Cyclic neutropenia

GENERAL INFORMATION

Description:

Cyclic neutropenia caused by defects in ELA2 is an autosomal dominant disease in which blood-cell production from the bone marrow oscillates with 21-day periodicity. Circulating neutrophils vary between almost normal numbers and zero. During intervals of neutropenia, affected individuals are at risk for opportunistic infection. Monocytes, platelets, lymphocytes and reticulocytes also cycle with the same frequency.

Alternative names:

- ELA2 related neutropenia
- Cyclic haematopoiesis

Classification:

- Defects of phagocyte function
  - Severe congenital and cyclic neutropenias
    - Cyclic neutropenia

Inheritance:

Autosomal dominant

OMIM:

- #162800 Cyclic hematopoiesis
- *130130 Elastase 2; ELA2

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Severe congenital neutropenias, including Kostmann syndrome

Incidence:

1: 1,000,000

CLINICAL INFORMATION

Description:

Symptoms associated with cyclic neutropenia may include fever, a general feeling of ill health (malaise), skin and oropharyngeal inflammation (mouth ulcers, gingivitis, sinusitis, and pharyngitis). In most cases, individuals with low levels of neutrophils (neutropenia) are abnormally susceptible to recurrent infections. Cyclic neutropenia is usually diagnosed within the first years of life based on recurrent fever and oral ulcerations occuring at 3 weeks intervals. Cellulitis is common during the neutropenic periods. Between neutropenic periods, individuals are generally healthy. Symptoms improve in adulthood. There is no risk of malignancy or conversion to leukemia.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Neutropenia cyclic, ORPHANET
- Neutropenia, eMedicine

Genetic:

- Laboratorio di Genetica Pediatrica "Angelo Nocivelli" - University of Brescia, EDDNAL

Therapeutic options:

- Treatment with recombinant human granulocyte colony-stimulating factor (GCSF) raises blood neutrophil levels, diminishes the number of new infections and improves survival and quality of life.
- Neutropenia, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies 2001-2004
- Research Program of Aprikyan and Associates, University of Washington

GENE INFORMATION

Names:

HUGO name: ELA2
Alias(es): SERP1, Elastase 2, neutrophil, Serine protease, Leukocyte elastase precursor, Neutrophil elastase, PMN elastase, Bone marrow serine protease, Medullasin

Localization:

Reference sequences:

DNA: Y00477 (EMBL) M20203 (EMBL) , **cDNA:** J03545 (EMBL) X05875 (EMBL) X05875 (EMBL) M34379 (EMBL) D00187 (EMBL) , **Protein:** AAS89303 (NCBI) Other Sequences

Chromosomal Location:

19p13.3

Maps:

ELA2 (Map View)

Other gene-based resources:

Ensembl: ENSP00000263621, GENATLAS: ELA2, GeneCard: ELA2, UniGene: 99863, Entrez Gene: 1991, euGenes: 1991, GDB: 118792

PROTEIN INFORMATION

Description:

Protein function:

Medullasin modifies the functions of natural killer cells, monocytes and granulocytes.

Catalytic activity:

Hydrolysis of proteins, including elastin. Preferential cleavage: val-|-xaa > ala-|-xaa.

Structures (PDB):

1HNE	Structure of human neutrophil elastase in complex with a peptide chloromethyl ketone inhibitor at 1.84-A resolution.
1PPF	X-ray crystal structure of the complex of human leukocyte elastase (PMN elastase) and the third domain of the turkey ovomucoid inhibitor.
1PPG	The refined 2.3 A crystal structure of human leukocyte elastase in a complex with a valine chloromethyl ketone inhibitor.
1B0F	Crystal Structure Of Human Neutrophil Elastase With Mdl 101, 146

Other features:

Signal peptide: 1-27

Propeptide: 28-29

Leukocyte elastase: 30-267

Disulfide bonds: 55-71, 151-208, 181-187, 198-223

N-linked (glcnac...) glycosylation sites: 88, 124, 173

Other related resourses:

PIR: ELHUL, InterPro: IPR001314; Chymotrypsin, InterPro: IPR001254; Ser_protease_Try, Pfam: PF00089; trypsin, SMART: SM00020; Tryp_SPc, PROSITE: PS50240; TRYPSIN_DOM, PROSITE: PS00134; TRYPSIN_HIS, PROSITE: PS00135; TRYPSIN_SER

Expression pattern for human:

Tissue	Exp. (%)	Clones
whole blood	50.84	6:2445
thymus	46.14	1:449
cervix	1.64	2:25325
bone marrow	1.04	1:19854
pool, liver+spleen	0.34	1:61327

Animal models:

Mouse:

MGD: ; Ela2

OTHER RESOURCES

Societies:

General:

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

Disease specific:

- Neutropenia Support Association, Canada
- Severe Chronic Neutropenia International Registry, USA
- Severe Chronic Neutropenia International Registry, Germany