Transforming Growth Factor-Beta-Induced Factor

Alternative Names
TGIF
TGIF1
TGFB-Induced Factor
TG-Interacting Factor

Record Category
Gene locus

WHO-ICD
N/A to gene loci

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

OMIM Number
602630

Mode of Inheritance
N/A to gene loci

Gene Map Locus
18p11.31

Description
Retinoid X receptors (RXRs) are nuclear receptors that function as transcriptional activators. In response to retinoids, they bind to specific cis-acting RXR responsive promoter elements of the cellular retinol-binding protein II promoter. The TGIF1 gene encodes an atypical homeobox protein that competitively inhibits this binding, thereby inhibiting the 9-cis-retinoic acid-dependent RXR alpha transcription activation of the retinoic acid responsive element. TGIF1 also acts as a transcriptional co-repressor of SMAD2. By carrying out its functions, the protein plays a role in the cellular response to growth factor stimulus and is thus an important embryonic development protein.

Mutations in the TGIF1 gene have been associated with Holoprosencephaly 4 (HPE4), an autosomal dominant neurological condition.

Molecular Genetics

The TGIF1 gene is located on the short arm of chromosome 18. It spans a length of 48.3 kb of DNA and its coding sequence is spread across 12 exons. The gene encodes a 43 kDa protein product comprised of 401 amino acids. Four distinct isoforms of the TGIF1 protein exist due to alternatively spliced transcript variants. The gene is expressed in various tissues, including the liver, lung, thymus, bone marrow and brain. Heterozygous mutations in the TGIF1 gene associated with HPE4 include deletions, missense variants and premature truncations that impair its function.

Epidemiology in the Arab World
Saudi Arabia
Monies et al. (2017) reported the genomic landscape of Saudi Arabia based on the findings of 1000 diagnostic panels and exomes. One patient, an 11-year-old male, suffered from hemimegalencephaly, developmental delay and ADHD. He also had abnormal pigmentation all over his body. Whole exome sequencing helped identify a dual molecular diagnosis in this patient. A heterozygous mutation (c.1557T>G, p.Y519X) was found in exon 8 of the patient's TYRP1 gene, associated with oculocutaneous albinism type 3, and a heterozygous variant (c.90G>A, p.W30X) was uncovered in exon 1 of the TGIF1 gene, associated with HPE4. Such dual molecular diagnoses were rare and only occurred in 1.5% of the cohort. Further, given the atypical presentation of the patient, this case helped in the phenotypic expansion of the HPE4 disorder.

References

Monies D, Abouelhoda M, AlSayed M, Alhassnan Z, Alotaibi M, Kayyali H, Al-Owain M, Shah A, Rahbeeni Z, Al-Muhaizea MA, Alzaidan HI, Cupler E, Bohlega S, Faqeih E, Faden M, Alyounes B, Jaroudi D, Goljan E, Elbardisy H, Akilan A, Albar R, Aldhalaan H, Gulab S, Chedrawi A, Al Saud BK, Kurdi W, Makhseed N, Alqasim T, El Khashab HY, Al-Mousa H, Alhashem A, Kanaan I, Algoufi T, Alsaleem K, Basha TA, Al-Murshedi F, Khan S, Al-Kindy A, Alnemer M, Al-Hajjar S, Alyamani S, Aldhekri H, Al-Mehaidib A, Arnaout R, Dabbagh O, Shagrani M, Broering D, Tulbah M, Alqassmi A, Almugbel M, AlQuaiz M, Alsaman A, Al-Thihli K, Sulaiman RA, Al-Dekhail W, Alsaegh A, Bashiri FA, Qari A, Alhomadi S, Alkuraya H, Alsebayel M, Hamad MH, Szonyi L, Abaalkhail F, Al-Mayouf SM, Almojalli H, Alqadi KS, Elsiesy H, Shuaib TM, Seidahmed MZ, Abosoudah I, Akleh H, AlGhonaium A, Alkharfy TM, Al Mutairi F, Eyaid W, Alshanbary A, Sheikh FR, Alsohaibani FI, Alsonbul A, Al Tala S, Balkhy S, Bassiouni R, Alenizi AS, Hussein MH, Hassan S, Khalil M, Tabarki B, Alshahwan S, Oshi A, Sabr Y, Alsaadoun S, Salih MA, Mohamed S, Sultana H, Tamim A, El-Haj M, Alshahrani S, Bubshait DK, Alfadhel M, Faquih T, El-Kalioby M, Subhani S, Shah Z, Moghrabi N, Meyer BF, Alkuraya FS. The landscape of genetic diseases in Saudi Arabia based on the first 1000 diagnostic panels and exomes. Hum Genet. 2017 Aug;136(8):921-939. PMID: 28600779.

Related CTGA Records

Holoprosencephaly 4 (OMIM 142946)

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=TGIF1

Contributors

Sayeeda Hana
18.09.2017