μ heavy-chain deficiency

GENERAL INFORMATION

Description:

Defects in the μ heavy-chain gene are a cause of autosomal recessive agammaglobulinemia. Agammaglobulinemia is characterized by failure to produce mature B lymphocyte cells and associated with a failure of Ig heavy chain rearrangement. An intact membrane-bound μ chain is essential for B-cell development. The recessive form is phenotypically identical to XLA but with possible autosomal origin. The μ heavy-chain gene on chromosome 14 is the most frequent abnormality in patients with agammaglobulinemia and decreased B cells who do not have a defect in BTK.

Alternative names:

- Immunoglobulin heavy μ chain deficiency
- Agammaglobulinemia due to early proB cell deffect
- Agammaglobulinemia, autosomal recessive

Classification:

- Deficiencies predominantly affecting antibody production
  - Agammaglobulinemia

Inheritance:

Autosomal recessive

OMIM:

- #601495 Agammaglobulinemia, non-bruton type
- *147020 Immunoglobulin MU; IGHM

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for X-linked agammaglobulinemia
- IDR factfile for X-linked hypogammaglobulinemia with growth hormone deficiency
- IDR factfile for BLNK deficiency
- IDR factfile for Igα deficiency
- IDR factfile for λ5 surrogate light-chain deficiency

Incidence:

1/2,000,000 births.

CLINICAL INFORMATION

Description:

Patients with mutations in μ heavy chain tend to develop symptoms earlier and are more likely to have severe symptoms. Symptoms present initially at the age of few months with pneumonia, otitis, gastroenteritis, chronic enterovirus enchephalitis, and Pseudomonas aeruginosa septic shock. Recurrent infections, mostly respiratory, with pyogenic bacteria, chronic diarrhoea and hypogammaglobulinemia are also present.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Agammaglobulinemia, autosomal recessive, ORPHANET

Genetic:

- Molecular Haematology Department - Royal Hallamshire Hospital (Sheffield), EDDNAL

Therapeutic options:

- (Intravenous) immunoglobulins and antibiotic therapy. Oral poliovaccine should not be given because of the risk of paralytic disease.
- Hypogammaglobulinemia, eMedicine

Research programs, clinical trials:

- Improved Healthcare for Patients with Primary Antibody Deficiencies through new Strategies Elucidating their Pathophysiology (IMPAD), IMPAD
- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: IGHM
Alias(es): μ, Immunoglobin heavy constant μ, immunoglobulin μ, Ig μ chain C region

Localization:

Reference sequences:

DNA: X57331 (EMBL) , **cDNA:** X17115 (EMBL) , **Protein:** P01871 (SWISSPROT) Other Sequences

Chromosomal Location:

14q32.3

Maps:

IGHM (Map View)

Variations / Mutations:

- IGHMbase; Mutation registry for μ heavy-chain deficiency

Other gene-based resources:

Ensembl: ENSG00000130076, GENATLAS: IGHM, GeneCard: IGHM, UniGene: 525648, Entrez Gene: 3507, euGenes: 3507, GDB: 120086, IMGT: IGHM

PROTEIN INFORMATION

Description:

Miscellaneous:

All 4 combinations of the s/g & v/g polymorphisms at positions 192 and 216 have been observed in human mu chains.

Domains:

Ch1 domain: 1-105

Ch2 domain: 106-218

Ch3 domain: 219-324

Ch4 domain: 325-454

Other features:

Disulfide bond interchain (with a light chain): 14

Disulfide bond interchain (with a heavy chain): 215

Disulfide bond interchain (with a heavy chain in another of the 5 tetrameric subunits of the molecule): 292

Disulfide bond interchain (with a heavy chain): 453

Disulfide bonds: 28-88, 135-198, 245-304, 352-414

Other related resourses:

PIR: MHHU, InterPro: IPR003006; Ig_MHC, InterPro: IPR003597; Ig_c1, Pfam: PF00047; ig, SMART: SM00410; IG_like, SMART: SM00407; IGc1, PROSITE: PS00290; IG_MHC

Expression pattern for human:

Tissue	Exp. (%)	Clones
lymph	15.97	618:64395
adipose	11.76	6:849
B-cells	10.37	103:16533
lymph node, pool of 10 lymphomas	8.22	2:405
head/neck	6.38	2:522
spleen	4.37	19:7229
genitourinary tract	4.36	10:3813
colonic mucosa with ulcerative colitus	4.10	3:1218
pancreas, exocrine	3.03	39:21418
lung with fibrosis	2.25	2:1479

Animal models:

Mouse:

MGD: ; Igh-6

Fly:

euGenes: ; Toll-7

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