Neutrophil-specific granule deficiency

GENERAL INFORMATION

Description:

Specific granule deficiency is a rare congenital disorder. The CEBPE gene encodes a transcription factor, which is expressed primarily during granulocytic differentiation. Individuals with specific granule deficiency express normal levels of lactoferrin and transcobalamin in their saliva but not in either their plasma or neutrophils. Specific granule deficiency involves morphological and functional abnormalities in neutrophils and eosinophils and is characterised by lack of specific or secondary granules in developing mature neutrophils.

Alternative names:

- SGD
- Specific granule deficiency
- Lactoferin-deficient neutrophils
- Neutrophil lactoferrin deficiency

Classification:

- Defects of phagocyte function

Inheritance:

OMIM:

- #245480 Specific granule deficiency, SGD
- *600749 Ccaat/enhancer-binding protein, epsilon; CEBPE

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Severe congenital neutropenias, including Kostmann syndrome
- IDR factfile for Cyclic neutropenia

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients have a lifetime of recurrent, pyogenic infections. Neutrophils from these individuals have abnormalities in nuclear morphology and lack primary, specific, and tertiary granule proteins including lactoferrin, collagenase, and defensins. They are defective in chemotaxis and killing of bacteria. Eosinophil-specific granule content, including eosinophil cationic protein, eosinophil-derived neurotoxin, and major basic protein (MBP), is deficient in specific granule deficiency (SGD) and have a defect in myelopoiesis. Due to impairment of the granulocytic and monocytic lineages, patients have profound defects in the innate-immune response, with severe and frequent bacterial infections.

Diagnosis:

Diagnostic laboratories:

Therapeutic options:

- Treatment with recombinant human granulocyte colony-stimulating factor (GCSF) elevates the granulocyte counts, diminishes the number of new infections and improve survival and quality of life. Some patients developed leukemia or myelodysplastic syndrome. Bone marrow transplantation could be an option.
- Inherited Neutrophil Disorders, Molecular Basis and New Therapies

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.

GENE INFORMATION

Names:

HUGO name: CEBPE
Alias(es): C/EBP-epsilon, CRP1, CCAAT/ enhancer binding protein (C/EBP), epsilon

Localization:

Reference sequences:

DNA: U48865 (EMBL) U48866 (EMBL) U80982 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** Q15744 (SWISSPROT)

Chromosomal Location:

14q11.2

Maps:

CEBPE (Map View)

Markers:

D14S990, RH75880

Variations / Mutations:

- CEBPEbase; Mutation registry for Neutrophil-specific granule deficiency

Other gene-based resources:

Ensembl: ENSG00000092067, GENATLAS: CEBPE, GeneCard: CEBPE, UniGene: 426867, Entrez Gene: 1053, euGenes: 1053, GDB: 132660, HomoloGene: 1367

PROTEIN INFORMATION

Description:

Protein function:

C/EBP are DNA-binding proteins that recognize two different motifs: the CCAAT homology common to many promoters and the enhanced core homology common to many enhancers

Subunit:

Binds DNA as a dimer and can form stable heterodimers with C/EBP delta.

Subcellular location:

Nuclear

Post-translational modification:

Phosphorylated

Tissue specificity:

Strongest expression occurs in promyelocyte and late-myeloblast-like cell lines.

Similarity:

Belongs to the bzip family. C/EBP subfamily.

Domains:

Leucine-zipper domain: 239-267

Other features:

DNA-binding region Basic motif: 208-228

Other related resourses:

InterPro: IPR004827; TF_bZIP, Pfam: PF00170; bZIP, SMART: SM00338; BRLZ, PROSITE: PS50217; BZIP, PROSITE: PS00036; BZIP_BASIC

Expression pattern for human:

Tissue	Exp. (%)	Clones
subchondral bone	77.55	2:5896
hippocampus	12.25	1:18660
embryonal carcinoma, cell line	9.68	1:23620
unclassified	0.52	2:879462
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Animal models:

Mouse:

MGD: , NCBI Gene: ; 239097 (93.24 % aminoacid similarity to human)

Rat:

NCBI Gene: ; 25410 (93.59 % aminoacid similarity to human)

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies

Other information sources:

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