and their prevalence among the asymptomatic populations from five Iraqi governorates (Najaf, Babylon, Qadisyia, Karbala and Baghdad governorates), as the asymptomatic patients globally represent about 80% from total HCV patients by using of viral genotyping through RT-PCR analysis. DESIGN: Cross-sectional study.
METHODS AND MATERIALS: Serum samples were collected from a total of 875 clinically asymptomatic individuals were included in this study that performed from the beginning of June 2009 to the end of August 2010, 517 ofthese samples were randomly taken from asymptomatic individuals (general population) of all ages, both sexes, different residences and the occupations whom attended to hospitals from five Iraqi governorates;, All samples were subjected to investigation of HCV genotypes by use of reverse transcription PCR (RT-PCR).
RESULTS: The genotype 4 was the predominant genotype that appeared in 89.4% of the patients followed by genotypes 1b, 2b, 3a and 6a which had been found in 6.79%, 2.91%, 2.91% and 1.94% of the asymptomatic patients, respectively.
CONCLUSION: The current study provides the first information in Iraq at least in the study areas about the presence of HCV genotypes 2b and 6a.

Keywords: HCV, Genotype, Reserve-transcription, PCR, Asympotomatic hepatitis

P77

Association of HLA with Nasopharyngeal Carcinoma in High-Risk Multiplex Families in Tunisia

[1]Nehla Mokni Baizig, [2]Mouna Makhlouf, [1]Said Gritli, [1]Michèle El May, [1]Mansour Ben Abdallah
[1]Cancer Institute, Tunisia, [2]Ch Nicolles Hospital, Tunisia

BACKGROUND AND PURPOSE:
Knowledge of familial NPC is limited in North Africa and the majority of HLA association studies concerned sporadic NPC. The aim of this study was to evaluate this association with familial NPC.

METHODS AND MATERIALS:
HLA types were determined by means of PCR-SSP. HLA-A ,-B were realized in 36 NPC cases and 72 unaffected members of their families. HLA-DRB1 concerned 36 NPC cases, 72 unaffected members from NPC families and 130 community controls. Allele frequencies between case and control groups were compared using the Khi2 or Fisher's exact test.

RESULTS:
Our results showed difference between NPC cases and unaffected family members regarding HLA-A 30 (25 % vs 7.25 %; p=0.03). Comparison of HLA-DRB1 allelic frequencies between NPC cases versus controls and between unaffected family members versus controls demonstrated that HLA-DRB1*10 was absent in our samples of NPC and unaffected members but this allele was present in 9.23% of controls. The differences were significant with p = 0.04 and p = 0.004 respectively. DRB1*03 was more frequent in NPC patients and in unaffected members of NPC families than in controls (41.66% vs 21.53%; p=0.02 and 58.33% vs 21.53%; p = 0.00). On the other hand, HLA-DRB1*11 was less frequent in NPC patients and in unaffected members of NPC families compared to control group (8.33% vs 27.69%; p=0.02 and 1.38% vs 27.69%; p = 0.00). The same results were found regarding DRB1*03 and DRB1*11 in sporadic NPC in our previous study.

CONCLUSION:
Considering the results of this study, we can suppose that a low allelic frequency of DRB1*10 is associated with NPC in high-risk families in Tunisia. .

Keywords: Nasopharyngeal carcinoma, High risk families, HLA, Alleles frequencies, Association

POSTERS

P78

A "De novo"Splice Site Deletion in the OFD1Gene is responsible for Oral-Facial-Digital type 1 Syndrome in an Emirati Child

[1]Mariam Aljneibe, [1]Khouloud Khozaimy, [1]Khouloud Al-Kathiri, [1]Bassam Ali, [2]Lihadh Al-Gazali
[1]Pathology Dept., CMHS, UAEU, [2]Paediatrics Dept., CMHS, UAEU, United Arab Emirates

BACKGROUND AND PURPOSE: Oral-facial-digital type 1 (OFD1) syndrome is an X-linked dominant disease characterized by dysmorphic face, oral cavity and digits. This syndrome is associated with polycystic kidney disease which is a typical feature of OFD1. Heterozygous mutations in the OFD1 gene, which is located on Xp22.2-22.3, are responsible for this condition. This gene encodes acentrosomal and basal body cilia protein that plays an important role in the early development of the brain, face, limbs and the kidneys. Particular mutations before residue 631 are lethal in males and cause OFD1 in females. Moreover, some mutations in the OFD1 gene have been associated with Joubert syndrome 10 and Simpson-Golabi-Behmel syndrome type 2.

METHODS AND MATERIALS: In this study we clinically evaluatedan affected female exhibiting OFD1 syndrome features from an Emirati Family. Screening the OFD1 gene for the causative mutation was carried out using Sanger sequencing. In addition, bioinformatics tools using HSF and ASSEDA softwares have been used to confirm the pathogenicity of the identified mutation.

RESULTS: We identified a heterozygous single-nucleotide deletion (c.2757+1delG) affecting the splice donor site of exon 20 in the affected child. DNA chromatograms showed that both parent were homozygous for the wild type sequence suggesting that the mutation in the child is 'de novo' in nature. Prediction programs showed that this deletion affects the authentic splice site leading to the creation of a cryptic splice site at position c.2756. Subsequently, this mutation will result in a frame-shift and premature termination codon (p.Lys920ArgfsX2).

CONCLUSION: We described the clinical features and molecular analyses of a sporadic case of an Emirati child with OFD1 syndrome. A heterozygous 'de novo' mutation in the OFD1 gene has been found to be responsible for the phenotype in the child.

Keywords: Oral-facial-digital type 1 (OFD1), OFD1 gene, Sporadic, "de novo" mutation, X-linked dominant

P79

Multiple Self-Healing Palmoplantar Carcinoma (MSPC): A Novel Inherited Skin Cancer with Palmoplantar and Conjunctival Lesions

[1,6]Ons Mamaï, [2]Lobna Boussofara, [3]Barry Merriman, [4]Wahiba Kraiem, [2]Rafiaa Nouira, [5]Badreddine Sriha, [2]Mohamed Denguezli, [1]Moez Gribaa, [1]Ali Saad, [6]Bruno Reversade
*[5]Badreddine Sriha, [2]Mohamed Denguezli, [1]Moez Gribaa, [1]Ali Saad, [6]Bruno Reversade [1]Laboratory of Human Cytogenetic, Molecular Genetics and Reproductive Biology, Farhat Hached University Hospital, Sousse, Tunisia, [2]Department of Dermatology and Venerology, Farhat Hached University Hospital, Sousse, Tunisia, [3]Department of Human Genetics, David Geffen School of Medicine, UCLA, California, USA, [4]Department of Dermatology and Venerology, Nabeul Regional Hospital, Nabeul, Tunisia, [5]Department of Pathological Anatomy and Cytology, Farhat Hached University Hospital, Sousse, Tunisia, [6]Institute of Medical Biology, A*STAR, Singapore*

Multiple keratoacanthoma (KA) and squamous cell carcinoma are phenotypically and histologically alike. The familial KAs are characterized by the appearance of epithelial tumors derived from adjoining hair follicles. They have a fast evolution, leaving atrophic scars after spontaneous regression.
To date, four familial variants of multiple KAs have been described:

- Ferguson-Smith disease (MIM#132800) caused by TGFBR1 mutations
- Muir-Torre syndrome (MIM#158320) caused by MSH2/MLH1 mutations
- Grzybowski syndrome and Witten-Zac syndrome whose aetiology are unknown We report here a fifth type.

In a five-generation Tunisian family comprising 14 affected patients with autosomal dominant transmission, we describe a novel familial KAs with primary palmoplantar and conjunctival lesions. Six out of 14 affected patients developed malignant tumors through metastatic transformation. We first excluded linkage to chromosome 9, 2 and 3 harboring respectively the TGFBR1 and MSH2/MLH1 genes. Through identical-by-descent haplotype mapping we identified a single allele on chromosome 17 which is fully segregating with the disease. On the basis of clinical presentations and genetic linkage data, we have named this new skin cancer predisposition: MSPC for Multiple Self-healing Palmoplantar Carcinoma. MSPC has the distinctive feature of affecting epithelial tissues which are devoid of hair. As more families are diagnosed with MSPC, we anticipate that its causative gene will be rapidly identified.

Keywords: Multiple self-healing palmoplantar carcinoma, Multiple keratoacanthoma, Linkage analysis, Haplotype mapping

POSTERS

P80

Methylenetetrahydrofolate Gene (MTHFR) C677T Polymorphism and Peripheral Artery Disease in East Algerian Population

[1,2]Hanachi Sabah, [1,2]Sifi Karima, [1]Zerdoud Nawel, [1]Zekri Salima, [1,2]Abadi Nouredine, [1,2]Cherifa Benlatreche, [3]Daoud Roula, [3]Nassira Kerrouaz

[1]Biochemistry Service, Ibn Badis Hospital, Faculty of Medicine, Algeria, [2]Laboratory of Biology and Molecular Genetics, Faculty of Medicine, Algeria, [3]Ibn Badis Hospital, Faculty of Medicine, Constantine, Algeria

BACKGROUND AND PURPOSE: MTHFR, is a key enzyme in catalyzing 5, 10- methylenetetrahydrofolate into 5 methyltetrahydrofolate, A missense mutation of MTHFR that converts alanine to valine (C to T substitution at nucleotide 677) encodes a thermolabile enzyme with lower specific activity. The MTHFR C677T polymorphism as a risk factor in peripheral artery disease (PAD) has been suggested, but direct evidence from genetic association studies remain inconclusive. The aim of this study is to analyze the prevalence of the MTHFR C677T gene polymorphism among a group of PAD patients in comparison to controls and to examinate the possible association between PAD and MTHFR gene mutation.
METHODS AND MATERIALS: 59 patients with PAD were included in the study. They were 44 males and 15 females with a mean age of 57.96 years. Forty eight patients (81.35%) were diabetic (type 2) and twenty two (37.3%) were hypertensive. MTHFR C677T gene polymorphism was analyzed by PCR in order to discriminate between homozygous (C/C and T/T) and heterozygous (C/T) genotypes in the study group. Eighty five healthy subjects (36 males and 49 females with mean age of 46 years) served as healthy controls.
RESULTS: The C677T mutation of MTHFR was not found to be different in patients with PAD and healthy controls. 31 patients with PAD (52.54%) and 44 healthy subjects (51.76%) had only the wild-type allele (C/C), 9 patients (15.25%) and fifteen healthy controls (17.65%) had two copies (T/T) of the T allele , and nineteen patients (32.20%) and twenty six healthy controls (30.59%) had one T allele (C/T) . patients with PAD were older compared to those without PAD. Diabetes status was significantly associated with PAD.
CONCLUSION: In the PAD population, MTHFR C677T gene polymorphism occurred in a pattern similar to that seen for healthy controls. No significant association was detected between the T/T genotype and PAD.

Keywords: Methylenetetrahydrofolate gene, MTHFR C677Tpolymorphism, Peripheral artery disease, PCR digestion, East Algerian population

P81

Analysis of Two Arab Families Reveals Additional Support for a DFNB2 Nonsyndromic Phenotype of MYO7A

[1]Bassam R Ali, [1]Salma Ben-Salem, [2]Heidi Rehm, [3]Patrick J Willems, [4]Zakaria A Tamimi, [5]Hammadi Ayadi, [6]Lihadh Al-Gazali

[1]Department of Pathology, College of Medicine and Heath Sciences, United Arab Emirates University, United Arab Emirates, [2]Partners`Laboratory for Molecular Medicine, and Harvard Medical School Boston, United States of America, [3]GENetic DIAgnostic Network (GENDIA), Antwerp, Belgium, [4]Department of Ophthalmology, Eye Specialty Hospital, Jordan, [5]Equipe Procédés de Criblages Moléculaires et Cellulaires, Laboratoire de micro-organismes et biomolécules, Centre de Biotechnologie de Sfax, Sfax, Tunisia, [6]Department of Paediatrics, College of Medicine and Heath Sciences, United Arab Emirates University, United Arab Emirates

BACKGROUND AND PURPOSE: Variants in the head and tail domains of the MYO7A gene encoding myosin VIIA cause Usher syndrome type 1B (USH1B) and nonsyndromic deafness (DFNB2, DFNA11). Congenital monogenic forms of deafness are the most common and the more severe forms of sensorineural hearing loss. To date, over 100 loci have been mapped and over 70 disease causing genes have been implicated in this condition. METHODS AND MATERIALS: In order to identify the genetic defect(s) underling profound deafness in two consanguineous Arab families living in UAE, we have sequenced a panel of 19 genes involved in Usher syndrome and nonsyndromic deafness in the index cases of the two families. RESULTS: Molecular analysis revealed a novel homozygous insertion of AG (c.1952_1953insAG; p.C652fsX11) in exon17 of the MYO7A gene in an Iraqi family, and a homozygous point mutation (c.5660C>T; p.P1887L) in exon 41 affecting the same gene in a large Palestinian family. Moreover, some individuals from the Palestinian family also harbored a novel heterozygous truncating variant (c.1267C>T; p.R423X) in the DFNB31 gene, which is involved in autosomal recessive nonsyndromic deafness type DFNB31 and Usher syndrome type II. CONCLUSION: Assuming an autosomal recessive mode of inheritance in the two inbred families, we conclude that the homozygous variants in the MYO7A gene are the disease-causing mutations in these families. Furthermore, given the absence of retinal disease in all affected patients examined suggests that family 2 may segregate a DFNB2 phenotype rather than USH1B. This finding further supports the premise that the MYO7A gene is responsible for two distinct diseases and gives evidence that the p.P1887L mutation in a homozygous state may be responsible for nonsyndromic hearing loss.

Keywords: Multiple self-healing palmoplantar carcinoma, Multiple keratoacanthoma, Linkage analysis, Haplotype mapping

POSTERS

P82

Differential miRNA Expression Profiles Related to Heart Failure in an Experimental Postinfarction Rat Model

[1]Dorota Tulacz, [1]Anna Fogtman, [2]Michal Maczewski, [1]Monika Gora, [1]Beata Burzynska

[1]*Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Poland,* [2]*Department of Clinical Physiology, Medical Centre of Postgraduate Education, Poland*

BBACKGROUND AND PURPOSE: MicroRNAs are endogenous small RNAs with biological function of post-transcriptional regulation of gene expression. Deregulation of miRNAs has been associated with various diseases, including cardiovascular diseases. The aim of the present study was to report miRNAs profiling performed on the left ventricle (LV) in a well validated model of postinfarction heart failure (HF). These findings might be useful in the understanding and in future diagnostics of HF.

METHODS AND MATERIALS: Ligation of the proximal left coronary artery in rats was used to induce a wide range of myocardial infarct sizes (small, moderated and large). Two months after the operation rats were anaesthetised and hearts were dissected. The development of HF was estimated by echocardiography and catheterization. The LV tissues were homogenized and total RNA was isolated using MagNA Pure Compact System (Roche Diagnostics). MicroRNA expression profiling was performed using Affymetrix GeneChip® miRNA 3.0 arrays according to the manufacturer's recommendations. The raw data was RMA normalized and differences in expression levels compared to sham-operated rats were calculated using Partek Genomics Suite software.

RESULTS: Rats with large myocardial infarction developed an extensive LV remodeling and heart failure, while rats with small or moderated infarct sizes compensated the LV injury. We identified several mature Rattus norvegicus-miRNAs (rno-miR) exclusively altered in rats with large myocardial infarct sizes. In contrast, no differences were detected in rats with small and moderate infarct sizes. We found miR-132, miR-199a and additional miRNAs potentially involved in HF condition.

CONCLUSION:
There are significant differences in miRNA expression profile in the left ventricle between rats with heart failure and rats with compensated heart injury. These findings suggest a potential functional role of selected miRNA in progression of heart failure and also in recovery after cardiac ischemic events.

Keywords: miRNA, Heart failure, Animal model

P83

Ataxia with Oculomotor Apraxia type 2:A clinical and genetics Study of 14 patients

[1]Mzahem Abderrahim, [1]Taghane Naima, [1]Boulefkhad Assia, [2]Koenig, [1]Hamri Abdelmadjid

[1]*Service Neurologie Hopital Benbadis CHU Constantine and Laboratoire de Génétique et de Biologie Moléculaire Université Mentouri,* [2]*Laboratoire de Diagnostic Génétique, Hôpital Civil, 67091 Strasbourg cedex, France*

Background and Purpose Ataxia with oculo-motor apraxia type 2 (AOA2) is a recently described autosomal recessive cerebellar ataxia (ARCA) defined by gait ataxia, oculomotor apraxia(OMA), polyneuropathy, elevated alpha-foetoprotein(AFP) levels and the mean age of onset is 15 years. The AOA2 gene is located on chromosome 9q34 and encodes the senataxin (AND/ARN helicase protein) we analyzed the phenotypic spectrum of 14 AOA2 patients from 5 unrelated families .The mean age at onset for all families was in the second decade. Cerebellar ataxia was progressive, slowly leading to disability which was aggravated by axonal polyneuropathy. OMA was present in 57% of the patients. Head tremor and dysarthria were observed in 35.07% and 78.57% of patients respectively. Areflexia at lower limbs were noted in all patients. Four different homozygous SETX mutations were found. Methods We analysed 91 Algerian families with a clinical presentation of autosomal recessive cerebellar ataxia (ARCA).Patients with clinical presentation reminiscent of AOA2 were screened for SETX mutation; we sequenced all exon of the SETX gene. Results The first signs described by the parents were abnormal falls, poor balance on walking and /or dysarthria. Almost all patients had ataxia of gait which was more disabling in the eldest ones, and mild ataxia of the limbs and trunk. OMA was observed in57.14 % of the patients, while convergent strabismus was present in 28.57% and nystagmus in 50 % of the patients. Skeletal deformities such as pes cavus occurring in 21.42 % and scoliosis in 21% of the patients. Pyramidal signs with a Babinski sign were observed in 42.85% patients. AFP blood levels were elevated in all patients. Functional disability seemed to correlate with disease duration Conclusions: AOA2 is relatively frequent in Algeria .Serum AFP is a good marker to suggest molecular studies of the SETX gene.

Keywords: Ataxia, Autosomal recessive, Oculomotor apraxia,Neuropathy, Senataxine

POSTERS

P84

The rs3027898 Polymorphism of the Interleukin-1 Receptor-Associated Kinase 1 Gene (IRAK1) is Associated with Increased Susceptibility of Psoriasis and Psoriatic Arthritis in the Tunisan Patients

[1]Chiraz Bouchlaka Souissi, [1]Myriam Ammar, [2]Slah Ouerhani, [3]Ines Zarra, [4]Ilhem Cheour [5]Raoudha Tekaya, [6]Hela Zeglaoui, [7]Hela Fourati, [6]Elyes Bouajina, [8]Nejib Doss, [3]Mourad Mokni, Slaheddine Sellami, [1]Amel Elgaaied, [1]Raja Marrakchi

[1]Laboratory of Genetics, Immunology and Human Pathologies, Faculty of Sciences, University of el Manar I, Tunis, Tunisia, [2]Pasteur Institute of Tunis, Laboratory of Molecular and Cellular Haematology, Tunis, Tunisia, [3]Dermatology Department, La Rabta Hospital, Tunis, Tunisia, [4]Osteoarthritis-osteoporosis Research Laboratory, Rheumatology Department, LaRabta Hospital, Tunisia, [5]Rheumatology Department, Charles Nicolle Hospital, Tunis, Tunisia, [6]Rheumatology Department, Farhat Hached Hospital, Sousse, Tunisia, [7]Rheumatology Department, Hedi Chaker Hospital, Sfax, Tunisia, [7]Dermatology Department, Military Hospital, Tunis, Tunisia

BACKGROUND AND PURPOSE: Psoriasis (Ps) and psoriatic arthritis (PsA) are complex immune diseases that result from interplay between multiple genetic and environmental factors. Both diseases are characterized by psoriasis skin involvement and PsA exhibit additional inflammatory arthritis. IRAK1 (interleukin-1 receptor associated kinase 1), is one of the miRNA-146a targets genes , and play an important role in the pathogenesis of both Ps and PsA, and therefore acts as a negative regulator in TLR and pro-inflammatory cytokine (IL-1) signaling pathway. This study aimed to investigate if the IRAK1 rs3027898 C/A polymorphism may contribute to Ps and PsA in the Tunisian patients. METHODS AND MATERIALS: We conducted a case-control association study in 280 Ps and PsA patients and 200 controls. The genotypes of the rs3027898 were determined by direct sequencing methods. The SPSS statistical package was used to test differences in polymorphism distribution between patients' groups and controls. RESULTS: Strong statistically significant difference in the distribution of the genotypes was observed in IRAK1 rs3027898 C/A polymorphism between patients and controls ($p = 0.001$ in Ps versus controls; $p=0,005$ in PsA versus controls). CONCLUSION: Our findings confirm that the IRAK1 rs3027898 C/A variant is associated with the development of both Ps and PsA in the Tunisian patients. The IRAK1 rs3027898 C/A localize in the target sequence of the mir146a, which inhibite IRAK1 expression, showing that Ps and PsA might be caused by an alteration of mirRNA regulation. Our results provide compelling evidence that although Ps and PsA are distinct clinical entities they also share common genetic factors that contribute to the pathogenesis of the two diseases.

Keywords: Psoriasis, Psoriatic arthritis, IRAK1 gene, Association study

P85

Factor V Leiden Heterozygous Mutation and MTHFR Gene C/T Polymorphism in the Vascular Disease of the Diabetes Mellitus

Boudaoud Khalida, Sifi Karima, Abadi Noureddine

Faculty of medicine, Algeria

INTRODUCTION:
Heterozygous mutation of factor V Leiden multiplies the risk of thrombosis by 5 - 10, this risk passes to 10-40 when it joins to other anomalies as those associated to the diabetes mellitus.

CARE REPORT:
Patient Z.A, born in 1955, presents, since 1994, diabetes mellitus, hypertriglyceridaemia and hypertension. In 2005, over a period of 6 months, he presents a cerebellar ischemic stroke then a thrombosis of the right upper limb to finish by a thrombophlebitis of the left lower limb. He was badly controlled on the level metabolic without obvious atherosclerosic complications (arterial echo-doppler of the supra-aortic trunks, the lower limbs and cardiac are normal, as well as the coronarography). The homocystéinemy is of 20.26 µmol / l. Antibodies antiphospholipids are negative. The rates of the protein S, the protein C, and the antithrombin III are 55 %, 122 %, 101 %, respectively. The Activated Protein C Resistance is of 101 seconds. He presents a heterozygous mutation 1691 G/A of the factor V and C/T polymorphism of the MTHFR gene C677T, without mutation 20210 G> A of the factor II. After 8 years of satisfactory metabolic control, the patient presents an ischemic heart disease and did not make any more thrombotic accidents. The family investigation reveals the same mutations at: -Tow hypertensive sisters, one of them made a transitory cerebrovascular ischaemia, -One brother presenting diabetes mellitus and hypertriglyceridaemia.

DISCUSSION:
There exists, at our patient, an additive effect with triple transmission of factor V Leiden, protein S deficit and MTHFR mutation, the bad metabolic control was a big factor which precipitated the occurrence of these thrombotic accidents. The search for acquired or congenital thrombophilia, particularly if it's recurring, is strongly recommended at patient without diabetic angiopathy. The relationship between these mutations and the cerebrovascular disease remain difficult to establish.

Keywords: Diabetes mellitus, Metabolic disorders, Thrombophilia, Genetics, Cerebrovascular accident

POSTERS

P86

Phenotypic Expression of Late-Onset Pompe Disease (PD)

[1]Yamina Sifi, [2]Karima Sifi, [2]A. Zouai, [2]Fatima Serradj, [2]Abdelmadjid Hamri

[1]Service of Neurology CHU of Constantine, Laboratory of Biology and Molecular Genetics, Faculty of Medicine, University of Constantine, Algeria, [2]Biochemistry Service, Ibn Badis Hospital, Constantine, Algeria

INTRODUCTION:
Pompe disease (PD), also known as glycogen storage disease type II, is caused by a deficiency of the enzyme lysosomal, acid-glucosidase (GAA) resulting in the accumulation of glycogen primarily in muscle tissue. The clinical presentation of (PD) is variable with respect to the age of onset and rate of disease progression. The objective of this study was to characterize the clinical presentation of patients with late-onset Pompe disease.

SUBJECTS AND METHODS:
During the period 2001- 2006 we diagnosed 04 adult cases of (PD). All patients profited from a complete clinical examination, electromyographic study, a systematic proportioning of muscular enzymes (CPK, LDH), muscular biopsy, hepatic assessment, abdominal and heart echography, pulmonary function testing (PFT) and leucocytic proportioning of acid maltase. Informed consent was obtained from all subjects.

RESULTS:
Four late-onset Pompe disease (PD) patients were included in this study; they are 02 sisters and their 02 cousins. The average age of the first symptoms was 22 years, muscle weakness has interested upper and lower extremity proximal in all cases, Three patients (patients 2, 3, and 4) also suffered from frequent respiratory infections with a death following a respiratory insufficiency. The muscular enzymes and the hepatic assessment were disturbed at 03 patients The diagnosis was confirmed by leucocytic proportioning of acid maltase.

CONCLUSION:
Pompe disease is a rare autosomal recessive disorder that results in lysosomal and cytoplasmic accumulation of glycogen. The clinical presentation of late-onset (PD) is heterogeneous and resembles that of other myopathies, therefore definitive diagnosis needs to be confirmed by biochemical or molecular methods.

Keywords: Glycogen storage disease type II, Adult- onset Pompe disease, Glycogenosis type II, Acid maltase deficiency, Myozyme

P87

Identification of the Loss of Heterozygosity in Marfan Syndrome

[1]Aicha Zoubeida BenMostefa, [2]Ann Curtis, [3]Maureen Boxer, [3]Carol Black, [2]John Burn

[1]University of Annaba, Algeria, Department of Human Genetics, [2]University of Newcastle upon Tyne and Northern Genetics Service, Royal Victoria Infirmary, Newcastle upon Tyne, England, [3]Molecular Biology Laboratory, Department of Pathology, Nine wells Hospital, Dundee, Scotland

BACKGROUND AND PURPOSE: Marfan syndrome (MFS) is an autosomal dominant disease. In 1991, MFS was linked to chromosome 15 and subsequently, the gene was shown to be FBN1. FBN1 is a large gene of 110 Kb, it codes for fibrillin 15 which is a component of the extra-cellular-matrix (ECM). Fibrillin 15 is synthesized in the fibroblast cells, then secreted as a monomer and assembled together in a specific configuration. This polymeric structure is then associated with others proteins to form the microfibrills which are incorporated in the ECM. A defect in the synthesis, the secretion or the incorporation will give rise to different phenotypes. Our study has been conducted to establish the Loss Of Heterozygosity (LOH),expected by the instability of the mutant allele, by analyzing the RsaI polymorphic site within the 3' untranslated region of FBN1.

METHODS: Genomic DNA and cDNA were amplified by Polymerase Chain Reaction (PCR) with specific primers then digested with the enzyme RsaI. The digests were separated in a 3% Nusieve agarose gel. Radioactive PCR were performed to ascertain the LOH, using radioactive labeled products.

RESULTS: Genomic DNA digests show specific bands pattern regarding the presence (+) or the absence (-) of the polymorphic restriction site. We have found 7 homozygotes (-/-) and 6 heterozygotes (+/-). However, there were no homozygotes (+/+). cDNA digests show the evidence of LOH in 3 patients.

CONCLUSION: The causative allele found at the genomic level is totally or partially lost at the cDNA level, proving that the mutant transcript is unstable. This is one way to regulate the expression of the causative allele so that its product will not disturb the ECM configuration. This study confirms the problematic correlation between genotype/phenotype of the MFS patients. This complexity is explained by the LOH, which has been clearly identified in our study.

Keywords: Marfan Syndrome, FBN1, Loss of heterozygocity, rtPCR, Radioactive PCR

POSTERS

P88

Clinical and Molecular Genetics of Kabuki syndrome: About Six Observations

[1]Imane Samri, [1]Laila Bouguenouc, [2]Sana Chaouki, [2]Mostapha Hida, [1]Karim Ouldim
[1]Medical Genetics and Oncogenetics Unit, Hassan II University Hospital, [2]Department of Pediatrics, Hassan II University Hospital, FEZ, Morocco

BACKGROUND AND PURPOSE: Kabuki Syndrome or Niikawa Kuroki syndrome is a rare genetic disorder. It combines characteristic facial dysmorphism, skeletal abnormalities and dermatoglyphics as well as mental retardation. We specify the characteristics of this syndrome by reporting six cases collected in medical genetics department of Fez Hassan II University Hospital.

OBSERVATIONS: We report seven cases: two girls and five boys with age range from 5 years to 12 years. All patients have mild mental retardation, suggestive dysmorphic features and dermatoglyphics abnormalities of where the clinical diagnosis of Kabuki syndrome. Other signs reported in the literature are present in our series including short stature, dental anomalies, the epilepsy and congenital heart disease association to this syndrome. The malformation assessment performed in our patients proved unremarkable. The molecular analysis of the six patients DNAand their parents in is in progress in collaboration with an Italian team. Monitoring children is provided by a multidisciplinary team including geneticists, pediatricians and pediatric neurologists.

RESULTS: Most reported cases of Kabuki syndrome are sporadic. Familial cases are published and are in favor of autosomal dominant inheritance. The genetic mechanism is still poorly understood but some MLL2 gene mutations have recently been described. However, a good clinical examination and collecting dysmorphologic signs can confirm alone the clinical diagnosis of the Kabuki syndrome.

CONCLUSION: Kabuki syndrome is a rare congenital malformation syndrome, whose etiology is unknown. The two main criteria for diagnosis are a characteristic facial appearance and developmental delay or mental retardation. It can be associated with several other events. The genes involved are still under study where the role of the clinical genetics in the diagnosis of this syndrome.

Keywords: Kabuki syndrome, Autosomal dominant, Fcaial dysmorphology, Mental retardation

P89

Oculocutaneous Albinism: About a Moroccan Family

Imane Samri, Laila Bouguenouch, Karim Ouldim
Medical Genetics and Oncogenetics Unit, Hassan II University Hospital, Morocco

BACKGROUND AND PURPOSE:
The oculocutaneous albinisms (AOC) present a set of hereditary defects of melanin biosynthesis characterized by a generalized reduction in pigmentation of hair, skin and eyes. The prevalence of all forms of albinism has been estimated at about 1/17 000. The clinical picture of the AOC is very variable, ranging from the most severe form (AOC Type 1A), with a total lack of melanin production throughout life and milder forms (OCA1B, OCA2, and AOC3 AOC4) in which a certain amount of pigment gradually accumulates. Clinical manifestations include eye abnormalities characteristics and hypo pigmentation of the skin and hair with varying degrees depending on the type of AOC. The incidence of skin cancer may be increased. The four types of OCA are inherited as an autosomal recessive disease. Diagnosis is based on clinical findings of hypopigmentation of the skin and hair and the presence of characteristic ocular symptoms. The molecular diagnosis is necessary to determine the genetic defect and the subtype AOC (At least four genes are involved: TYR, OCA2, TYRP1 and MATP). Genetic counseling and prenatal diagnosis are possible when the mutations causing the disease have been identified in the family. People with AOC require regular ophthalmological and dermatological supervision. The life expectancy, development, intelligence and fertility are quite normal.

METHODS AND RESULTS:
We report the case of a Moroccan family with consanguineous marriage and having three albinos' children and a healthy child. The clinical diagnosis is established and the molecular study is underway.

CONCLUSION:
Albinism is a genetic disease for which it is desirable that research projects develop. This study should focus both on the genetics of the disease but also on therapeutic and preventive care of it.

Keywords: Kabuki syndrome, Autosomal dominant, Fcaial dysmorphology, Mental retardation

POSTERS

P90

The Qatar Genome Browser: A Next-Gen Bioinformatics Resource in MENA

Jillian Rowe, Greg Smith, Pankaj Kumar, Karsten Suhre, Hanif Khalak
Weill-Cornell Medical College – Qatar

BACKGROUND AND PURPOSE:
Weill-Cornell Medical College in Qatar has conducted a number of next-gen medical genomics projects, including family and cohort studies of diabetes, obesity, inherited neuropathies, and cancer. These studies have generated data on hundreds of new whole genomes, exomes, and methylomes - tools are required to visualize and analyze this data, particularly in the context of publicly available genome data and annotation.

METHODS AND MATERIALS:
We designed and implemented a customized genomic data portal interface based on the Catalyst web framework using Perl and the Bio::Perl packages, and generated visualizations in Javascript using the D3 and Jbrowse visualization libraries. Reference and private study genome data, many standard annotation tracks, group-based access policies and custom comments for genomic features are stored using JSON-formatted files and a mySQL database.

RESULTS:
WCMC-Q has established the Qatar Genome Browser (QGB) to address a critical need in next-gen data analysis for the visualization of genetic and genomic study datasets, particularly in the context of genome annotation and data from other populations and published studies. Custom features in the portal include authenticated group-based access to primary and summary data, genomic feature linking and searching, private data upload, custom comments on features, and secondary analytics (e.g., LD heatmaps)

CONCLUSION:
The Qatar Genome Browser is a web-based data portal which provides a dynamic interface to public and study-focused next-gen'omics data. QGB is the first of its kind in the MENA region, giving access to summary views of data from HapMap, 1000 Genomes, and a number of regional studies representing 100s of sequenced genomes, as well as user's own data tracks in genomic context.

Keywords: Qatar genome browser, Genomic data portal, Next generation data analysis

P91

Polymorphism Thr241Met of the XRCC3 Gene and Lack of Association with Colorectal Cancer Risk in Algerian Population

[1]Moghtit Fatima Zohra, [1]Louhibi Lotfi, [2]Robert Jacques, [2]Lemorvan V, [2]Bellot R, [3]Boushaba A, [3]Megaiz A, 1Mehtar Nadhira, [1,4]Aberkane Meriem Samia
[1]*Laboratory of Molecular and Cellular Genetics, University of Science and Technology (Mohamed Boudiaf) Oran, Algeria,* [2]*Institut Bergonié, INSERM U916, 229 cours de l'Argonne, Bordeaux Cedex, France,* [3]*Centre régional de lutte contre le cancer ' EL Emir Abdelkader, Algeria,* [4]*Faculté de Médecine, Université d'Es sénia ,Oran, Algérie*

BACKGROUD AND PURPOSE: Colorectal cancer (CRC) is one of the most common causes of death due to cancer in both men and women throughout the world. It is a complex, multifactorial disease influenced by genetic and environmental factors. Genetic variation like Single Nucleotide Polymorphisms (SNP) in candidate genes such as DNA repair genes are thought to play an important role in individual variation in colorectal cancer susceptibility and in response to therapy. Many epidemiological studies have explored the association between XRCC3 (X-ray repair complementing defective repair in Chinese hamster cells 3) polymorphisms and colorectal cancer risk in various populations. The aim of this case control study was to investigate the effect of XRCC3 T<C (Thr241Met, rs861539) polymorphism on the development of CRC among West Algerian patients.

METHODS: Genomic DNA was extracted from blood samples collected from 80 sporadic CRC patients and 99 normal controls. The Thr241Met Polymorphism was determined by pyrosequencing technology.

RESULTS: The distribution of genotypes (Thr/Thr, Thr/Met and Met/Met) among CRC cases (10%, 51%, 39% respectively) was not significantly different from those among controls (12%, 57%, 31% respectively) (P>0,05).The variant genotype combinations did not show any significant association with CRC susceptibility risk suggesting that the XRCC3 codon 241 polymorphism does not convey moderate increase in susceptibility to CRC in West Algerian population.

CONCLUSION: This is the first study on XRCC3 gene polymorphism in our population suggesting that the Thr241Met polymorphism of XRCC3 gene may not be associated with the colorectal cancer risk in West Algerian population. Further research with a larger sample size is needed to reveal more.

Keywords: XRCC3 Thr241Met, Association, Colorectal cancer risk, Algerian population

POSTERS

P92

RET Genetic Screening in Patients with Medullary Thyroid Cancer: The Algerian Experience

Karima Sifi, Noredine Abadi, Al kacem Lezzar, Khalida Boudaoud, Chérifa Benlatreche, Nassim Nouri, Hanachi Sabah, Zerdoud Nawel, Zekri Salima
Laboratory of Biology and Molecular Genetics, Faculty of Medicine, University Mentouri 3 of Constantine, Algeria

BACKGROUND AND PURPOSE: Medullary Thyroid Carcinoma (MTC) can occur in hereditary (25%) or sporadic form (75%). In the hereditary forms, MTC is the major component of the Multiple Endocrine Neoplasia Syndrome type 2 (MEN 2). MEN 2 is caused by autosomal dominant gain-of-function mutations of RET proto-oncogene. Early prophylactic total thyroidectomy before the development of MTC is currently the only curative treatment. The aims of this study: -Determine the frequency and the localization of the detected RET proto-oncogene changes in MTC case index and theirs relatives and to compare them with the data of the literature. -Present the phenotype–genotype correlation in Algerian MEN2 families.

METHODS AND MATERIALS: DNA was extracted from the peripheral blood lymphocytes of a total of 40 persons, including 25 MTC probands and 15 of their unaffected kindred's. Exons 8,9,10, 11, 13, 14, 15 and 16 of the RET gene were amplified by PCR and sequenced. Informed consent was obtained from all subjects.

RESULTS: The C634Y RET exon11 germline mutation was detected in 8% of our MTC index cases and in 46.66% of their relatives. In MEN2, RET G691S/S904S haplotype is more frequent. In relatives G691S and S904S polymorphisms identical to those of MEN2 index cases were found but in the homozygous state, suggesting that this haplotype have a modifying effect on the age of onset of MTC in MEN2A. That is what was observed in our relatives. In sporadic MTC, the exon 11 non synonymous G691S SNP, was strongly present. Several studies have shown that this SNP is associated with predisposition to sporadic MTC. In our patients, the C634Y mutation was significantly associated with the presence of pheochromocytoma, which is consistent with the literature data.

CONCLUSION: The identification of the C634Y mutation allowed us to offer to the mutated case index and their relatives prophylactic thyroidectomy

Keywords: MTC, MEN2A, MEN2B, RET proto-oncogene, Sequencing

P93

Molecular and Cellular Analysis of a Novel Mutation in DDR2 causing Spondylo-Meta-Epiphyseal Dysplasia with Short Limbs and Abnormal Calcifications (SMED-SL)

[1]Adila Al-Kindi, [2]Praseetha Kizhakkedath, Anne John, [1]Abeer AlSayegh, Maha Al Awadi, [3]Lihadh Al-Gazali, [1]Bassam R. Ali
[1]Department of Genetics, Sultan Qaboos University Hospital, Oman, [2]Department of Pathology, College of Medicine and Heath Sciences, United Arab Emirates University, UAE, [3]Department of Paediatrics, College of Medicine and Heath Sciences, United Arab Emirates University, UAE

BACKGROUND AND PURPOSE: The rare autosomal genetic disorder, Spondylo-meta-epiphyseal dysplasia with short limbs and abnormal calcifications (SMED-SL), is reported to be caused by missense or splice site mutations in the human discoidin domain receptor 2 (DDR2) gene. DDRs are plasma membrane bound receptor tyrosine kinases (RTKs) that recognize collagens as their ligands. Previously our group has established that trafficking defects and loss of ligand binding are the underlying causes of several SMED-SL causing mutations. METHODS AND MATERIALS: Clinical evaluation including imaging has been used to evaluate two Omani children of consanguineous parents with suspected SMED-SL. All the coding exons and splice sites of the DDR2 gene were sequenced by Sanger sequencing. Subcellular localization of the mutated DDR2 protein was determined by confocal microscopy.
RESULTS: In addition to the typical features of SMED-SL, one of the patients has an eye phenotype including visual impairment and glaucoma optic atrophy. The eye abnormalities have not been previously reported in SMED-SL expanding the clinical spectrum of this condition. In addition, a novel homozygous recessive mutation (c.CT 2468Del; p.S823C FS) on exon 16 of DDR2 gene has been identified in both patients. The mutation resulted in frameshift leading to premature termination of translation and a predicted amino acid change S823C. Subcellular localization of the mutant protein was analysed in mammalian cell lines and the protein was found to be largely retained in ER as evidenced by colocalization with an ER marker, suggesting protein trafficking defects as a possible contributing factor to the disease pathology. CONCLUSION: We have elucidated the molecular and cellular cause underlying SMED-SL in Omani patients. In addition, we have expanded the phenotype to include eye involvement. The eye findings can be attributed directly to the function of DDR2 as a collagen receptor to collagen II which is found in vitreous humor of the eye.

Keywords: Spondylo-meta-epiphyseal dysplasia with short limbs and abnormal calcifications, DDR2 gene, mutation

POSTERS

P94

Study of Methylation Differences in Qatari Population

Shaza Zaghlool, Mashael Al-Shafai, Wadha Al Muftah, Pankaj Kumar, Karsten Suhre
Weill Cornell Medical College Qatar

BACKGROUND AND PURPOSE:
Differentially methylated regions can be indicative of disease state. However, there are other factors that can differentially contribute to alternative phenotypes such as age, gender, bmi, smoking status, and even cellular heterogeneity. These known factors can differ by disease status acting as confounders while investigating DNA methylation differences. Along with these known factors, there could be hidden variables or confounders that must also be controlled and accounted for.

METHODS:
Two Illumina 450K methylation datasets consisting of 145 subjects were collected from the Qatari population with varying diabetes and obesity states. Because the DNA samples were collected from whole blood, they consisted of heterogeneous cell populations in varying proportions. The Methyl Spectrum tool [Houseman 2012] was used for inferring cell distributions based on DNA methylation patterns. Then, MethylPCA [Chen 2013] was used for control of potential confounders in the light of the already known factors. This tool performs data reduction and uses principle component analysis to capture the unmeasured sources of variation in methylation data. It then performs association tests using multiple regression with the provided covariates to test the association between the studied disease and each methylation site, while adjusting for the covariates.

RESULTS:
The methylation difference between cases and controls showed a sufficient reduction in the epigenome-wide association signals before and after the adjustment using the estimated cell proportions. Up to 10 principle components representing potential confounders were computed although the first 2 or so principle components explained the majority of unexplained variance in methylation patterns.

CONCLUSIONS:
Epigenome-wide methylation studies can reflect useful information on the disease state under the circumstance that known factors contributing to other differences are corrected for. Confounders unrelated to the disease may also lie in the data possibly explaining the variance.

Keywords: Differential methylation, Diabetes, Obesity, Covariates

P95

A Novel Refsum-Like Disorder: Clinical and Genetic Study of Three Algerian Families

[1]Naima Taghane, [1]Abderrahim Mzahem, [1]Assia Boulefkhad, [2]M Koenig, 1Abdelmadjid Hamri
[1]*Centre Hospitalouniversitaire Ibn Badis Constantine, Algeria,* [2]*Iinstitut De Genetique Et De Biologie Moleculaire Et Cellulaire. Illkirch, Strasbourg, France*

BACKGROUND AND PURPOSE:
Polyneuropathy, hearing loss, ataxia, retinitis pigmentosa and cataract (PHARC) is a neurodegenerative disease marked by early-onset in the late teen and involvement of both the central and peripheral nervous system. The purpose is to report clinical and genetic study of three Algerian families with progressive autosomal recessive ataxia that we aseertained initialy as a phenocopy of Refsum disease.

METHODS AND MATERIALS:
We describe clinical data and ABHD 12 gene mutation analysis of five persons belonging to a three families with PHARC. Concurrent mapping studies were performed with Genechip 10kx bal arrays followed by analysis on selected individuals with the gene chip6.0 arrays; these patients defined a 5,5Mb linkage interval in the 20p11,21q12 region on chromosome 20.
RESULTS:
The disorder in our families shows an earlier onset that has both central and peripheral characteristics. cerebral corticalfunction appears to be spared with onlyone patient having mental retardation. A predominantly demyeliniating peripheral neuropathyis present in all adult patients. our five patients are homozygous for a 7bp duplication(e,846-852 dup TAAGAGC) in ABHD12 gene with replaces Histidine residue at codon 285 with stop codon

CONCLUSION:
The ABHD12gene causes PHARC. The discovery of the genetic defect in this new disorder provides additional insights into pathogenesis of disease affecting the retine and peripheral and central nervous systems.

Keywords: ABHD 12 gene, Polyneuropathy hearing loss ataxia retinitis pigmentosa and cataract, Linkage analysis

POSTERS

P96

Characterization of Wilson Disease Causing ATP7B Gene Mutations in Qatar

[1]Shabeer Padariyakam, [2]Khalid Abou Hazima, [2]Kamal Hassan, [2]Khitam Abu Khadija, [1]Zafar Nawaz
[1]Cytogenetics & Molecular Cytogenetics Laboratory, Hamad Medical Corporation, Qatar, [2]Department of Pediatrics, Hamad Medical Corporation, Qatar

INTRODUCTION:Wilson Disease (WD) is an autosomal recessive disorder caused by mutations in the copper-transporter (ATPase) encoded by ATP7B gene. Its clinical manifestations are highly variable. The current commonly used diagnostic biochemical investigations have limitations. Therefore, direct molecular diagnosis is considered the most decisive tool There are more than 500 WD disease-causing mutations that have been described in various ethnic populations. However, only few studies described WD mutations in the Arab population and the Middle East.

OBJECTIVES:
1. To characterize ATP7B gene mutations in Qatar.
2. To decipher possible genotype -phenotype co-relation.

METHODS AND MATERIALS: The study was conducted at Hamad General Hospital, which is the only tertiary hospital in Qatar. Ethical approval was obtained. Blood samples were obtained from consented WD patients for DNA sequencing of ATP7B gene. The sequencing was performed on all 21 exons and promoters including 50 nucleotides on each sides of exons. The data analysis was performed manually and using EsqScape software by ABI.,

RESULTS:
Mutations have been identified in 8 patients from different ethnic groups in Qatar. Of interest, a novel mutation was identified in 2 Yemeni brothers, c.2987-8 ins C, leading to frame shift and disruption of protein synthesis. This mutation had not been described before. The elder brother was diagnosed in early adulthood with neurological manifestations, while the younger presented at 10 years with hepatic involvement. Studies on the parents and siblings are underway to confirm variants and their relationship with clinical phenotypes.

CONCLUSION:
This study highlights the importance of molecular genetic diagnosis of patients with WD. Because of clinical heterogeneity the clinical picture of a patient may not always be suggestive of WD even within same family. The presence of new disease mutation with variable presentation may be of help to establish a genotype -phenotype correlation and better understanding of WD.

Keywords: APT7B, Mutations, Arab, Sequencing, Genetics

P97

A Novel ALS2 Splice-Site Mutation in a Turkish Infantile-Onset Hereditary Spastic Paraplegia Family

[1]Fatema Al-Salmi, [2]Süleyman Ersin Ünlü, [1]Aisha Alkhayat Alshehhi, [3]Andrew Crosby, [4]Hatice Koçak Eker
[1]Department of Biology, College of Science, Sultan Qaboos University, Muscat, Oman, [2]Elvankent Ayyýldýz Family Health Center, Ankara, Turkey, [3]Institute of Biomedical and Clinical Science, University of Exeter Medical School, Exeter, UK, [4]Ankara Pediatric Health and Diseases Hematology Oncology Education and Research Hospital, Department of Medical Genetics, Ankara, Turkey

Recessive Mutations in ALS2 are Causative for Early-Onset Upper Motor Neuron Diseases, Including Infantile-Onset Ascending Hereditary Spastic Paralysis (IAHSP). IAHSP is a rare disorder characterized by progressive muscle weakness and stiffness in the arms, legs, and face with onset within the first 2 years of life. We studied a consanguineous Turkish family with four affected individuals presenting with IAHSP. A high density genome-wide SNP analysis in all affected family members identified a 14.7 Mb homozygous region of chromosome 2q32.2-2q33.2, delimited by recombinant SNP markers rs10931426 and rs16840921, likely to correspond to the disease locus. This expanse of chromosome 2 is predicted to contain 153 genes including ALS2, which has previously been associated with IAHSP. To determine if mutation of ALS2 was responsible oligonucleotide primers were designed flanking all 34 coding exons as well as associated intronic splice junctions for PCR and dideoxy sequence analysis. This revealed a novel homozygous c.2351+2 C>A sequence alteration affecting the splice donor site of intron 11, which cosegregated with the disease phenotype, and is predicted to result in alteration of the reading frame and the introduction of premature stop codon.

Keywords: Infantile-onset ascending hereditary spastic paralysis, ALS2 gene, Mutation, GWAS

POSTERS

P98

Accurate and High Resolution Copy Number Variants by Combining SNP Array and Next Generations Sequencing Technology and Incorporating Family Information

Pankaj Kumar, Khalid Fakhro, Hanif Ghalak, Mashael Al-Shafai, Karsten Suhre
Weil Cornell Medical College in Qatar, Qatar

BACKGROUND AND PURPOSE:
Recently Copy Number Variants (CNV) has gained considerable interest and have demonstrated a role in functional diversity. Currently, technology of choice for detecting CNV is either SNP array for fast and accurate detection or Next Generation Sequencing (NGS) for high resolution. Also, studies have shown correction in CNV calls by incorporating family or pedigree information.

METHODS AND MATERIALS:
CNVs were detected from Illumina SNP array using their proprietary software GenomeStudio. CNVs from NGS data were obtained using GenomeStrip sfotware in combination with GATK and Queue. Hidden Markov Model(HMM) and Gaussian Mixture Model (GMM) were used to correct the questionable CNV after incorporating pedigree information.

RESULTS:
Combination of SNP array and Sequencing technology improves quality of CNV detection. HMM and GMM helped in assessing previously unknown CNVs. In several cases, where the breakpoint determined by SNP array was obscure, NGS data helped in resolving the issue. Incorporation of family information using GMM further improves the quality of CNV by correcting mendelian inconsistencies without affecting the detection of de novo mutation.

CONCLUSION: The quality of CNV detection is can be enhanced significantly by utilizing data from multiple platforms and by tackling statistical challenges using suitable algorithm..

Keywords: CNVs, SNP array, Next generation sequencing, Next generation data analysis

P99

The Anti-Inflammatory Effects of Statins Therapy in Patients with Acute Myocardial Infarction

[1]Agata Maciejak, [2]Grazyna Sygitowicz, [3]Maciej Pawlak, [4]Janina Piniewska, [1]Beata Burzynska
[1]*Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland,* [2]*Department of Biochemistry and Clinical Chemistry, Medical University of Warsaw, Warsaw, Poland,* [3]*1st Chair and Department of Cardiology, Medical University of Warsaw, Warsaw, Poland,* [4]*Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland*

BACKGROUND AND PURPOSE: Inflammation is involved in the pathogenesis of acute coronary syndrome (ACS). Myeloperoxidase (MPO) and C-reactive protein (CRP) may play critical roles in generation of oxidative stress and development of systemic inflammatory response. Statins, inhibitors of HMG-CoA reductase, have pleiotropic benefits independent of cholesterol levels, including anti-oxidant and anti-inflammatory effects. The aim of our study was to investigate the effect of statins therapy on serum CRP concentrations, MPO gene expression and plasma levels in patients with acute myocardial infarction (AMI).

METHODS AND MATERIALS: Thirty-seven patients (mean age 55.7±10.9 yrs, n=10 women, n=27 men) with first AMI receiving statins treatment: atorvastatin 40mg/day (n=31), simvastatin 20mg/day (n=3), rosuvastatin 20mg/day (n=3) and followed up for 1 month. The relative MPO gene expression in peripheral blood mononuclear cells (PBMCs) was examined using qRT-PCR. The plasma concentrations of MPO were measured using a chemiluminescent microparticle immunoassay (CMIA), serum high-sensitivity CRP (hsCRP) concentrations were determined by immunoturbidimetric assay. RESULTS: The median serum level of hsCRP was significantly lower after 1-month statins therapy in all patients [11.3 (2.2-68.4) mg/L vs. 1.9 (1.2-7.2) mg/L; $p<0.001$, respectively]. The MPO gene expression was down-regulated in 18 patients [48.6%] and also MPO plasma levels were decreased in 17 patients [45.9%]. In the total population, a significant correlation was observed between MPO plasma levels and gene expression ($r=0.403$, $p<0.05$), hsCRP ($r=0.565$, $p<0.05$). CONCLUSION: Short-term statins therapy exhibit anti-inflammatory activity in patients with AMI. Our studies also show differential response to statins treatment in individual patients and it may be related with inter-individual variability. The molecular mechanisms of this phenomenon are not yet defined and require further research.

Keywords: Myeloperoxidase, C-reactive protein, Statins, Acute myocardial infarction, Real-time PCR

POSTERS

P100

Ring Chromosome 13: An Eventual Risk for Intellectual Disability, Surdity, Congenital Malformations and Leukemia

Inesse Ben-Abdallah-Bouhjar, Hanene Hannachi, Hela Ben-Khelifa, Ali Saad, Hatem Elghezal
Department of Cytogenetic and Reproductive Biology, Farhat Hached University Teaching Hospital, Tunisia

BACKGROUND AND PURPOSE:
The 13q deletions syndrome are currently known to share several common semiologic features, including, in particular intellectual disability ranging from moderate to severe, marked short stature, neural tube, brain and heart defects, microcephaly, genital malformations in males including undescended testes and hypospadias and characteristic facies.

METHODS AND MATERIALS:
in this study we report the cytogenetics investigations of three cases of ring chromosome 13 and we compare the growth and clinical features of these patients with previously reported cases, with a similar deletion on the long arm of chromosome 13.

RESULTS:
The patient karyotypes were 46,XY,r(13)(p11;q34) dn for the patient 1, 46,XX,r(13)(p11;q34) dn for the patient 2 and 46,XY,r(13)(p11:q14) dn for the patient 3, as a result of the deletion in the telomeric regions of chromosome 13. They were, therefore, monosomic for the segment 13q3413qter, in addition for the patient 3 the deletion was more large encompassing the segment 13q1413qter. Fluorescence in situ hybridization analysis showed loss of a specific subtelomeric 13q region in r(13) in three cases and loss of a specific locus 13q14/RB1 in the patient 3, who died from Acute leukemia during the cytogenetic analysis. Array CGH exploration of DNA's of patient 2 revealed a loss of at least 2.9 Mb on the short arm of chromosome 13 and a deletion of 4.7 Mb on the long arm of the same chromosome 13. Initially FISH defined, the chromosome breakpoints and were precisely localized by array CGH on 13q11 [arr 13q11q11 (18601703- 21593561)×1 dn] instead of 13p11, and 13q34 [arr 13q34 (109599699- 113964366)×1 dn].

CONCLUSION:
In our patients the deletion included the gene EFNB2, GJB6, ARHGEF and MYO16 are probably involved respectively in genital development, hearing loss, microcephaly and growth retardation.

Keywords: Ring chromosome 13, 13q deletion, FISH, Karyotype,

P101

Promoter Methylation of CASP8, FAS, BRCA1 Genes in Cervical and Esophageal Cancer

Anastassiya Perfilyeva, Lilia Skvortsova, Olzhas Ixan, Feruza Muratova, Bakytzhan Bekmanov
Institute of General Genetics and Cytology, Kazakhstan

Oncological diseases continue to be a major cause of morbidity and mortality all over the world. The problem is particularly acute in Kazakhstan: the mortality rate from this type of disease is higher in comparison with many other countries of the CIS and Asia. The aim of this study was to investigate the methylation status of the genes of DNA repair, cell cycle control and apoptosis (Fas, BRCA1, Casp8) in epithelial tumors of the esophagus and cervical cancer among residents of Almaty city and Almaty region (Kazakhstan). The objects of the study were samples of tumor and normal esophageal epithelium from 52 people and samples of cervical epithelium from 30 people. DNA samples were isolated from clinical material by standard method.

To detect the promoter methylation status of the genes Fas, BRCA1 and Casp8 was used a method of methyl-sensitive PCR. It is shown that a significant increase in the risk of esophageal cancer is associated with promoter methylation of the genes Fas (OR = 13,22; CI 95% = 0.71 - 245.12, p = 0.02) and Casp8 (OR = 7,70; CI 95% = 1.91 - 31.01, p = 0.003). The increase of the risk of developing cervical cancer is associated (high reliability) with the presence of promoter methylation of the genes BRCA1 (OR = 11.38; CI 95% = 1.17 - 110.42, p = 0.02) and Casp8 (OR = 41,89; CI 95% = 1.95 - 897.66, p = 0.0008). Determination of the methylation status of tumor suppressor genes will allow early diagnosis of the esophagus and cervix cancer, as well as to predict the dynamics of its development. Furthermore, the study of the methylation of tumor suppressor genes may promote in solving problems of gene therapy, in particular the possibility of applying demethylating drugs in the treatment of these cancers.

Keywords: DNA repair, Apoptosis, Cancer, Genes, Methylation

POSTERS

P102

Association of ACE Gene I/D Polymorphism and Hypertension in Diabetic Peripheral Neuropathy

Serbulent Yigit, Ahmet Inanir, Nursah Basol, Nevin karakus
Gaziosmanpasa University, Turkey

BACKGROUND AND PURPOSE: Diabetic peripheral neuropathy (DPN) is one of the most common diabetic chronic complications. The aim of the present study was to investigate the possible association between ACE gene I/D polimorphism and DPN and evaluate if there was an association with clinical features in a relatively large cohort of Turkish patients. METHODS AND MATERIALS: The study included 235 patients affected by DPN and 281 healthy controls. Genomic DNA was isolated and genotyped using polymerase chain reaction (PCR) assay for the ACE gene I/D polimorphism. Gender, age, disease duration, height, weight, BMI, hemoglobin, serum creatinine, HbA1C, triglyceride, total-HDL-LDL cholesterol, type of diabetes mellitus, history of retinopathy, history of hypertension, medications and smoking of patients were analyzed. RESULTS: The frequency of II genotype was significantly higher in patients with positive history of hypertension than the patients with negative history of hypertension (p=0.013). The frequencies of DD, ID and II genotypes in the patients were 43.0%, 38.7%, and 18.3% and in the controls were 33.8%, 43.8%, and 22.4%. Statistically significant difference was not observed between patients and controls according to genotype frequencies (p=0.096). CONCLUSION: Baseline characteristics of the patients according to ACE genotypes were similar, except for history of hypertension. The frequency of II genotype was significantly higher in patients with positive history of hypertension than the patients with negative history of hypertension (p=0.013). As a result, It showed that II genotype of ACE gene I/D polymorphism was a susceptibility factor for hypertension in DPN patients.

Keywords: DNA repair, Apoptosis, Cancer, Genes, Methylation

P103

Genetic Variants Involved in Interindividual Variability in Lutein Bioavailability in Healthy Men

[1,2,3]Patrick Borel, [1,2,3]Charles Desmarchelier, [1,2,3]Marion Nowicki, [1,2,3]Romain Bott
[1]*INRA, France,* [2]*INSERM, France,* [3]*Aix-Marseille University, France*

BACKGROUND AND PURPOSE:
The carotenoid lutein (LUT) is recovered at high concentration in the human macula. There is a huge interindividual variability in its bioavailability. The aims were i) to describe the interindividual variability in LUT response to dietary LUT, ii) to assess its effect on long term LUT status, and iii) to identify genetic variants involved in this phenomenon.

METHODS AND MATERIALS:
In a randomized, 2 test-meal clinical study, 39 healthy males volunteers eated either a test meal in which was added 15 mg free LUT as a supplement, or the same meal in which was added 100 g tomato purée. LUT was measured in plasma chylomicrons (CM) isolated at regular interval times, up to 8 h after meal intake. The association of SNPs, in or near genes assumed to play a role in postprandial CM LUT response (3055 SNPs), with the low (< mean response - 1 SD) vs normal postprandial CM LUT response (0-to-8 h postprandial area under the curve) was assessed by partial least squares discriminant analysis (PLS-DA).

RESULTS:
The subject CM LUT responses to the test meals were very variable. The subject CM LUT responses measured after the two test-meals were positively correlated (P<0.0001). The subject fasting plasma LUT concentrations were positively correlated to their CM LUT responses measured after both meals (P<0.05). A significant (P=1.65 x 10-7) and validated PLS-DA model, which included 32 SNPs in 13 genes, explained 74% of the variance in the CM LUT response.

CONCLUSION:
The interindividual variability in CM LUT response to dietary LUT is an intrinsic characteristic of the subjects. The ability to responds to dietary LUT likely affects the long term blood status in LUT. A combination of SNPs in 13 genes, 9 of them related to postprandial CM metabolism, explains a significant part of this characteristic.

Keywords: Nutrigenetic, Personalised nutrition, Lutein, Bioavailability, Single nucleotide polymorphisms

POSTERS

P104

Lack of Association Between -2383 (rs 3761549) C>T Promoter Polymorphism of Foxp3 Gene with Breast Cancer- A South Indian Study

[1]VR Vinish Ramachander, [1]G Maruthi, [2]TSR Murthy, [1]Parveen Jahan
[1]*Department of Genetics, Osmania University, India,* [2]*Railway Central Hospital, Lalaguda, Hyderabad, India*

BACKGROUND AND PURPOSE:
Breast cancer, a malignant breast neoplasm is one of the leading causes of female death worldwide accounting for 3.1% annual global increase in developing countries like India. It was estimated that 29% of the new cancer cases identified in women will be of breast cancer. Etiology of the breast cancer depends on various epidemiological factors however; genetic susceptibility plays a major role in development of the disease. Transcription factor Foxp3 a tumor suppressor gene which controls the function of Treg cells is down regulated in Breast Cancer. The main aim of the study is to evaluate the potential influence of Foxp3 -2383 (rs 3761549) C>T polymorphism with Breast Cancer in South Indian Population.

METHODS AND MATERIALS:
Present study was conducted on a total of 322 individuals including 202 patients and 120 controls. 2ml of peripheral blood sample was collected in EDTA vacutainer and genomic DNA was isolated by salting out method using standard established protocol. All the samples were genotyped for the Foxp3 -2383 C>T polymorphism with specific primers using PCR-RFLP and data was analyzed using Chi-Square test and Odds Ratio calculator.

RESULTS:
The frequency of CC, CT and TT genotypes were 2%, 98%, 0% and 1.7%, 98.3%, 0% respectively in patients and controls respectively. TT genotype was found to be completely absent in this study. The results showed that there is no association with Foxp3 -2383 C>T polymorphism between controls and breast cancer patients and within the patients with respect to premenopausal and postmenopausal group.

CONCLUSION:
In conclusion our finding suggests that there is no association between Foxp3 -2383 (rs 3761549) C>T polymorphism and breast cancer in South Indian Population.

Keywords: Breast cancer, FOXP3, Assosiation study, South Indian population

P105

CNV-Merger: A Copy Number Variation Merging and Analysis Tool

[1,4]Noha A. Yousri, [2]Khalid A. Fakhro, [3]Ronald G Crystal, [1]Karsten Suhre
[1]*Weill Cornell Medical College in Qatar, Department of Physiology and Biophysics, Doha, Qatar,* [2]*Weill Cornell Medical College in Qatar, Department of Genetic Medicine, Doha, Qatar,* [3]*Weill Cornell Medical College, Department of Genetic Medicine, New York,* [4]*Computer and System Engineering, Faculty of Engineering, Alexandria University, Egypt*

BACKGROUND AND PURPOSE: Copy number variations are structural variations in the human genome, and may be characteristic to each population, or to disease phenotypes. CNVs are detected using both array and next generation sequencing (NGS) technologies. A number of processing steps are needed to transform individual CNVs into CNVRs (CNV Regions) and annotate them in aggregate to determine the impact of their frequency, genomic overlap and gene perturbation on population phenotypes. METHODS AND MATERIALS: A comprehensive R tool, CNV-Merger, is developed for processing CNVs from both array and NGS sources, by: a) Merging CNVs, including any number of relevant phenotypic features, into CNVRs, b) Analyzing CNVRs by providing counts, histograms and other statistical features relevant to downstream data analysis, c) Integrating CNVs from different platforms to redefine breakpoints, and d) Performing clustering and PCA analysis to detect possibly related CNVRs. Additionally, the tool is being optimized to integrate with existing annotation tools to help parse annotation features and provide basic counts and tables for all CNVRs within a population. RESULTS: CNV-Merger is tested on CNVs of 108 Qataris obtained from high and low resolution platforms. The high resolution set is leveraged to set accurate breakpoints within the low resolution CNVRs. Histograms and PCA analysis were used to reveal the structure of copy number deletions and duplications in Qatari subpopulations. Functional annotation from external databases is used to detect novel CNVRs, and for gene and disease enrichment analysis. CONCLUSION: An R tool for processing and merging CNVs is developed and tested on CNVs obtained from Qatari population using high and low resolution detection platforms. The tool's small footprint and speed are ideal for processing, mapping and generating distributions of population level CNVs in an efficient packaged environment. Once accomplished, the tool will be publicly available.

Keywords: CNVs, Next generation sequencing, Annotation, Next generation data analysis

POSTERS

P106

Genetics of Obesity in Qatari Families

[1,2]Mashael Al-Shafai, [2]Mario Falchi, [1]Karsten Suhre, [2]Philippe Froguel, [1]Khaled Machaca
[1]*Weill Cornell Medical College in Qatar, Qatar,* [2]*Imperial College London, UK*

BACKGROUND AND PURPOSE:
Obesity is a major health problem that has reached epidemic levels worldwide. Genetic studies have demonstrated the high heritability and heterogeneity of obesity. Despite the success in identifying many genetic loci involved in obesity, they can only account for about 2% of the estimated heritability of body mass index (BMI), suggesting that much remains to be revealed. In this study, we developed a cohort to focus on identifying novel rare obesity variants in Qatari families in order to further elucidate the heritability of the disease.

METHODS AND MATERIALS:
Qatari families (n=8) with multiple obese members were ascertained through an obese proband (adult with BMI>30 kg m-2 or child with BMI>2SD above the mean), and were recruited through home visits. Genome wide genotyping was performed for a total of 64 subjects using illumina HumanOmni2.5-8 BeadChip and whole genome sequencing (WGS) using illumina hiseq2500 platform (35x coverage). Linkage analysis was performed using Merlin to obtain candidate obesity regions. The identified regions will be further analyzed using the sequencing data, to find potential genetic variants involved in obesity.

RESULTS:
Nonparametric linkage analysis and variance component linkage analysis for obesity related traits have identified a group of candidate obesity regions, thus, narrowing down variants of potential interest. A prioritization strategy will be applied to the obtained variants based on frequency and functionality to focus on a reduced number of most likely candidates.

CONCLUSION:
The detection of obesity variants in a small sample size is unlikely to be simple and will be highly dependent on the nature of the causative variants. However, this study is one of the first studies conducted on the genetics of obesity in a Qatari cohort, and can serve as a pilot for future studies to provide better understanding of the underlying genetic determinants of obesity.

Keywords: Obesity, Genetic variants, Linkage analysis

P107

A Study of mtDNA Control Region HVR-1 Molecular Profile in Omani Population

Aisha Alkhayat AlShehi, Aisha AlHosni
Sultan Qaboos University

The analysis of mitochondrial DNA genome, in particular the control region, has been widely used in forensic analysis and population genetics, where it is used as genetic marker to describe human variation, population substructure and migration pattern and to trace maternal lineages. Studies of mitochondrial DNA variation have proven to be useful in examining evolutionary process in human and reconstructing population histories. Arabian Peninsula is assumed to be one of the first inhabited regions following the expansion of early Homo sapiens out of Africa. Oman is located in the southeast coast of the Arabian Peninsula. This project, we investigated the hypervariable segment of the control region, HVR-1 (16024-16569) in the mitochondrial DNA (mtDNA) sequence, in 114 unrelated individuals to determine genetic variation and types of haplogroups found in Omani population. This region, HVR-1, contains highly polymorphic sites due to accumulative point mutations. MtDNA was extracted from saliva by safe, non-toxic and efficient method using salt and protinase K, amplified by PCR and directly sequenced. DNA sequences were aligned against the revised human Cambridge Reference Sequence (rCRS), (>gi|13959823|ref|NC_001807.3| human mitochondrion, complete genome. The Haplogroups were scored using online software tools and the frequency of the haplogroups were determined using standard statistical tools. So far 51 variable sites were reveled for HVRI (16024-16569) when compared to reference sequence. SNP used in haplogroups detection showed that the Omani population is a mix of African, Asian and Eurasian haplogroups with highest frequency of haplogroups U and J that is similar to other Arab populations.

Keywords: Mitochondrial DNA, Population migration, HVR-1, Haplogroups

POSTERS

P108

Cellular Impact of Missense Mutations in the Very Low Density Lipoprotein Receptor (VLDLR) Gene Associatedwith Disequilibrium Syndrome

[1]Ali S. Al-Blooshi, [1]Ahmed Al Hosani, [1]Ahmed M. Al-Nuaimi, [1]Anne John, [2]Lihadh Al-Gazali, [1]Bassam R. Ali
[1]*Department of Pathology, College of Medicine and Heath Sciences, United Arab Emirates University, UAE,* [2]*Department of Pediatrics, College of Medicine and Heath Sciences, United Arab Emirates University, UAE*

BACKGROUND AND PURPOSE: Disequilibrium syndrome is a genetically heterogeneous condition that combines autosomal recessive nonprogressive cerebellar ataxia with mental retardation and the subclass disequilibrium syndrome type 1(CAMRQ1) has been attributed to mutations in the VLDLR gene. The low density lipoprotein receptor (LDLR) gene family consists of cell surface proteins involved in receptor-mediated endocytosis of specific ligands. Previously our group has identified the first homozygous missense founder mutation (c.2117 G>T; p.C706F) in VLDLR to cause DES without quadrupedal locomotion in two unrelated Omani families from UAE. The affected cysteine residue is highly conserved and according to the predicted structure of the VLDLR domains, the mutation is likely to result in the mis-folding of the protein and degradation by ER quality control machinery leading to the loss of its biological function.
METHODS AND MATERIALS: To test the ER quality control hypothesis, we generated the p.C706F mutant along with other reported pathogenic missense mutants (P.D487Y and p.D521H) by site directed mutagenesis. The mutant constructs were generated using wild type VLDLR having a C-terminal GFP or HA epitope tag. The mutant and wild type constructs were transiently transfected into HeLa cells and the subcellular localization of the proteins were determined by confocal microscopy. Calnexin was used as a marker for Endoplasmic Reticulum (ER).
RESULTS: All the three missense mutants were found to be predominantly retained in ER, as confirmed by co-localization with the ER marker calnexin, and the localization pattern was distinct from the plasma membrane localization of the wild-type VLDLR. This suggests the involvement of the ER quality control machinery in Disequilibrium Syndrome pathology.
CONCLUSION: ER retention and the subsequent ER-Associated protein Degradation (ERAD) are likely to be the cellular mechanisms underlying the three missense mutations causing Disequilibrium Syndrome.

Keywords: Breast cancer, FOXP3, Assosiation study, South Indian population

P109

Genetic and Functional Characterization of Orphan Diseases

[1]Carine Bonnard, [2]Hanan Hamamy, [3]Hulya Kayserili, [1]Bruno Reversade
[1]*Institute of Medical Biology, A*STAR, Singapore,* [2]*Department of Genetic Medicine and Development, Geneva University, Geneva, Switzerland,* [3]*Medical Genetics Department, Istanbul Medical Faculty, Istanbul University, Turkey*

Although Genetic Orphan Diseases are rare, the pathologies they cause are often very common. Using revolutionary tools such as SNP genotyping and next generation sequencing, we aim to identify the genes and rare variants associated to fully penetrant diseases, but most importantly we are interested on understanding the biological pathways and mechanisms which underlie the pathology of these disorders. Besides disclosure of a gene function in the context of normal embryonic development and disease state, we intend to reveal new biological nodes whose variation contributes to more frequent pathologies. To achieve this aim, we have implemented a set of workflows according to the disease type and availability of samples. Biological specimens are collected from patients and unaffected relatives and stored in a Biobank together with pedigree and detailed clinical manifestations. Upon identification of the causative gene, primary cells are generated for functional validation and downstream application.

For instance, derivation of induced pluripotent stem cells from primary fibroblasts is now commonly performed in our laboratory to model genetic disorders. Besides in vitro modelling, we have demonstrated pathogenicity of different diseases using genetic engineering in animal models such as mouse, zebrafish and Xenopus. Phenocopying human syndromes does not only help to understand the disease origin and mechanisms but may also reveal unsuspected anomalies in patients. Finally, since different genes can result in similar disease phenotypes, we investigate the functional link between the encoded proteins by using BioID technique. This innovative approach allows us to validate direct or indirect protein interactions and to elaborate a protein network for a common phenotype, offering alternative surrogates for diagnostic and therapeutic solution. To conclude, we trust that by studying rare genetic diseases using these biological and engineering tools, we will elucidate new pathological mechanisms that can contribute greatly to research and treatment for more common diseases

Keywords: Consanguinity, Hereditary, Congenital, Rare disease, Biobank

POSTERS

P110

Association Analysis of Methyl CpG Binding Domain 2(MBD2) gene polymorphisms with schizophrenia in South Indian Population

[1]Sarada Lekshmi K R, [1]Sanish Sathyan, [2]Indu K R, [3]Chandrasekharan Nair, [1]Moinak Banerjee
[1]*Rajiv Gandhi Centre for Biotechnology, India,* [2]*Mental Health Centre, Thiruvananthapuram, India,* [3]*Nair's Hospital, Cochin, India*

Schizophrenia is one of the most debilitating disorders affecting about 1% of the world population. The etiology is complex involving a major genetic contribution as well as environmental factors interacting with the genetic susceptibility. Epigenetic processes may contribute to environment induced phenotypic variation by modifying gene expression. The capacity to respond to environmental cues is often heritable, indicating a genetic basis for epigenetic modifications.DNA methylation is the most common epigenetic modification and aberration that have been implicated in the pathophysiology of various complex disorders including schizophrenia. These variations might be due to extrinsic factors like diet, age etc or due to intrinsic variations in the genes involved in maintenance of DNA methylation. Methyl CpG Binding Domain 2 is a methylated DNA binding protein and has been found to be functioning as a demethylating enzyme.
The objective of the study was to investigate the association of polymorphisms in MBD2 gene with schizophrenia in a south Indian population. DNA was isolated from 300 patients and 300 healthy controls after obtaining informed consent.

Only patients suffering from schizophrenia diagnosed by DSM-IV/ ICD 10 have been enrolled for this study.Age, Sex and ethnicity matched controls were recruited for the study. We selected 6 SNPs from MBD2 gene based on their functional relevance and tagging status. Samples were genotyped using allele specific amplification followed by fluorescence detection (KASPar) and PCR-RFLP. rs1259938, an SNP found in 3'UTR was found to be associated with the disease in allelic, genotypic ($p<0.001$) combinations.

Keywords: Schizophrenia, MBD2 gene, epigenetics, SNPs, Association study

P111

ACE Gene Polymorphism and Serum ACE Level in Egyptian Type 2 Diabetic Patients with and those without Nephropathy

[2]Olfat Shaker, [3]Manal F. Ismail, [1]Esmat Ashour 4Heba M. Yousif , [3]Mai Afify, [1]Weaam Gouda Ali
[1]*Biochemistry Dept., National Research Centre, Dokki, Giza, Egypt,* [2]*Medical Biochemistry Dept., Faculty of Medicine, Cairo University, Egypt,* [3]*Biochemistry Dept., Faculty of Pharmacy, Cairo University, Egypt,* [4]*Internal Medicine Dept., Faculty of Medicine, Cairo University,*

BACKGROUND AND PURPOSE: One of the most common complications of diabetes mellitus (DM) is diabetic nephropathy (DN). Angiotensin- converting enzyme (ACE) gene was the first candidate gene of renin-angiotensin system (RAS) for predisposition to DN. Investigation whether the ACE insertion/deletion (I/D) polymorphism is associated with Egyptian type 2 diabetic mellitus (T2DM) patients and nephropathy as a complication. In addition, the study investigated the relationship between variants of ACE I/D gene polymorphism, serum ACE level and the progression of nephropathy in Egyptian T2DM patients.

METHODS AND MATERIALS: A total of 180 T2DM patients (96 with nephropathy and 84 without nephropathy) besides 80 healthy (non-diabetic) age-matched subjects were recruited for this study for comparison. The (I/D) polymorphism of the ACE gene was investigated using PCR and serum ACE levels were determined using ELISA.

RESULTS: The frequency of ACE DD genotype and D allele was significantly higher in both DM without nephropathy and DN patients when the results of each group was compared to control healthy subjects, while the frequency of ACE DD genotype and D allele in patients with DN was not significantly different from diabetic patients without nephropathy. In addition our results showed that in both T2DM with and without nephropathy the mean values for serum ACE levels were higher in D allele versus to I allele when the results of each group were compared to control subjects.

CONCLUSION: The present study showing a strong association between the D allele and/or DD homozygous of ACE gene and diabetic patients with and those without nephropathy, most probably, is due to T2DM itself. In addition, individuals with D allele have higher levels of serum ACE compared to those having I allele. ACE gene polymorphism and serum ACE levels may serve as a susceptibility biomarker for T2DM, yet not a risk factor for susceptibility to diabetic nephropathy

Keywords: Diabetic nephropathy, Type 2 diabetes mellitus, Angiotensin-converting enzyme, Gene polymorphism, Serum ACE level

POSTERS

P112

Inflammatory Responses in Vitiligo- A Study in South Indian Population

[1]Yashwanth Ala, [1]Khalid Pasha, [2]Vijayalaxmi Valluri, [1]Parveen Jahan
[1]*Department of Genetics, Osmania University, India,* [2]*Lepra India-Blue Peter Public Health and Research Centre, Cherlapally, Hyderabad*

BACKGROUND AND PURPOSE:
Cytokines are the important mediators of immunity. Disequilibrium in cytokine network may paramount autoimmune disease susceptibility and severity. Vitiligo is an acquired depigmenting disorder resulting in the destruction of melanocytes in the epidermis affecting 1-4% worldwide with no prediction for sex or race. The incidence of vitiligo is found to be 0.5 to 2.5% in India with a high prevalence of 8.8% in Gujarat and Rajasthan. The cause of the vitiligo remains obscure although the autoimmunity hypothesis has been now recognized as the most influential pathogenic mechanism. The present study was conducted to determine the equilibrium between two important cytokines IFN-gamma and IL-10 in vitiligo. Our aim to determine the relationship between IFN-gamma and IL-10 in Vitiligo patients.

METHODS AND MATERIALS:
Estimation of IFN-y and IL-10 levels in human serum from 60 vitiligo patients and healthy controls using ELISA. Data analysis was performed using One-way ANOVA and t-tests.

RESULTS:
Vitiligo patients showed increased levels of IFN- y (11.7±5.2 pg/ml), whereas the IL-10 levels were increased in controls. Moreover, ratio of IFN-y to IL-10 was also significantly higher in patients (1.5±0.7 pg/ml) indicating pro inflammation.

CONCLUSION:
Enhanced production of pro inflammatory cytokine (IFN-γ) in patients plays a vital role in the progression and the severity of the disease suggesting Th1 mediated immune response in the pathogenesis of vitiligo.

Keywords: Vitiligo, IFN-gamma, IL-10, Inflammatory response

P113

Amyotrophic Lateral Sclerosis Family Form

Assia Boulefkhad, Naima Taghane, Yamina Sifi, 1Abderahim M'zahem, Fatima Serradj
University Hospital Center, Algeria

BACKGROUND AND PURPOSE:
Amyotrophic lateral sclerosis (ALS) is a degenerative motor neuron disease causing muscle deficit, muscular with a charge of death usually within 3 to 5 years after the onset of respiratory disease symptoms. It mainly affects adults aged 50 to 60 years. Approximately 10% of ALS cases are familial (SLA F), transmission is autosomal dominant in most cases, and it is very rarely autosomal recessive or X-linked. 15 to 20% of familial cases, a mutation in the gene encoding the protein superoxide dismutase Cu / Zn (SOD1) have been identified. Mutations in other genes have been described. To describe the phenotype of ALS F in 2 Algerian families with autosomal dominant transmission to guide genetic diagnosis.

METHODS AND MATERIALS:
Six patients from two consanguineous families who have more vertical transmission of the disease, with involvement of the mother, maternal uncle, sister and the first index case in the 1st family, the father and 2nd the index case in the second.

RESULTS:
4 patients from the 1st family began their disease at an early age (around 40 years) by the lower limbs and presented a few months breathing and bulbar problems causing the death of three patients. 2 patients from the 2nd family began their illness to 45 years by the upper limbs with a much longer evolution and later respiratory disorders causing the death of one patient. Genetic diagnosis is in progress.

CONCLUSION:
The difference in the clinical presentation in two families and after results of genetic diagnosis may favor the analysis of a gene or another depending on the phenotype.

Keywords: Amyotrophic lateral sclerosis, Family, Algerian

POSTERS

P114

Lack of Association of MDR1 C3435T Polymorphism with Chronic Myeloid Leukemia

[1]Samia Dorgham, [2]Meriem samia Aberkane, [1]Wefa Boughrara, [1]Abdallah Boudjema
[1]*Molecular and Cellular Genetics Laboratory, University of Science and Technology of Oran-Mohamed Boudiaf (USTO-MB) Algeria,* [2]*Department of Molecular Biology and Cytogenetic, Establishment University Hospital of Oran, Algeria*

BACKGROUND AND PURPOSE:
MDR1 (miltidrug resistance) gene encodes a transmembrane active efflux pump for a variety of environmental toxins and xenobiotics. A number of studies have evaluated its association with cancer risk. Chronic myeloid leukemia (CML) is a myeloproliferatif disorder, although the clinical and biological aspects are well documented, little is known about individual susceptibility to this disease. Many investigations have reported the relationship between MDR1 and response to treatment of CML but only a few was reported about its relationship with CML risk.In our study through a case-control study we analyzed the prevalence of the polymorphism MDR1 C3435T in Algerians CML patients.

METHODS AND MATERIALS:
Using TaqMan® allelic discrimination assay, we investigate MDR1 C3435T polymorphism distribution in 85 cases of CML and 100 healthy subjects, all from Algeria. RESULTS: The results demonstrated no statistical difference in MDR1 C3435T frequency distribution between patient and control groups.

CONCLUSION: Our findings suggest that MDR1 C3435T gene variants have no significant influence on the susceptibility to CML in the Algerian population.

Keywords: Chronic myeloid leukemia, MDR1 C3435T polymorphism, Association study

P115

Evaluation of Serum Neural S-100B and TGF-B1 levels to Assess Brain Injury in Egyptian Patients with Phenylketonuria

[1]Lamiaa Mageed Ibrahim, [1]Nagwa Meguid, [1]Esmat Ashour, [2]Mohga S Abdallah, [2]Hayat M Sharada
[1]*National Research Centre, Egypt,* [2]*Helwan University, Egypt*

BACKGROUND AND PURPOSE: Phenylketonuria (PKU) is an inherited metabolic disorder characterized by high phenylalanine (Phe) levels in blood. Tissue accumulation of L- Phe is the biochemical hallmark of human PKU, clinically characterized by mental retardation and other neurological features. The mechanisms of brain damage observed in this disorder are poorly understood. Serum neural protein (S-100B) and transforming growth factor beta-1 (TGF-B1) proteins are highly specific for nervous tissue where their roles are not yet fully understood. Purpose: To evaluate serum S-100B and TGF-B1 protein levels in PKU patients as brain injury biomarkers. METHODS AND MATERIALS: Nineteen (n=19) PKU patients from 15 families were selected from the Children with Special Needs Clinic and Clinics Department, National Research Centre. Their age ranged between 2 and 21 years, in addition to 15 healthy controls with same age. Blood samples were drawn to investigate circulating serum levels of S-100B and TGF-B1 using ELISA technique for all the studied cases. RESULTS: Statistical significant increase of serum S-100B and TGF-B1 concentrations were present in PKU patients compared to controls. Regarding sensitivity and specificity, in PKU patients, S-100B showed high sensitivity and specificity values compared to TGF-B1. In addition, there was a negative correlation between S100B and Phe and a positive correlation between TGF-B1 and Phe CONCLUSION: Serum S-100B and TGF- B1 protein levels could be useful peripheral markers of nervous system damage in patients with phenylketonuria

Keywords: Phenylketonuria, Phenylalanine, Serum neural protein (S-100B), Transforming growth factor beta-1, Brain injury

POSTERS

P116

The Role of Consanguinity in Transmitting Genetic Diseases: Are Saudis Aware?

Fahad Alfares, Muneera Alhusain, Saleh Alhasan
King Saud University, Saudi Arabia

BACKGROUND AND PURPOSE:
Saudi Arabia is considered one of the highest rate countries with genetic and metabolic diseases due to high rate of consanguinity, ultimately resulting in burden of chronic and complicated mentally and physically disabled children. This study was set to evaluate the awareness of Saudis about the relationship between consanguineous marriages and transmitting genetic diseases, and the awareness about the current limitation of the premarital screening program.

METHODS AND MATERIALS:
Structured questionnaire contains 31 questions were set to assess the level of awareness about consanguinity and its role in transmitting genetic diseases, and the awareness about the current limitation of the premarital screening program. The questionnaires were distributed among participants to the premarital screening clinics in Riyadh.

RESULTS:
Our data suggest that 71.7% of participants had low awareness, 17.1% had moderate awareness, and 11% had high awareness. Male gender, old age, high educational level, non-consanguineous parents and family history of genetic disease were significantly associated with high level of awareness (p value <0. 05). 64% of participants were not aware about the limitation of the current premarital screening program. More than 60% agreed on the importance of genetic counseling in reducing the incidence of genetic diseases. Personal preference was the strongest motivation toward consanguineous marriages.

CONCLUSION:
Since the most effective way to reduce the incidence of genetic diseases is through prevention, defined comprehensive educational programs to educate the public about the benefits and risks of consanguineous marriages as well as the limitations of the current premarital screening program should be addressed to the population. More emphasis should be on high school and college students , special attention to families with known genetic diseases.

Keywords: Birth defect, Unusual phenotype, Exome sequencing, Animal model, Physiopathology

P117

Looking for More Families with Congenital Birth Defects or Unusual Phenotype

[1]Nathalie Escande-Beillard, [1]Mohammad Shboul, [2]Hanan Hamamy, [3]Hulya Kayserili, [1]Bruno Reversade
*[1]IMB, A*STAR, Singapore, [2]Department of Genetic Medicine and Development, Switzerland, [3]Department of Medical Genetics, Istanbul, Turkey*

Our group research focus is to understand the principles that govern normal embryogenesis in humans. Thanks to the crucial help of clinicians, we take advantage of rare human's congenital birth defect from highly consanguineous population to characterize novel gene mutations by high throughput exome sequencing. Next, our goal is to address the clear mechanistic underlying the physiopathology of the diseases by using appropriate animal models and tools from biochemistry and molecular biology.

We have already identified:
PYCR1 causing an autosomal recessive form of premature ageing, CHSY1 as a novel NOTCH modulator essential for limb patterning, IRX5 as crucial transcription factor for craniofacial development, TGFBR1 responsible for multiple self-healing squamous epithelioma and AGAAB causing heterogeneous forms of punctate palmoplantar keratoderma. We have many more ongoing projects and in order to unravel more causative genes, we wish to increase our patient's cohorts with any unusual phenotype or family inherited disorders such as skin, ageing, cancer, cardiovascular, neurocognitive and craniofacial disorders.

Keywords: Birth defect, Unusual phenotype, Exome sequencing, Animal model, Physiopathology

POSTERS

P118

The Relationship between the MTHFR and MDR1 Polymorphisms and Response to Methotrexate Treatment in RA Algerian Population, and their Correlation with Activity of the Disease

[1]Wefa Boughrara, [1]Chahinez Dahmani, 2Meriem Aberkane, [3]Ahmed Benzaoui, [1]Abdallah Boudjema

[1]University of Science and Technology of Oran-Mohamed Boudiaf (USTO-MB), Algeria, [2]Department of Pharmacy, University Es Senia of Oran, Algeria, [3]Department of Rheumatology CHUO (Oran), Algeria

BACKGROUND AND PURPOSE: Methotrexate (MTX) is the most used worldwide among disease-modifying antirheumatic drugs for treatment of rheumatoid arthritis (RA). As an analog of dihydrofolic acid, it generates an anti-inflammatory effect, catalyzes the conversion of homocysteine to methionine and prevents the conversion of UMP to TMP. Several aspects about the pharmacology of MTX are not clear. The mechanisms most frequently involved in variability in clinical response to MTX are a modification of the expression of target enzymes intervening in the pharmacokinetics of MTX. The aim of this study is to determine the impact of C677T and A1298C polymorphisms in the methylenetetrahydrofolate reductase gene (MTHFR), and C3435T polymorphism in multidrug resistance 1 (MDR1) on response to MTX treatment. The impact of these polymorphisms on height activity of RA is also tested.

METHODS AND MATERIALS: One hundred teen patients with RA and one hundred one controls are enrolled in this study. The efficacy is evaluated using the disease activity score 28 according with EULAR criteria. Genotyping was performed by real time PCR (Taqman). Data were analyzed by χ2-test and genotype relative risk.

RESULTS: Our findings suggest that there is no evident distribution of alleles/genotypes of these polymorphisms between responder/non responder. However the 1298C allele of MTHFR gene is associated with height activity of RA (39.74% vs 26.8%, p=0.03, OR=1.8), this result was confirmed by genotypes analysis (71.79% vs 48.45%, p=0.01, OR= 2.63). Additionally, the MDR1 genotypes 3435TT+3435CT seems to increase activity of RA (29.09% vs 53.46%, p=0.04, OR=2.09); nevertheless the C667T is not correlated with RA activity.

CONCLUSION: This study revealed, for the first time in the Algerian population that none of the tree polymorphisms tested shows any association with response of MTX treatment, but the A1298C and C3435T polymorphisms could influence on activity of RA

Keywords: Rheumatoid arthritis, Methotrexate, MTHFR, MDR1

P119

Genetics of Type 2 Diabetes among Qatari Families

[1,2,4]Wadha Al Muftah, [1]Mario Falchi, [3]Cindy McKeon, [1]Philippe Froguel, [2]Karsten Suhre

[1]Department of Genomics of Common Disease, Hammersmith campus, Imperial College London, Qatar, [2]Department of Physiology and Biophysics, Weill Cornell Medical College in Qatar, [3]Clinical Research Core, Weill Cornell Medical College – Qatar, [4]Qatar Science Leadership Program, Qatar Foundation, Qatar

BACKGROUND AND PURPOSE:
T2D has become a major challenging health issue worldwide in the current decade. Several approaches have been used to identify genetic variants involved in the patho-physiology of T2D and glucose hemostasis, such as linkage analysis and genome wide association studies. In this project we aim to identify novel genetic variants and shared novel mutations between different individuals among different Qatari families.

METHODS AND MATERIALS:
Multi-generational consanguineous Qatari families (n=9) were included in this project. Families with 50 subjects were investigated using Illumina HumanOmni2.5M bead chip platform to perform genome-wide genotyping. Also, whole genome sequencing was performed using Illumina HiSeq2500 system with a minimum average coverage of (40x). Linkage analysis was performed using MERLIN software to identify chromosomal regions associated with the disease phenotype.

RESULTS:
Model free linkage analysis and variance component analysis were run for discrete trait and diabetes trait (Hba1c), respectively. Regions of interest were identified and analyzed further to detect novel variants associated with T2D.

CONCLUSION:
Although the sample size is small and difficult to identify significant linkage regions, investigating Qatari population may identify novel causative variants associated with T2D.

Keywords: Diabetes mellitus Type 2, Linkage analysis, Genetic variant

POSTERS

P120

Genetics of Obesity in Saudi Arabian Population

[1]Haya Al-Saud, [1]Philippe Froguel, [1]Mario Falchi, [2]Aayed Al-Qahtani
[1]Imperial College London, Department of Genomics of Common Disease, United Kingdom, [2]King Saud University, Saudi Arabia

BACKGROUND AND PURPOSE:
Obesity is a complex polygenic trait with high heritability rate estimated at 40-70%. Candidate gene, linkage and genome wide association (GWAS) studies have helped identify large set of genes and genomic regions associated with obesity. In this study we employed the strategy of using 'extreme' sub-groups of obese patients (syndromic or Mendelian) to identify new genes and loci for obesity in the population of Saudi Arabia.

METHODS AND MATERIALS:
Here we investigated the contribution of copy number variation (CNV) to obesity in Saudi 80 adults/children that have mental retardation, dysmorphic features and obesity or morbid obesity and 71 normal controls. We used PennCNV algorithm to detect CNVs from Affymetrix 6.0 whole genome SNP array. CNVs detected were later validated by Multiplex Ligation-dependant Probe Amplification (MLPA). We also investigated 10 Saudi multiplex consanguineous families, with children that have extreme obesity, to seek causative loci for new Mendelian forms of obesity using linkage analysis, whole exome sequencing and Sanger sequencing.

RESULTS:
We report 1 individual with a CNV heterozygous deletion in chromosome 16p11.2. We later assessed the contribution of chromosome 16p11.2 heterozygous deletion to common forms of obesity in a set of 200 obese Saudi, Sudanese and Yemeni samples and found a couple of these samples carrying this deletion. From the linkage analysis and whole exome sequencing, one family carried a novel homozygous mutation in a known monogenic gene. This mutation is the first report in Saudi Arabia.

CONCLUSION:
Using the two aspects of this study, we have identified novel and first reports of obesity causing variants. In the future we hope to further identify new highly-penetrant causes of obesity, which might also be observed as a component of population collections of "common" obesity

Keywords: Obesity, GWAS, CNVs, Genetic variants

P121

Validation of High Resolution aCGH Technology for Detecting Copy Number Changes in DMD Gene Causing Becker and Duchenne Muscular Dystrophy

Khitam Abu Khadija, Shabeer Padariyakam, Sarmad Ali, Zafar Nawaz
Cytogenetics and Molecular Cytogenetics Laboratory, Hamad Medical Corporation, Qatar

The oligonucleotide array comparative genomic hybridization (aCGH) have been adopted readily by genetic diagnostic laboratories as a rapid, cost-effective, highly sensitive and accurate approach for studying chromosomal abnormalities as well as for the detection of single- and multiexon deletions or duplications in single gene disroders. We have successfully validated and implemented a aCGH based assay for detecting single- and multi-exon deletions and duplication in DMD gene, an X-linked gene causing Duchenne and Becker muscular dystrophy, DMD and BMD diseases, affecting approximately 1 in 3,500 males. The DMD gene is composed of 79 exons. The mutational spectrum of disease is complex. Deletions account for approximately 65% of DMD mutations and 85% of BMD mutations. Duplications occur in approximately 6–10% of males with either DMD or BMD. The aCGH analysis of DMD gene can be used to confirm a clinical diagnosis of DMD, characterize the type of DMD gene mutation and perform prenatal testing and carrier testing for females.

Keywords: DMD, BMD, aCGH, Microarray, Monogenic

POSTERS

P122

Sero-Prevalence of Sexually Transmitted Disease (HIV, Syphilis, Hepatitis-B and Hepatitis-C) in Volunteer Blood Donors of Jail Inmates and Student Community in Punjab Province, Pakistan

[1]Shahida Hasnain, [2]Humaira Yasmeen, [2]Imran Qadeer
[1]*Women University Multan, Pakistan,* [2]*Department of Microbiology & Molecular Genetics, University of the Punjab Lahore, Pakistan*

BACKGROUND AND PURPOSE:
Cohort studies of prisoner and student community volunteer blood donors recruited in 2007-2012 in 30 jails and 30 educational institues of Punjab province were done. In Punjab, there are 32 prisoners jail that are nearly three times overcrowded with 62500 prisoners (undertrial, convict and condemned prisoners). A number of studies indicate that even in prisons of developed countries prevalence of transmission of sexually transmitted infections is high.

METHODS AND MATERIALS:
Ten thousand (10,000) apparently healthy blood donors were assessed for the sero-prevalence of human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphillus (RPR) using a commercially available Enzyme Linked Immunosorbent Assay (ELISA)-based kit. Information was obtained for risk factors using structured questionnaire.

RESULTS:
Out of the 5,000 samples screened in each community, 337 (6.74%) in student community and 1424 (28.48%) in prisoner community were sero-positive. Subjects aged 15-45 years recorded 2.20% HBV, 4.12% HCV, 0.42% RPR and no HIV positivity in students while in prisons 5.28% HBV, 12.32% HCV, 0.18% HIV and 10.70% RPR positivity. Subjects aged 15-25 years are more HBV positive (2.51%) and (7.94%) while subjects aged 25-35 years were more HCV positive (4.88%) and (14.18%) in student and prisoner community respectively. Unfortunately, sero-prevalnce rate is high in prisoner community as compared to student community.

CONCLUSION: Overcrowding, poor hygienic and close living conditions stake prisoners at a very high risk for acquisition of sexually transmitted infections as compare to student community. Public awareness and vaccination programme should be improved in the community on urgent basis.

Keywords: STDs, ELISA, Sero-prevalence

A Single Source For Your Lab

GULF SCIENTIFIC CORPORATION

Research

Luminex Multiplex Testing: Neoplex for newborn screening, GPP (Gastrointestinal pathogen Panel), Cystic Fibrosis, Cancer Makers, Gene Expression, Endocrine Assay, Cell Biology and Cell Studies and Immunoassay
Millipore: Lab Water, Lab Filtration, Drug Discovery and Development, Antibodies, Cell Culture, Flow Cytometry, Immunoassays & Multiplex Solutions, Western Blotting, Multiwell Plate Solutions, Pathways, Stem Cell Research, and Toxicity
Affymetrix and Panomics: Molecular Genomics
Caliper: *In Vivo* Imaging
MOBIO and USB: DNA, RNA & Protein isolation, PCR & Cloning Reagents
Autogen: Automated DNA and RNA Isolation

Translational

Luminex Multiplex Testing: Neoplex for newborn screening, GPP (Gastrointestinal pathogen Panel), Cystic Fibrosis, Cancer Makers, Gene Expression, Endocrine Assay, Cell Biology & Cell Studies and Immunoassay
Affymetrix and Panomics: Molecular Genomics
Gen-Probe: HLA Genotyping
Asuragen: Multiplex Cancer Testing
Progenika: Multiplex Pharamacogenomics Testing
Theradiag and Zeus: Multiplex Autoimmune and Infectious Disease Testing
Chromsystems: HPLC LC-MS/MS Diagnostics
Autogen: Automated DNA and RNA Isolation

Diagnostics

Luminex Multiplex Testing: Neoplex for newborn screening, GPP (Gastrointestinal pathogen Panel), Cystic Fibrosis, Cancer Makers, Gene Expression, Endocrine Assay, Cell Biology & Cell
Affymetrix and Panomics: Molecular Genomics
Gen-Probe: HLA Genotyping
Theradiag & Zeus: Multiplex Autoimmune and Infectious Disease Testing
Asuragen and Progenika: Multiplex Cancer and Pharmacogenomics Testing
Grifols: RBC and HPA genotyping
Autogen: Automated DNA and RNA Isolation
ASI: Spectral Imaging, Karyotyping, FISH Analysis, Pathology

Gulf Scientific Corporation
P.O. Box 17010, Jebel Ali - Dubai, UAE
Tel: +971 4 881 5270 ; Fax: +971 4 881 6778 ; Toll Free Number (within UAE): 800 4776
Email: marketing@gulf-scientific.com ; Website: www.gulf-scientific.com

116

Workshop

RD-CONNECT: An integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research

Although individually uncommon, rare diseases collectively affect as many as one person in every 17, which equates to about 30 million people in Europe. They span all areas of medicine and their impact on public health, society and national economies is substantial. Their rarity and diversity pose specific challenges for healthcare provision and research, and for the development and marketing of treatments. Many patients with rare diseases lack timely and accurate diagnosis and even fewer receive tailored treatments influencing survival and quality of life. Eighty percent of rare diseases have a genetic component, and the genomics revolution has brought the hope of gene-based treatments for many rare diseases a step closer. The first sequencing of a human genome completed in 2003 required the work of hundreds of scientists for more than 10 years at a cost of over €3 billion. The same task is now feasible on a single sequencing instrument within days at a cost of less than €10,000, and this cost is continuing to decrease.

The newly emerging omics technologies are generating data on a huge scale unprecedented in biomedical research. Despite the advances in computing technology, the processing and analysis of data, or even its transfer from one location to another, is not trivial and remains far from routine. To date several thousand complete human genomes have been sequenced. This has led to an explosion of data by several orders of magnitude in recent years, and this rapid growth is expected to continue. The limiting factor is now our ability to analyse these vast quantities of data, rather than the capacity to produce it. Bioinformatics processing costs associated with next-generation sequencing represent the highest associated costs, ranging from €10,000 to €100,000 per genome. As a consequence, new and innovative bioinformatics solutions are required.

What is also becoming increasingly evident, however, is that sequencing is only the first part of the story. It does not replace clinical expertise – being able to combine genetic data with clinical data is more important than ever. Additional complexity arises from the fact that the genome sequence of each individual has a few hundred thousand "private" variants that are not found in the general population. The majority of these changes are not directly disease-causing and often classed as polymorphisms, but may still be relevant for gene regulation and may modify phenotypes or cause a condition when in combination with other variants. Our current understanding of the underlying biology is often too limited for making appropriate predictions for an individual.

In order to advance knowledge the combination and integration of genomics, transcriptomics, proteomics and metabolomics and detailed phenotype (phenomics) data across centres and across diseases is key. While competition between different research groups is a driving force to advance science, harmonisation and sharing of data is ultimately required to compare, combine and make best use of the results. This is especially true in rare diseases, where individuals with the conditions may be scattered across the world. Transnational and trans-disease efforts are thus essential to make optimal use of resources. Patient registries, biobanks and bioinformatics analysis tools are the key infrastructure tools required for omics research. More than 100 rare disease biobanks and 500 patient registries already exist in Europe alone, and progress towards infrastructure harmonisation has been made in several areas thanks to collaborative initiatives in specific disease groups (e.g. Huntington's disease, cystic fibrosis and neuromuscular disease).

A continued bottleneck for cutting-edge research towards diagnosis and therapy development is that at present these individual efforts continue to multiply while remaining largely "siloed", with very little interoperability and almost no systematic connection of detailed clinical information (deep phenotyping) with genetic information, biomaterial availability or research/trial datasets. To deliver concrete benefits to patients in terms of diagnosis and therapy development, the ability to link omics data with clinical data and biomaterials of individual patients or well-defined patient cohorts is crucial. Outside the rare disease field, a number of major research infrastructures – IHEC, the International Human Epigenome Consortium; ICGC, the International Cancer Genome Consortium; and BBMRI, the Biobanking and Biomolecular Resources Research Infrastructure, have shown that robust tools for large-scale data and sample sharing across multiple research projects can succeed.

RD-Connect (www.rd-connect.eu; Coordinator: Prof. Hanns Lochmüller) is a unique global infrastructure project that links up databases, registries, biobanks and clinical bioinformatics data used in rare disease research into a central resource for researchers worldwide. In a six-year project funded by the European Union but uniting researchers across the world, it will develop an integrated research platform in which complete clinical profiles are combined with -omics data and sample availability for rare disease research, in particular research funded under the International Rare Diseases Research Consortium (IRDiRC).What RD-Connect must achieve is both the uniting of the multiple existing infrastructures and the integration of the latest tools in order to create a robust and comprehensive combined biobanking, data analysis and patient registry platform for for rare disease that is used by researchers across the world.

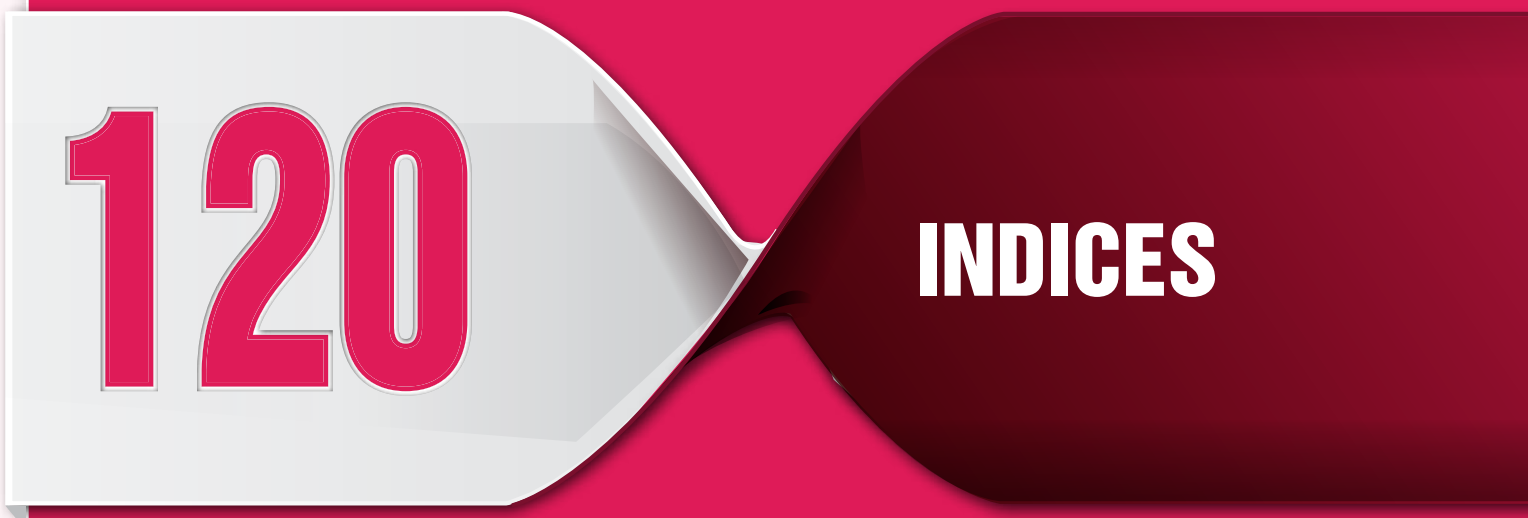
RD-Connect is part of a multi-million Euro initiative aiming to bring together researchers from across the world to develop new diagnostic tools and new treatments for people with rare diseases and to connect research data in this area on a global scale. With a total of 38 million Euro funding for research towards new treatments and for the development of a central global rare disease hub involving 70 institutions, RD-Connect, together with the other two multicenter projects, namely Neuromics (www.rd-neuromics.eu; Coordinator: Prof. Olaf Riess) and EURenOmics (www.rd-eurenomics.eu; Coordinator: Prof. Franz Schaefer) will allow scientists to share data from their genomics research projects. This will lead to faster diagnosis and better treatments and improve the quality of life for patients with rare diseases.

NeurOmics: -omics Research for Diagnosis and Therapy in Rare Neuromuscular and Neurodegenerative Diseases – an EU-Funded FP7 Project

Olaf Riess
Head of the Institute of Medical Genetics and Applied Genomics, University Hospital Tuebingen, Germany

NeurOmics is an EU-funded translational research project which has the primary aim of greatly improving understanding of neuromuscular and neurodegenerative diseases. The research will study around 1100 exomes in its aim to discover disease causing and disease modifying genes, develop new therapies, undertake deep phenotyping of patients, increase patient cohorts for clinical trials and develop new biomarkers for clinical application. The project focusses on 10 rare, genetic neuromuscular and neurodegenerative disease groups: frontotemporal lobe degeneration; Huntington's disease; ataxias; hereditary spastic paraplegias; spinal muscular atrophy and lower motor neuron diseases; hereditary motor neuropathies; congenital myasthenic syndromes; muscular dystrophies and muscular channelopathies. The project brings together the leading research groups in Europe, five highly innovative SMEs and overseas experts to work together using the most sophisticated -omics technologies employing genomics, transcriptomics, proteomics and metabolomics.

The consortium is coordinated by Olaf Riess at Tuebingen University. NeurOmics is working closely with RD-Connect, the rare-disease platform, in order to develop a global infrastructure for the wide sharing of research outputs of NeurOmics, and other rare disease projects.


120
INDICES

122 Author Index

129 Keyword Index

136 Country Index

Author Index

Abbes S	P64
Abdalla E	O10
Abdalla H	O18
Abdallah B	P69
Abdallah MS	P115
Abdelmadjid H	P73, P83
Abdelwahab M	P41
Abderrahim M	P83
Abderrahmanne RK	P27, P71
AbdRaboh N	P43
Abdul Wahab A	P20
Abdulsada KM	P76
Aberkane MS	P91, P114, P118
Abou Ghoch J	O11
Abou Hazima K	P96
Abou Jamra R	O7, O27, P29
Abourazzak S	P18
Abu Issa N	P33
Abu Khadija K	O20, P96, P121
Abushama H	P41
Abuthuraya R	O26
Afify M	P111
Agosto-Perez F	P13
Ahmad AH	P29
Ahmed O	P73
Akawi N	O16, O23
Akawi NA	P70
Al Aqeel AI	L15
Al Arrayed S	P60
Al Awadi M	P93
Al Dossari H	O26
Al hashem A	O9, P26
Al Hosani A	P108
Al Husseini K	P68
Al kacem L	P92
Al Khateeb MA	P29
Al Marzouqi A	L20
Al Muftah W	P9, P94, P119
Al Radhi AA	P76
Ala Y	P112
Al-Aama J	P23
Al-Abdulhadi S	P16
Alam NC	O11
Al-Araimi M	P19
Al-Blooshi AS	P108
Albrechten A	O24
Al-Dewik N	P63
Aleem A	P9
Alfares F	P116
Al-Gazali L	O8, O14, O16, O23, P65, P70, P78, P81, P93, P108
Al-Hadyan K	P7
Al-Hammadi M	O19
Al-Harbi K	O17
Al-Harbi N	P7
Alhasan S	P116
AlHosni A	P107
Alhousani M	P61
Alhusain M	P116
Alhwij I	O2
Ali WG	P111
Ali BR	O8, O14, O16, O23, P65, P70, P78, P81, P93, P108
Ali S	O20, P121
Ali S	P121
Aljaibeji H	O16
Aljneibe M	P78
Al-Kathiri K	P78
Al-Kindi A	P93
Al-mola GA	P76
Al-Mulla F	L8, P31
Almuriekhi M	O21
Al-Nuaimi AA	P108
Al-Owain M	O18
Al-Qahtani A	P120
Al-Qahtani S	P7
Al-Saffar M	P14
Al-Salmi F	P97
Al-Saud H	P120
AlSawalhee N	O12
AlSayegh A	P93
Alsbeih G	P7
Al-Shafai M	P9, P94, P98, P106
Al-Shamsi AM	P65
Al-shboul M	P12
Alshehhi AA	P97, P107
Al-Yahyaee SA	O14
Alzaidan H	O17
Al-Zeheimi N	P68
Ammar M	P84
Ammari A	P26

Author Index

Amouyel P	P66, P75
Anwar A	O22
Arif A	P30
Ashelford K	P32
Ashour E	P111, P115
Assia B	P83
Ayadi H	P81
Ayari-Jeridi H	P55
Azhar A	P30
Azzedine H	O17, P54
Baizig NM	P77
Baker D	P31
Bakhiet M	P39
Bakur K	P23
Banerjee M	P110
Baqir S	P68
Baraban J	P54
Barakat A	O25
Barkovich J	P14
Baroudi O	P55
Bartesaghi L	P54
Basol N	P102
Bauer P	P3
Bayoumi F	P37
Bayoumi R	O14
Baysal E	L3
Baz P	O13
Bdier A	P23
Behery AK	P72
Bejjani-Doueihy N	P4
Bekmanov B	P101
Bellot R	P91
Ben Abdallah M	P77
Ben Salem S	O14
Ben-Abdallah-Bouhjar	P100
Benammar-Elgaaïed A	P55
Benchekor SM	P66, P67
Ben-Khelifa H	P100
Benlatreche C	P80
BenMostefa AZ	P87
Ben-Omran T	O21
Bensaber S	P52
Ben-Salem S	P65, P81
Benseddik K	P71
Bensenouci S	P51
Benzaoui A	P118
Bernard-Marissal N	P54
Beshkar A	P22
Bhuiyan Z	P23
Bijarnia S	P8
Black C	P87
Bonnard C	P109
Borel P	P103
Bott R	P103
Bouajina E	P84
Bouaouina N	P5
Boubekeur AM	P27, P71
Boudjema A	P114, P118
Bougatef K	P64
Boughrara W	P114, P118
Bouguenouch L	P17, P18, P88, P89
Bouguila H	P55
Boulefkhad A	P95, P113
Boulenouar H	P66, P75
Boushaba A	P91
Boussofara L	P79
Bouzayene H	P55
Boxer M	P87
Brand A	K2
Brockschmidt FF	P29
Buchert R	O7, O27, P29
Bueno S	P44
Burn J	P87
Burzyns B	P82
Burzynska B	P99
Capranico G	P44
Cassinat B	P63
Cécile GED	P51
Chaabouni HB	L17
Chahrour M	P47
Chandy N	P14
Chaouki S	P17
Charradi K	P55
Cheour I	P84
Cherifa B	P73, P74, P92
Chillemi G	P44
Choo KHA	P61
Chouchane L	L1, P5
Chouery E	O11
Chrast R	P54
Claeys KG	P54
Cooper DN	K1

Author Index

Costa JL	P53
Costello E	P49
Cottel D	P75
Crosby A	P97
Crystal R	P13, P15
Crystal RG	P105
Curtis A	P87
Daama S	O3
Dahmani C	P118
Dallongeville J	P75
Darwish M	P4
Dash P	P8
de Bot ST	O14
de Brouwer APM	O14
de Vondervoort I	O14
de Vrie BBA	O14
Deenadayal A	P45
Deepika MLN	P50
Denguezli M	P79
Desmarchelier C	P103
Dhaini H	P4
Diophode S	P20
Djabaria Naïma FEL	P75
Djamel K	P74
Dorgham S	P114
Doss N	P84
Dridi W	O3
Drmanac R	L6
Eftekhaari TE	P10, P59
Eker HK	P97
Ekici AB	O7, O27, P29
El Ansary M	P6
El Ayoubi H	P63
El Gharbawi N	P6
El Kebir FZ	P62
El Kharadly R	O6
El May M	P77
Elalaoui SC	O29
Elewisy S	P7
Elgaaied A	P84
Elghezal H	P100
Elhady G	P72
Elhannan S	P39
Elhassan A	P41
El-Helou R	P70
Elsenousy W	P37
Elshafei SAS	P72
Ermeli N	P52
Escande-Beillard N	P117
Fahiminiya S	O21, O30
Fahmy P	P6
Fakhro K	P13, P15, P98, P105
Falchi M	P106, P119, P120
Farah F	P4
Farhat G	P4
Ferrari M	L13
Fitouri S	P52
Fodil Faouzia Z	P69
Fogtman A	P82
Fourati H	P84
Froguel P	P106, P119, P120
Gaafar M	P46
Gaafar T	P37
Gati A	O29
Gbaj A	P52
Geissler K	O7
Geraghty MT	O14
Ghalak H	P98
Ghalim N	O25
Ghandour F	P4
Gjesing A	O24
Gora M	P82
Gosadi IM	P36
Goumidi L	P66, P75
Gouttenoire EA	P54
Goyder EC	P36
Gravanis A	L16
Grenier-Boley B	P66, P75
Gribaa M	P79
Gritli S	P77
Guillausseau P-J	O13
Hadj T	P69
Hagen F	P20
Hagos S	O26
Hajizadeh F	P59
Hakonarson H	O3
Halaby G	O13
Hallak B	O27, P29
Hamamy H	L11, P12, P109, P117
Hamdan S	P29
Hamri A	P86, P95
Hamzeh AR	L19

Author Index

Hanachi S	P92
Hannachi H	P100
Hansen T	O24
Hara T	O18
Hashishe MM	P72
Hasnain S	P122
Hassan K	P96
Hassen E	P5
Hayward B	O10
Hemedi S	P43
Hemida M	O19
Hemimi N	P43
Hermann A	P52
Hermant X	P66, P75
Hertecant J	P65
Hida M	P17, P18, P88
Higgs DR	L4
Hill RS	P14
Hills LB	P14
Horikawa Y	O24
Hou C	O3
Housawi Y	O3
Houti L	P66, P75
Hudson D	P61
Hui H	P42
Humphreys P	O14
Hussein H	P6
Ibrahim LM	P115
Inanir A	P102
Indu KR	P110
Ismael A	O7, P29
Ismail MA	P46
Ismail MF	P111
Ismail S	P22
Ismail SR	O6
Ixan O	P101
Jacques R	P91
Jaeda M	P52
Jahan P	P45, P50, P104, P112
Jahrami M	P35, P40
Jaouad IC	O29
Javid J	O15
Jerome-Majewska L	O30
Jiang WG	O1
John A	P70, P93, P108
Joshi K	P34
Julier C	O13
Kakegawa W	P14
Kalitsis P	P61
Kamsteeg EJ	O14
Kanaan MN	L10
Kar B	O5
Karima S	P73, P74, P80, P85
Karmakar B	P24
Kayasseh MA	P2
Kayserili H	P109, P117
Kerrouaz N	P80
Khalak H	P90
Khalida B	P85, P92
Khalil S	P25
Khan AO	O17
Kholeif S	O6
Khozaimy K	P78
Kiladjian J-J	P63
Kim C	O3
Kizhakkedath P	P93
Kobyliansky E	P24
Koenig M	P83, P95
Kohli S	O12
Komaravalli PL	P45
Konno K	P14
Kordi-Tamandani DM	P1, P38
Kraiem W	P79
Kumar P	P9, P90, P94, P98
Kundavi S	O5
Kurdi A	P26
Lakshmana Rao SS	P50
Lam AN	P14
Lamba P	P48
Lardjam Hetraf SA	P66, P67, P75
LeGuern E	P54
Lemorvan V	P91
Ligtenberg M	P53
Lim-Melia E	P14
Lohmann D	P55
Lotfi L	P91
Louhibi L	P27, P51, P71
Lukacs G	P21
Lyahyai J	O29
Machaca K	P106
Machado JC	P53
Maciejak A	P99

Author Index

Maczewski M	P82
Mahfoudh W	P5
Mahmoud A	P6
Mahmoudi K	P27, P51
Majewski J	O30
Majid S	O26
Makeeva OA	P56
Makhlouf M	P77
Makowski E	P54
MalekZadeh K	P57, P58
Malik M	O1
Malkin I	P24
Mamaï O	P79
Manzo S	P44
Marinello J	P44
Markova VV	P56
Marrakchi R	P84
Maruthi G	P104
Mason J	P19
Masri A	P14
McKeon C	P119
McKibbin M	P19
Mdimegh I	P55
Mediene-Benchekor S	P75
Medjaoui IH	P66, P67, P75
Megaiz A	P91
Megarbane A	O11
Meguid N	P115
Mehtar N	P91
Mehtar NS	P27
Meirhaeghe A	P66, P67, P75
Menif S	P64
Menon PK	P48
Mensenkamp A	P53
Meriem A	P69
Meroufel DN	P66
Merriman B	P79
Mezey J	P13
Mezey J	P15
Mfadi D	P33
Milhem R	O8
Mir R	O15
Mochida G	P14
Moftah B	P7
Mogthit F	P71
Mohamed H	P41
Mohamed R	P28
Mohamed Z	P28
Mokni M	P84
Morcos B	P37
Morisson H	O7
Mostafa I	P22
Mostefa F	P69
Mrema I	P52
Muhammad S	P29
Muratova F	P101
Murthy TSR	P104
M'zahem A	P95, P113
Naima M	P75
Naima T	P83
Nair C	P110
Najar I	O15
Nakamura M	O18
Nasir R	P14
Nassim N	P92
Nassr EMA	P72
Naveed M	L5
Nawar M	O10
Nawaz Z	O20, O21, P96, P121
Nawel Z	P80
Nazmy N	O6
Nedjadi T	P49
Nelen M	P53
Neoptolemos J	P49
Nevinkarakus	P102
Nijhof B	O14
Nikbakht M	P57, P58
Nikhat F	O12
Nikuei P	P10, P59
Nordine A	P74
Noredine A	P92
Nöthen MM	P29
Nouira R	P79
Noureddine A	P73, P80, P85
Nowicki M	P103
Omrane I	P55
Osman O	P41
Otieno G	O3
Ouatou S	O25
Ouchene H	P53
Ouerhani S	P64, P84
Ouhaïbi-Djellouli H	P66, P67, P75

Author Index

Ouldim K	P17, P18, P88, P89
Padariyakam S	O20, P96, P121
Papadopoulos P	O29
Partlow JN	P14
Pasha K	P112
Pato MV	P54
Patrinos G	L2, O29
Pawlak M	P99
Pedersen O	O24
Perfilyeva A	P101
Piniewska J	P99
Pinto N	P54
Plante-Bordeneuve V	P54
Poirot O	P54
Poulter J	P19
Pramathan T	O14
Puri R	P8
Qadeer I	P122
Rabeh W	P21
Rajaei M	P59
Ramachander VRV	P104
Ramzan K	O26
Ratbi I	O29
Rauch F	O30
Ray PC	O15
Razavi MS	P1
Reddy R	P50
Reed E	P32
Rehm H	P81
Reis A	O7, O27, P29
Reversade B	P12, P79, P109, P117
Rhaissi H	O25
Riecken L	O7
Riess O	P3
Rivolta C	P54
Robay A	P13, P15
Rodriguez-Flores J	P13, P15
Roky R	O28
Ropers H	L9
Rouba H	O25
Roula D	P80
Rowe J	P90
Saad A	P79, P100
Sabah H	P80
Sabrina B	P74
Sadiq M	P33
Sadoon A	P20
Sager M	O3
Sahms A	O10
Said G	P54
Saidan MM	P26
Saidi Mehtar N	P75, P66, P51
Salih M	O17
Salima Z	P80
Salwa	P48
Samri I	P17, P18, P88, P89
Sana Chaouki S	P88
Sanyoura M	O13
Sarada Lekshmi KR	P110
Sastry K	L1
Sathyan S	P110
Sawalhi S	P11
Saxena A	O15
Saxena R	O12, P8
Schmitz-Abe K	P47
Schöls L	P3, P54
Schumacher J	O7, P29
Schuurs-Hoeijmakers J	O14
Schwartzentruber J	O14
Schwarze B	O27
Seddiki S	P62
Sefiani A	O29
Sellami S	P84
Senderek J	P54
Senee V	O13
Serradj F	P86, P113
Shaker O	P111
Shan J	L1, P5
Sharada HM	P115
Shboul M	P117
Sheif M	P37
Sheikhha M	P10
Shekari M	P57
Shoukri M	P26
Sifi K	P86, P92
Sifi Y	P113, P86
Sivamani S	O5
Skvortsova L	P101
Sleiman P	O3
Smith AC	O14
Smith G	P90
Soleimanian S	P5, P10, P59

Author Index

Soltani I	P64
Soosay A	O2
Souissi CB	P84
Sriha B	P79
Sticht H	O7, P29
Stoler JM	P14
Strom T	P29
Sturm M	P3
Suhre K	O4, P9, P15, P90, P94, P98, P105, P106, P119
Sygitowicz G	P99
Synofzik M	P3
Tabarki B	O9
Taghane N	P95, P113
Taha S	P39
Tajaldeen SJ	P20
Tamaddon M	P10
Tamimi ZA	P81
Tariq S	O14
Tarish HR	P76
Tawamie H	O7, O27, P29
Teare MD	P36
Tekaya R	P84
Thomas L	P32
Tian L	O3
Toomes C	P19
Torbey P-H	P4
Tulacz D	P82
Tzimas G	O29
Uebe S	O7, O27, P29
Ünlü SE	P97
Upadhyaya M	P32
Usha Rani V	P45, P50
Valluri V	P112
van der Graaf M	O14
van Schaik RH	L12
Varma T	O5
Vasiliou V	L14
Vasquez L	O3
Venturina N	P7
Venturini G	P54
Verma I	O12, P8
Vermeer S	O14
Viennas E	O29
Villard L	O11
Walsh CA	P47
Wang J	L7
Watanabe M	P14
Wei W	P42
Wenjing C	P42
Wilde A	P23
Willems PJ	P81
Winston J	P32
Woudstra C	O13
Ya G	P42
Yamina S	P73
Yanhua C	P42
Yasmeen H	P122
Yassin M	P63
Ye L	O1
Yigit S	P102
Yousif HM	P111
Yousri N	P15
Yousri NA	P46, P105
Yu T	P47
Yuzaki M	P14
Zaghlool S	P94
Zain S	P28
Zalloua P	O13
Zarra I	P84
Zavadakova P	P54
Zeglaoui H	P84
Zehra S	P30
Zekri S	P92
Zenker J	P54
Zerdoud N	P92
Zohra MF	P91
Zouai A	P86
Zyada A	P29

Keyword Index

13q deletion	P100
56C>G SNP	O25
ABHD 12 gene	P95
Abortion	P59
aCGH	O20, O22, P121
Acid maltase deficiency	P86
Acute anterior uveitis	P48
Acute lymphoblastic leukemia	P57, P58
Acute myocardial infarction	P99
ADAMTSL2	P65
Adult- onset Pompe disease	P86
AFLP fingerprinting	P20
Age	P73
AHT	O25
Aldehype dehydrogenase	L14
Algerian population	P73, P75, P80, P91, P113
algorithm	P46
Alleles frequencies	P77
Alpha globin	L4
Alpha thalassemia	L4,
ALS2 gene	O26, P97
Alstrom syndrome	O13
Alternating hemiplegia of childhood	O9
Alzheimer's disease	P73
Amyotrophic lateral sclerosis	O26, P113
Angiotensin-converting enzyme	P102, P111
Animal model	P82, P117
ANKRD26 gene	O3
Annotation	P104, P105
Antibody response	P41
Antigen	P61
Anti-mullarian hormone	P45
APOA5 gene	O25
APOE polymorphisms	P74, P75
Apoptosis	P101
APT7B	P96
Arab	L19, P13, P96, P116
Arabian genome	P31
Aromatase	P50
Array-based Genotyping	P9
Association study	P77, P84, P91, P102, P110, P114
Asthenoteratozoospermia	O5
Asthma	P16
ASUN	P12
Asympotomatic hepatitis	P76
Ataxia	P3, P83
ATP1A2	O9
Autism	P47
Autosomal dominant	P70, P88
Autosomal recessive	L11, O7, P29, P81, P83
Autosomal recessive disorders	O21
Autosomal recessive intellectual disability	O27
Awareness	P116
Ayurveda	P34
Azidopine tritiée	P62
Basal cell carcinoma	P71
Becker muscular dystrophy	P17
Bedouin	P13
Benign tumours	P32
Bioavailability	P103
Biobank	P109
Biodosimetry	P7
Birth defect	P26, P117
Bladder tumours	P64
BMD	P121
BMPR2 (Bone Morphogenetic Protein Receptor Type 2)	P70
BNP gene	P66
Brain injury	P115
BRCA genes	L1, P52, P53
Breast cancer	L1, L8, L10, P33, P52, P104, P122
Brilliant cresyl blue	P68
Brugada syndrome	L13
C6orf221 gene	O10
Calling Algorithms	P9
Camptodactyly-arthropathy-coxa vara-pericarditis syndrome	O23
Cancer	L14, O1, P101
Cancer stem cell marker	L14

Keyword Index

Cardiovascular diseases	P74
Cardiovascular risk factors	P73, P75
Carrier detection	L11
CD4+CD25+ T-cell	P37
Cell mis-segregation	P61
Cell signaling protein	P30
Centromere	P61
Cerebellar ataxia and tonic upgaze	P14
Cerebrovascular accident	P85
Cerebrovascular disease	P74
CFTR gene	P21
Charcot-Marie-Tooth disease	P42, P54
Chemical chaperones	O8
Chemokine	P16
Chemokine receptor	P16
Chemomarkers	P62
Childhood-onset ataxia syndromes	O17
Cholesterol	P73
Chorionic villus sampling	O12
Chromosomal aberrations	P7
Chromosome	P61
Chronic myelogenous leukemia	O15
Chronic myeloid leukemia	P64, P114
Cilia	P12
Clinicotype	P2
CNVs	O11, O30, P15, P98, P105, P120
Colorectal cancer	P71, P91, P64
Common diseases	P60
Comparative genomic hybridization	O2, L11
Congenital	P109
Congenital heart diseases	P30
Congenital muscular dystrophy	O23
Congenital Myopathy	P8
Consanguinity	L10, L11, L17, O21, P26, P36, P109, P116
Covariates	P94
Coxsachievirus B3	O19
CpG-island promoters	P44
C-reactive protein	P99
Cryptic	P30
Crypto	P30
Cumulus cells	P68
Cutaneous leishmaniasis	P41
CYP2C19	P34
CYP3A4	P4
CYP3A5	P4
Cystic fibrosis	P20, P21
Cytochrome P450	P34
Cytogenetic	P7, P72
Cytogenetic abnormalities	O6
Cytokines	P49
DDHD2	O14
DDR2 gene	P93
de novo mutation	P78
Deafness	P81
Deafness infertility syndrome	O5
Deep sequencing	O24, P13
Dermatoglyphic asymmetry	P24
Developmental delay	O11, O20
Dextro transposition of great arteries	P30
DFNB2	P81
DFNB31	P81
Diabetes	O13, P66, P67, P85, P94, P36, P111, P119
Diabetic complication	P35
Diabetic nephropathy	P111
Diabetic peripheral neuropathy	P102
Diagnosis	O6, O20, P18
diagnosis panels	P3
Diagnostic NGS	L9
Diagnostics	P23, P31, P53
Dicentric chromosomes	P7
Differential methylation	P94
Disease progression	O15
Disease screening	L5
Disequilibrium syndrome	P108
Diversity traits	P24
DMD	P121
DNA diagnostics	P48
DNA repair	P101
DNA topoisomerase I	P44
Dopamine receptor	P38
Doxorubicin	P62

Keyword Index

Duchenne muscular dystrophy	P17
Dysmorphic	O20
Dystrophin	P17
ELISA	P123
Endogamy	L17
Endoplasmic Reticulum Associated Degradation (ERAD)	O8, P70, P108
Endotype	P2
Ensemble selection	P46
Epigenetic modification	L4, O15, P110
Epigenetic status	P57
ERK (Extracellular signal Regulated Kinase)	P39
Ethics	O28
Exome sequencing	L8, P8, P47, P117
EZR	O7
F8	P69
FAM44A	P61
familial correlation coefficients	P24
Family	P113
FBN1	P87
Facial dysmorphology	P88
FGFR2 gene	P122
FISH	O6, P100
Fluorescence uni-probes	P52
FMR1	P45
FOXP3	P104
FPAH (Familial pulmonary arterial Hypertension)	P70
Fragile X syndrome	P45
French population	P75
Frizzled family receptor (FZD4)	O8
Gastrointestinal stromal tumor	P11
Geleophysic Dysplasia	P65
Gene	P1
Gene expression	P5, P68
Gene polymorphism	P111
Gene-diet interaction	P67
Genes	P101
Genetic counseling	O12, P40
Genetic counseling	P40
Genetic diagnosis	O13
Genetic disorders	L19, O29, P116
Genetic mutations	P60
Genetic risk assessment	P56
Genetic risk factor	P73
Genetic testing	P56, P60
Genetic variance	O4, P106, P119, P120
Genetics	L8, O20, P59, P85, P96
Genetics Database	L19
Genetotype	P2
Genistein	P57
Genital ambiguity	P18
Genome Wide Association Studies	O4, L7, P97, P120, P122
Genomic data portal	P90
Genomic DNA nanoarrays	L6
Genomic services	P60
Genomic studies	O28
Genomics	L15, P47
Genotype	P76
Genotype-phenotype correlation	L13, P23
Glutamate receptor	P38
Glycogen storage disease type II	P86
Glycogenosis type II	P86
Glycoprotein P	P62
GRID2	P14
Gulf Arabs	P15
Haplogroups	P107
Haplotype analysis	P16
Haplotype mapping	P79
Haplotypes	L8
HCV	P76
HCV core protein	O18
Heart failure	P82
Hematopoietic cells	L4
Hemoglobinopathies	L3
Hemophilia A	P69
Hemorrhagic destruction of the brain	O23
Hereditary	P109
Hereditary hearing loss	L10
Hereditary spastic paraplegia	O26
High risk families	P77
High throughput genome sequencing	L11

Keyword Index

HLA	P77
HLA B-27	P48
HLA-F	P35
Homozygosity	O26
Homozygosity mapping	L10, L17, O27, P14, P19, P29, P54
HRM	P63
hTERT	O18
HVR-1	P107
Hybrid strategies	P15
hypermethylation	P58
Hypertension	P35, P102
Identity by descent	L17
IFN-gamma	P1, P112
IgG	P41
IL-1 gene	P37
IL-10	P1, P112
Imaginotype	P2
Imatinib	P11
Imprinted genes	O2
Inbreeding	P24, P36
Infantile-onset ascending hereditary spastic paralysis	P97
Infectious diseases	P60
Inflammatory response	P112
Informed consent	O28
Inhibition	O7
Insulin	P66
Intellectual disability	O7, O11, O23, L9, P29, P47
Intron 1 inversion	P69
Intron 22 inversion	P69
Invasiveness	O1
Ion Torrent PGM	P53
iPla1	O14
IRAK1 gene	P84
ISOR study	P67
IVF failure	P10
JAK2 exon 12 mutations	P63
Jak2V617F mutation	P63
Jordanian	P33
Kabuki syndrome	P88
Karyotype	P100
Karyotyping	O5
KIT	P11
KRAS gene	P64
L.donovani	P41
L.major	P41
LCA5	P19
Leber's congenital amaurosis	P19
Leptin gene	P43
Leukemia	P25
Linkage analysis	L5, P16, P79, P95, P106, P119
Lipid metabolism	O27
Lipid parameters	P75
Lipoprotein	P74
LL genotype	P50
Loss of heterozygocity	O2, O22, P87
Lutein	P103
Male infertility	P33
Malignant peripheral nerve sheath tumours (MPNSTs)	P32
Management	L1
MAPKs (Mitogen-Activated Protein Kinases)	P39
Marfan Syndrome	P87
Massively parallel sequencing technology	L10, P53
Maternal	P59
Maturity-onset diabetes of the young	O24
MBD2 gene	P110
MDR1	P114, P118
MEN2A	P92
MEN2B	P92
Mental retardation	O20, P88
Metabolic disorders	L14, O14, P47, P85
Metabolic individuality	O4
Metabolic syndrome	P43
Metabolomics	O4
Methotrexate	P118
Methotrexate metabolism	P34
Methylation	P101
Microarray	O20, P121
Micro-array datasets	P46
MicroRNA	O19, P82

Keyword Index

Mitochondrial DNA	P107
Mitochondrial marker	P68
Modulation	O19
Mohr	P12
Molar pregnancy	O10
Molecular	P72
Molecular genetic testing	P23
Molecular genetics	O5
Molecular heterogeneity	P25
Monogenic	P121
Monogenic diabetes	O24
Monogenic disease	O13
Moroccan population	O29
Motoneuron	O26
MPL mutation	P63
MPNs	P63
MST1	P58
MST2	P58
MTC	P92
MTHFR	P10, P33, P80, P118
Multi variant logistic regression analysis	P26
Multiple epiphyseal dysplasia	O23
Multiple keratoacanthoma	P79
Multiple self-healing palmoplantar carcinoma	P79
Muscle skeletal receptor tyrosine kinase (MUSK)	O8
Mutagenesis	P70
Mutation	O26, P12, P19, P65, P93, P96, P97
Mutation analsyis	P27, P51, P55
Mutation database	O29
Mutational spectrum	P64
Muzeina tribe	P24
Mycoplasma fermentans	P37
Myeloperoxidase	P99
MYO7A	P81
Myocarditis	O19
Myopathy	P17
Myozyme	P86
Nanoparticles	P57
Nasopharynegeal carcinoma	O2, P77
Nephropath	P35
Neuroblastoma	P4
Neurodegenerative diseases	L16
Neurofibromatosis type 1	P11, P32
Neutrophins	L16
New technologies	L15
Next generation data analysis	P90, P98, P104, P105
Next generation sequencing	L6, L13, O3, O27, P3, P9, P13, P29, P31, P53, P98, P104, P105
NLRP7 gene	O10
Non-alcoholic fatty liver disease	P28
Non-coding variants	O30
Nutrigenetic	P103
Obesity	P94, P106, P120
Oculocutaneous albinism	P89
Oculomotor apraxia,Neuropathy	P83
OFD1 gene	P78
Olfactory receptor gene	P35
Oocyte	P68
Oral-facial-digital syndromes	P12, P78
Ouest Algerien population	P66
Pancreatic cancer	P49
Paraplegia	P3
Pathogenesis	O19
Patient education	P40
PCOS	P50
PCR	P69, P72, P76, P80
Peripheral artery disease	P80
Personal genomes	L6, L7
Personalised nutrition	P103
Personalized medicine	L2, L12, L15
Pharamacogenetic markers	L12
Pharamacogenetics	O16, L12
Pharamacogenomics	L2, P34
Pharmacogenomic markers	L2
Phenotype	P43
Phenotype genotype correlation	P23
Phenotypic spectrum	O17
Phenylalanine	P115
Phenylketonuria	P115

Keyword Index

Physiopathology	P117
PIAS (Protein Inhibitor of Activated Signal Transducer and Activator of Transcription)	P39
PLA2G6	O17
Plasmalogen synthesis	O27
Platelet	O3
Platelet-derived growth factor receptor-alpha	P11
PLEKHG5	P54
PNPLA3	P28
Polymorphic variants	L5
Polymorphism	L8, P1, P10, P43, P66, P67, P74
Polyneuropathy hearing loss ataxia +retinitis pigmentosa and cataract	P95
Population migration	P13, P107
Population study	O4
Predictive diagnostics	P56
Premature ovarian failure	P45
Prenatal diagnosis	L3, O12
Preventable health condition	P56
Prevention	L15
Progesterone	P62
Promoter hypermethylation	P38, O15
Protein misfolding	O8
Protein rescue	P21
Pseudomonas aeruginosa	P20
Psoriasis	P84
Psoriatic arthritis	P84
Public Health Genetics	P60
Qatar	O21, P15
Qatar genome browser	P90
Radiation exposure	P7
Radioactive PCR	P87
Rare disease	P109
Rare genetic disorders	O30
Rare recessive disorders	O23
RAS/MAPK	O7
Rb gene	P27
RB1	P55
Real-time PCR	P99
Recurrent hydatidiform mole	O10
Repeated pregnancy loss	P59
Reserve-transcription	P76
RET proto-oncogene	P92
Retinoblastoma	P27, P55
Rheumatoid arthritis	P37, P118
Ring chromosome 13	P100
Risk of CAD	O25
RIZ1	O15
RQ-PCR	P63
rtPCR	P87
RYR1 gene	P8
S100A8	P49
S100A9	P49
Saudi Arabia	P116
SBF2 gene	P42
Schizophrenia	P1, P38, P110
Semaphorins	O1
Senataxine	P83
Sequencing	P92, P96
Sero-prevalence	P123
Serum ACE level	P111
Serum neural protein (S-100B)	P115
Sex assignment	P18
Sex differentiation disorders	P18
Short stature	P65
Sickle Cell anemia	P40
SNP array	P98
SNPs	L7, P28, P52, P103, P110, P122
Social awareness	P40
South India	P50
Sp1	O18
Spastic paraplegia	O14
SPG54	O14
Spinal muscular atrophy	P17
Split-hand /foot malformation with long-bone deficiency	L5
Spondylo-meta-epiphyseal dysplasia with short limbs and abnormal calcifications	P93

Keyword Index

Sporadic	P78
SPP1	P32
STAT (Signal Transducer and Activator of Transcription)	P39
Statins	P99
STDs	P123
STR(TTTA)n polymorphism	P50
Strategic plan	P40
SUZ12	P32
Syria	P29
TCF7L2	P67
TCH2	O3
Telomerase	O18
Tetralogy of fallot	P30
Tetra-nucleotide microsatellite	P43
TGF beta signaling pathways	P65
Thalassemia	L3
Therapeutic response	P2
Therapeutic targets	P32
Thrombocytopenia	O3
Thrombophilia	P85
TNRC9	L1
Top1-DNA cleavage complexes	P44
TP53 variants	P71
TRAFs (TNF Receptor-Associated Factors)	P39
Transcription	O18
Transcriptional control	L4
Transforming growth factor beta-1	P115
Translational genomics	L15
Turner	P72
United Arab Emirates	O23
Unusual phenotype	P117
variants	L13
VEGF	P10
Vitiligo	P112
VKORC1	O16
VLDLR gene	P108
Warfarin	O16
Whole exome sequencing	L9, O21, O22, O23, O30, P42
Whole genome analysis	L6, L8, O21
Wolfram syndrome	O13
X chromosome abnormalities	P5
X Inactivation	P5
Xeroderma pigmentosum	P51
X-linked dominant	P78
XPC gene	P51
XRCC3 Thr241Met	P91
Y chromosome	P72

Country Index

Algeria	P27, P51, P62, P66, P67, P69, P71, P73, P74, P75, P80, P85, P86, P87, P91, P92, P95, P113, P114, P118
Australia	P61
Austria	P52
Bahrain	P35, P39, P40, P60
Belgium	O29, P81
Canada	O14, O21, O30, P21
China	L7, P42
Denmark	O24
Egypt	O10, O18, O19, O6, P6, P37, P46, P72, P105, P111, P115
France	O11, O13, P54, P63, P66, P67, P71, P75, P83, P95, P103
Germany	L9, O7, O27, P3, P29, P54, P55
Greece	L2, L16, O29
India	O5, O12, O15, P8, P24, P34, P45, P50, P104, P110, P112
Iran	P1, P10, P38, P57, P58, P59
Iraq	P76
Israel	P24
Italy	L13, P44
Japan	O18, O24
Jordan	P14, P33, P81
Kazakhstan	P101
Saudi Arabia	L15, O3, O9, O17, O19, O26, O31, P7, P16, P23, P25, P26, P36, P49, P116, P120
Kuwait	L8
Lebanon	O11, O13, P4
Libya	P52
Malaysia	O2, O22, P28
Morocco	O25, O29, O32, P17, P18, P88, P89
Oman	L18, O14, P19, P68, P107
Pakistan	O1, P30, P122
Plaestine	L10
Poland	P82, P99
Portugal	P53, P54
Qatar	L1, O4, O20, O21, P5, P9, P13, P15, P20, P46, P63, P90, P94, P96, P98, P105, P106, P119, P121
Russia	P56
Singapore	P12, P79, P117
Sudan	P41
Switzerland	L11, O31, P12, P23, P54, P109, P117
Syria	O7, O27, P29
The Netherlands	K2, L12, 014, P20, P23, P53
Tunisia	L17, P5, P55, P64, P77, P79, P84, P100
Turkey	P97, P102, P109, P117
United Arab Emirates	L3, L5, L19, L20, O8, O12, O14, O16, O23, O28, P2, P11, P14, P21, P43, P48, P61, P65, P70, P78, P81, P93, P108
United Kingdom	K1, L4, O1, O10, O28, P19, P31, P32, P49, P87, P97, P106, P120
United States of America	L6, L14, O3, O18, P13, P14, P15, P47, P54, P81

Notes

138

Sponsors' Profiles

140 Gold Sponsor: Gulf Scientific Corporation (GSC)

141 Silver Sponsor: Neo Science and Group

142 Exhibitors:
Sengenics
DNA Genotek
Interactive Biosoftware
Alliance Global

Gold Sponsor

GULF SCIENTIFIC CORPORATION
Serving the scientific community since 1990

Gulf Scientific Corporation (GSC)

Established in 1990 with a mission of providing complete and customized laboratory solutions, GSC is a leading provider of Life Science and Analytical solutions across the MENA region. Our unrivaled support structure and philosophy centered on innovative technologies, education and service makes GSC a preferred choice for research and diagnostic customers alike. Through adopting a systems approach and strategic partnering with the leading industry principals, GSC strives to offer complete laboratory solutions ranging from molecular and cell biology studies all the way to in vivo imaging of animal models. Our esteemed partners include Affymetrix, Waters, Merck Millipore, Luminex, Perkin Elmer, Agilent and many more.

Affymetrix is a pioneer in microarray technology and a leader in genomics analysis, now developing and providing innovative technologies that enable multiplex and parallel analysis of biological systems at the cell, protein, and gene level, facilitating the rapid translation of results into biology for a better world. The extensive portfolio of translational and clinical solutions enables scientists and clinicians to rapidly translate their research into understanding underlying disease mechanisms, identifying biomarkers for personalized medicine, creating novel molecular diagnostic tests, and improving genetic marker-assisted breeding programs in agriculture for human health and wellness.

Silver Sponsor

Neo Science and Group

Neo-Science and Group is a trusted provider of high quality tools and services to the Life Science research, Clinical Diagnostics. We offer one stop solutions to meet the changing needs of the clinical, scientific community.

Neo-Science and group was incorporated in 2013 by founding member and CEO Nadia Abu Hijleh. It consolidates Gulf Scientific for Laboratories in Saudi Arabia, previously known as GSE in operation since 2010, Qatar Scientific in operations since 2005, new offices to serve the U.A.E, Kuwait and Oman. The company has a strong presence across the GCC region and has acquired a solid reputation for delivering innovative products, integrated solutions and professional support across a broad range of sectors including: Life Science, Healthcare and Informatics.

We now employ over 75 highly qualified professionals. Our collaborative approach has enabled us to build a strong support network of distinguished local offices and agents in the GCC countries we operate in with the main focus on Saudi Arabia , Qatar and the UAE.

We are headquartered in Dubai which enables us to operate effectively across the UAE, Kingdom of Saudi Arabia, Qatar, Kuwait, Bahrain and Oman

Exhibitors

Sengenics

Sengenicsis the 1st Asia-based Genomics Research & Molecular Diagnostics Company outside of the United States (US). The 2 key focus areas for the company are 'Genomic Diagnostics' involving non-invasive pre-natal diagnostics, post-natal diagnostics, cardiac and cancer risk tests, developmental delay diagnostics using next-generation sequencing and microarrays, and 'Proteomic and Genomics based Research Services'using protein array based immune-proteomics and clinical trial immune response monitoring. The company has now built a portfolio of more than 400 genetic tests for Developmental Delay, Rare Genetic Disorders, Cardiac risk, Thalassemia and Cancer. The business model of the company also leverages the translation of joint research projects into patented and commercialized diagnostics tests. Sengenics has established a wide network of partners in the US, Europe and Asia as channels for its products and services. The company has sales offices and genetic testing facilities in four countries.

DNA Genotek

DNA Genotek, based in Ottawa, Canada, provides high-quality biological sample collection, stabilization and preparation products for human genetics, microbiology and animal genetics. The company's products protect and stabilize multiple sample types for long-term storage at ambient temperature to ensure the highest quality results for genetic analysis and testing. The products' reliability and ease-of-use have resulted in rapid adoption by thousands of academic, biotechnology, diagnostic, agriculture, and other leading institutions around the globe.

Exhibitors

Interactive Biosoftware

Interactive Biosoftware is the creator of Alamut®, the original mutation interpretation software used by leading genetic scientists around the world. The Alamut® software expedites mutation interpretation, providing a rich and very user-friendly graphical environment to easily assess the effects of genomic variants. It is used in diagnostic and research genetics laboratories worldwide. A specialized version for high throughput annotation, named Alamut-HT, is an essential tool in the NGS era.

Alliance Global

The AGBL Group of companies is the largest biomedical gateway to the emerging markets of the Middle East, Africa and Asia. The group is dedicated to bringing innovative technologies and products to researchers, clinicians, and diagnostic users in the emerging healthcare markets within the Middle East, African and Asian region. The group employs more than 80 specialists and has nine regional offices offering distribution, consultation and product development services. Our network of sister and subsidiary companies that are strategically serving the region are: AGBL-HQ, AGBL-Egypt, AGBL-Levant, AGBL-Afrique, AGBL-Arabia, AGBL-Pakistan, AGBL-South Africa, AGBL-East Africa and AGBL-Asia. We cover the market's needs through four main divisions: Diagnostics, Life Sciences, Food Safety and Emerging Medical Technologies. The company helps biomedical technology manufacturers and suppliers introduce their products and services to emerging markets, reflecting on the healthcare standards within those markets.

Notes