Dedicator of Cytokinesis 8

Alternative Names
DOCK8

Record Category
Gene locus

WHO-ICD
N/A to gene loci

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

OMIM Number
611432

Mode of Inheritance
N/A to gene loci

Gene Map Locus
9p24.3

Description
The DOCK8 gene encodes a protein belonging to the DOCK180 family of guanine nucleotide exchange factors (GEF). Members of this family function as activators of small G proteins and are components of intracellular signaling networks. Similar to other members of this family, DOCK8 is made up of two domains called the DOCK homology regions (DHR). While DHR1 is responsible for downstream signaling and biological activity, DHR2 contains the catalytic site for GEF activity.

Mutations in the DOCK8 gene are associated with autosomal recessive hyper IgE syndrome (AR-HIES). This primary immunodeficiency disorder is characterized by recurrent viral infections, chronic eczema, elevated serum IgE levels and defective T cell activation. The disease has a high morbidity and mortality rate. AR-HIES patients with DOCK8 mutations usually have little or no DOCK8 protein. This shortage of DOCK8 is believed to affect T-cell structure and migration, B cell maturation, and antibody production, thereby leaving the individual severely immunocompromised.

Molecular Genetics
The 214 kb long DOCK8 gene is located on the short arm of chromosome 9. Its coding sequence is made up of 46 to 48 exons. The encoded protein product is approximately 238 kDa in size and made up of 2099 amino acids. Several different isoforms exist due to alternative splicing. The DOCK8 gene has been found to be highly expressed in cells of the immune system, especially in lymphocytes. More than 110 DOCK8 mutations (both homozygous and compound heterozygous) have been associated with AR-HIES. Most of these are deletions that result in a truncated protein.

Epidemiology in the Arab World

Saudi Arabia

Alsum et al. (2013) studied the clinical and molecular characteristics of 25 patients diagnosed with AR-HIES. A genetic analysis revealed DOCK8 mutations in 13 of the 17 screened individuals. Of these, seven patients from three families carried the 5625T>G (Y1875X) mutation in exon 44. Two patients of the same tribe carried the mutation 5132C>A (S1711X) in exon 40 while one patient had a splice site mutation c.827+6 T>C. All three mutations were novel and were predicted to result in a truncated protein. This was confirmed in the patient with the splice site mutation by western blot analysis, which found no DOCK8 expression. In three patients, large deletions were discovered which would abolish DOCK8 expression. An additional four patients were assumed to be DOCK8 deficient due to siblings with confirmed DOCK8 mutations and similar clinical presentations.

References
Alsum Z, Hawwari A, Alsmadi O, Al-Hissi S, Borrero E, Abu-Staiteh A, Khalak HG, Wakil S, Eldali AM, Arnaout R, Al-Ghonaium A, Al-Muhsen S, Al-Dhekri H, Al-Saud B, Al-Mousa H. Clinical, immunological and molecular characterization of DOCK8 and DOCK8-like deficient patients: single center experience of

twenty-five patients. J Clin Immunol. 2013; 33(1):55-67. PMID: 22968740

Related CTGA Records

Hyperimmunoglobulin E-Recurrent Infection Syndrome, Autosomal Recessive

External Links

http://www.genecards.org/cgi-bin/carddisp.pl?gene=DOCK8
https://ghr.nlm.nih.gov/gene/DOCK8

Contributors

Sayeeda Hana: 20.8.2016