TLR3 deficiency

GENERAL INFORMATION

Description:

Herpetic encephalopathy is a cerebral infection caused by herpes simplex virus type 1 (HSV1). This disease, which affects only a small minority of HSV1-infected individuals, could result from a genetic predisposition. A mutation in the UNC-93B gene, inducing impaired production of interferon, an anti-infectious factor necessary to fight the herpetic virus infection in nervous tissue, may be responsible for the disease. Another mutation was found in a gene encoding toll-like receptor 3 (TLR3).

Alternative names:

- TLR3D
- Influenza associated encephalopathy
- HSV encephalitis, Herpes simplex encephalitis, Herpes simplex neuroinvasion, Herpetic encephalopathy Herpetic encephalopathy, idiopathic

Classification:

- Defects of innate immune system, receptors and signaling components

Inheritance:

Autosomal dominant

OMIM:

- *603029 Toll-like receptor 3; TLR3
- *603029 Toll-like receptor 3; TLR3

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for UNC-93B deficiency
- IDR factfile for IFNγ1-receptor deficiency
- IDR factfile for IFNγ2-receptor deficiency
- IDR factfile for Interleukin-12 p40 deficiency
- IDR factfile for Interleukin-12 receptor beta 1 deficiency
- IDR factfile for STAT1 deficiency

Incidence:

1 in 250 000 and 1 in 500 000.

CLINICAL INFORMATION

Description:

Onset may occur at any age but is most common in adults. It presents as an acute necrosing temporal encephalitis, after a primary or recurrent infection. Onset is rapid (less than 48 hours) with a fever of 40 oC, headaches, and behavioural, language and memory problems. These initial manifestations are followed by numbness and coma, which may be accompanied by convulsions and paralysis.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Herpetic encephalopathy, ORPHANET, France
- Herpes simplex encephalitis, eMedicine, USA

Genetic:

- IDdiagnostics

Therapeutic options:

- Emergency treatment should involve intravenous administration of acyclovir, as soon as the diagnosis is suspected
- Herpes simplex encephalitis, eMedicine, USA

Research programs, clinical trials:

- Herpetic encephalopathy, ORPHANET, France
- HSEPID - Herpetic encephalitis in children : a new group of immune diseases

GENE INFORMATION

Names:

HUGO name: TLR3

Localization:

Reference sequences:

DNA: D0124 (IDRefSeq) , **cDNA:** U88879 (EMBL) , **Protein:** O15455 (SWISSPROT)

Chromosomal Location:

4q35

Maps:

TLR3 (Map View)

Variations / Mutations:

- TLR3base; Mutation registry for TLR3 deficiency/Influenza associated encephalopathy

Other gene-based resources:

Ensembl: ENSG00000164342, GENATLAS: TLR3, GeneCard: TLR3, UniGene: 657724, Entrez Gene: 657724, euGenes: 7098, GDB: 9864746, HomoloGene: 20696

PROTEIN INFORMATION

Description:

Protein function:

Participates in the innate immune response to microbial agents. May be involved in the recognition of ds-rna. Acts via myd88 and traf6, leading to nf-kappa-b activation, cytokine secretion and the inflammatory response (by similarity)

Subunit:

Binds myd88 via their respective tir domains (by similarity)

Subcellular location:

Membrane; single-pass type i membrane protein (by similarity)

Tissue specificity:

Expressed at high level in placenta and pancreas. Also detected in cd11c+ immature dendritic cells. Only expressed in dendritic cells and not in other leukocytes, including monocyte precursors

Similarity:

Belongs to the toll-like receptor family

Structures (PDB):

1ZIW .
2A0Z .

Domains:

TIR domain: 754-896

Other features:

Signal peptide: 1-23

Toll-like receptor 3: 24-904

N-linked (glcnac...) glycosylation sites: 52,57,70,124,196,247,252,265,275,291,398,413,507,636,662

Other related resourses:

InterPro: IPR001611; LRR, InterPro: IPR000483; LRR_C, InterPro: IPR000372; LRR_cys_N, InterPro: IPR003591; LRR_typ, InterPro: IPR000157; TIR, Pfam: PF00560; LRR_1, Pfam: PF01463; LRRCT, Pfam: PF01582; TIR, PRINTS: PR00019; LEURICHRPT, SMART: SM00369; LRR_TYP, SMART: SM00082; LRRCT, SMART: SM00013; LRRNT, SMART: SM00255; TIR, PROSITE: PS50104; TIR

Expression pattern for human:

Tissue	Exp. (%)	Clones
trachea	31.34	10:51029
placenta	19.51	23:188546
spleen	6.54	2:48893
bladder	6.44	1:24827
adrenal_gland	5.15	1:31044
kidney	3.32	4:192682
colon	3.24	2:98776
connective_tissue	3.23	2:99154
muscle	3.19	2:100230
unclassified	2.66	1:60167

Animal models:

Mouse:

MGD: ; Tlr3

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies (IPOPI)
- Immune Deficiency Foundation
- European Society for Immunodeficiencies
- NIH/National Institute of Allergy and Infectious Diseases

Other information sources:

- Immunodeficiencies+TLR3 deficiency