IRAK4 deficiency

GENERAL INFORMATION

Description:

NEMO, IKBA and IRAK4 (IL-1-receptor-associated kinase-4) mutations result in novel primary immunodeficiencies affecting the NF-kB signalling pathway. The infectious phenotypes associated with each of the three genetic disorders are markedly different. IRAK4 deficiency patients are susceptible to pyogenic bacteria and resistant to most other common microorganisms, including mycobacteria, viruses and fungi.

Alternative names:

- IRAK4D

Classification:

- Defects of innate immune system, receptors and signaling components

Inheritance:

Autosomal recessive

OMIM:

- #607676 IRAK4 deficiency
- *606883 Interleukin 1 receptor-associated kinase 4

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Nemo deficiency

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Three unrelated children with IRAK4 deficiency developed multiple life-threatening infections with pyogenic bacteria, with no developmental signs such as EDA, osteopetrosis or lymphoedema. These patients were mostly infected with encapsulated Gram-positive S. pneumoniae and S.aureus bacteria. No infections with H. influenzae were reported, but one patient presented severe infections with other Gram-negative bacteria. These infection occured early in life, but the condition improved with age.

Diagnosis:

Diagnostic laboratories:

Therapeutic options:

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Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies, coord. Edvart Smith

GENE INFORMATION

Names:

HUGO name: IRAK4
Alias(es): LOC51135, NY-REN-64, REN64, Interleukin-1 receptor associated kinase 4 , Hypothetical protein FLJ20521, Interleukin-1 receptor associated kinase 4 mutant form 1, Interleukin-1 receptor associated kinase 4 mutant form 2

Localization:

Reference sequences:

DNA: AF445802 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** Q8TDF7 (SWISSPROT)

Chromosomal Location:

Chr.4

Maps:

IRAK4 (Map View)

Variations / Mutations:

- IRAK4base; Mutation registry for IRAK4 deficiency

Other gene-based resources:

Ensembl: ENSG00000198001, GENATLAS: IRAK4, GeneCard: IRAK4, UniGene: 138499, Entrez Gene: 51135, euGenes: 51135, GDB: 11510556

PROTEIN INFORMATION

Description:

Protein function:

Involved in IL1R-induced NF-kappa-B (NFkB) activation as well as the activation of mitogen-activated protein (MAP) kinase pathways. Phosphorylates IRAK1.

Subunit:

Interacts with TRAF6 and IRAK1.

Belongs to the Ser/Thr protein kinase family. Pelle subfamily.

Other features:

Other related resourses:

InterPro: IPR000719; Prot_kinase, InterPro: IPR001245; Tyr_pkinase, Pfam: PF00069; Pkinase, ProDom: PD000001; Prot_kinase, PROSITE: PS50011; PROTEIN_KINASE_DOM

Expression pattern for human:

Tissue	Exp. (%)	Clones
ovary	34.27	1:880
natural killer cells, cell line	11.01	2:5480
neuroepithelial cells	9.91	1:3043
leukopheresis	7.76	2:7769
embryonic stem cells	6.28	1:4803
from chronic myelogenous leukemia	4.92	1:6125
glioblastoma	4.26	1:7072
hypernephroma, cell line	3.76	1:8027
leukocyte	3.41	1:8838
endometrium, adenocarcinoma cell line	2.99	1:10072
ovary	34.27	1:880
natural killer cells, cell line	11.01	2:5480
neuroepithelial cells	9.91	1:3043
leukopheresis	7.76	2:7769
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leukocyte	3.41	1:8838
endometrium, adenocarcinoma cell line	2.99	1:10072

Animal models:

Mouse:

MGD: ; Irak4

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies