Ubiquitination Factor E4A

Alternative Names
UBE4A
UFD2, S. Cerevisiae, Homolog Of
Ubiquitin Conjugation Factor E4
E4

Record Category
Gene locus

WHO-ICD
N/A to gene loci

Incidence per 100,000 Live Births
N/A to gene loci

OMIM Number
603753

Mode of Inheritance
N/A to gene loci

Gene Map Locus
11q23.3

Description
Ubiquitination is a cellular process by which a small regulatory protein called ubiquitin is attached to a substrate protein. This protein modification can target the substrate for degradation through the proteasome, alter its cellular location, affect its activity or promote/prevent protein interactions. Ubiquitination requires several enzymes, namely: ubiquitin-activating enzymes, or E1s, ubiquitin-conjugating enzymes, or E2s, and ubiquitin-protein ligases, or E3s. UBE4A encodes an additional E4 conjugation factor, required for efficient polyubiquitination that would enable proteasomal targeting of a substrate. The EF enzyme binds to the ubiquitin moieties of preformed conjugates and works in conjunction with E1, E2 and E3 to catalyze the ubiquitin chain assembly.

Molecular Genetics
The UBE4A gene is located on the long arm of chromosome 11 at position 11q23.3. The gene spans a length of 39.6 kb of DNA and its coding sequence is contained in 20 exons. The protein product encoded by this gene has a molecular mass of 122 kDa and is made up of 1066 amino acids. Alternative splicing results in an additional isoform of the UBE4A protein with 1073 amino acids. The gene is found to be overexpressed in the brain and bone.

Epidemiology in the Arab World
Saudi Arabia
Anazi et al. (2016) researched 337 Intellectual Disability (ID) patients and found genomic tools to have a higher diagnostic yield than standard clinical evaluations. By using exome sequencing, the authors found a homozygous c.384G>A (p.Trp128*) mutation in the UBE4A gene of a 14 year old boy and his 10 year old sister. The mutation was a loss-of-function variant that segregated fully with the phenotype and had a minor allele frequency <0.001 based on 1500 Saudi exomes. The patients belonged to a consanguineous family and both suffered from global developmental delay, seizures, obesity, prominent teeth and small hands and feet. The boy also exhibited microcephaly and PWS features.

References
Anazi S, Maddirevula S, Faqeih E, Alsedairy H, Alzahrani F, Shamseldin HE, Patel N, Hashem M, Ibrahim N, Abdulwahab F, Ewida N, Alsaif HS, Al Sharif H, Alamoudi W, Kentab A, Bashiri FA, Alnaser M, AlWadei AH, Alfadhel M, Eyaid W, Hashem A, Al Asmari A, Saleh MM, AlSaman A, Alhasan KA, Alsughayir M, Al Shammari M, Mahmoud A, Al-Hassnan ZN, Al-Husain M, Osama Khalil R, Abd El Meguid N, Masri A, Ali R, Ben-Omran T, El Fishway P, Hashish A, Ercan Sencicek A, State M, Alazami AM, Salih MA, Altassan N, Arold ST, Abouelhoda M, Wakil SM, Monies D, Shaheen R, Alkuraya FS. Clinical genomics expands the morbid genome of intellectual disability and offers a high diagnostic yield. Mol Psychiatry. 2016 Jul 19. PMID: 27431290.

Related CTGA Records

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=UBE4A

Contributors
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