GFI1 deficiency

GENERAL INFORMATION

Description:

Defects in protooncogene GFI1, are a cause of autosomal dominant severe congenital neutropenia (SCN). ELA2 mutations cause cyclic hematopoiesis and about two thirds of severe congenital neutropenia (SCN) cases. Mutations in WAS (different from those causing Wiskott-Aldrich thrombocytopenia) also cause severe congenital neutropenia (SCN). Mutations in GFI1 produce immature neutrophils and monocytes. The combined neutropenia and immunodeficiency resembles WHIM (syndrome of warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis), but neutrophils have an undifferentiated appearance different from the hypermature appearance of neutrophils in WHIM syndrome. Neutropenia causing GFI1 causing mutations are heterozygous.

Alternative names:

- SCN
- severe congenital neutropenia

Classification:

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

Inheritance:

Autosomal dominant

OMIM:

- #202700 Neutropenias, severe congenital ; SCN
- *600871 Growth factor-independent 1; GFI1
- *130130 ELASTASE 2; ELA2

Cross references:

Phenotype related immunodeficiencies:

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

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients with GFI mutations present by age of three month recurrent bacterial infections. The most common sites of infection are the mouth and perirectum. The patients have also anemic symptoms (fatigue, weakness, dyspnea on exertion) and symptoms of thrombocytopenia (petechia, purpura, epistaxis).

Diagnosis:

Diagnostic laboratories:

Clinical:

- Kostmann syndrome, ORPHANET
- Kostmann disease, eMedicine

Therapeutic options:

- Treatment with recombinant human granulocyte colony-stimulating factor (GCSF) elevates the granulocyte counts, helps resolve preexisting infections, diminishes the number of new infections and results in significant improvements in survival and quality of life. Some patients have developed leukemia or myelodysplastic syndrome following treatment with GCSF.
- Kostmann disease, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies 2001-2004, coord.Edvard Smith.

GENE INFORMATION

Names:

HUGO name: GFI1

Localization:

Reference sequences:

DNA: U67369 (EMBL) BC032751 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** Q99684 (SWISSPROT)

Chromosomal Location:

1p22

Maps:

GFI1 (Map View)

Variations / Mutations:

- GFI1base; Mutation registry for GFI1 deficiency

Other gene-based resources:

Ensembl: ENSG00000162676, GENATLAS: GFI1, GeneCard: GFI1, UniGene: 73172, Entrez Gene: 2672, euGenes: 2672, GDB: 389574, HomoloGene: 3854

PROTEIN INFORMATION

Description:

Protein function:

May be a transcription factor involved in regulating the expression of genes active in the S phase during cell cycle progression in T cells. May be involved in tumor progression. Represses ELA2 transcription.

Subcellular location:

Nuclear

Similarity:

Contains 6 c2h2-type zinc fingers.

Domains:

GLY/ALA-RICH domain: 158-209

Other features:

Zinc finger region C2h2-type 1: 255-278

Zinc finger region C2h2-type 2: 284-306

Zinc finger region C2h2-type 3: 312-334

Zinc finger region C2h2-type 4: 340-362

Zinc finger region C2h2-type 5: 368-390

Zinc finger region C2h2-type 6: 396-419

Other related resourses:

InterPro: IPR007110; Ig-like, InterPro: IPR007087; Znf_C2H2, InterPro: IPR001878; Znf_CCHC, Pfam: PF00096; zf-C2H2, ProDom: PD000003; Znf_C2H2, SMART: SM00355; ZnF_C2H2, SMART: SM00343; ZnF_C2HC, PROSITE: PS00028; ZINC_FINGER_C2H2_1, PROSITE: PS50157; ZINC_FINGER_C2H2_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
tHYMUS	70.72	2:2217
pooled	13.75	1:5703
bone_Marrow	5.34	2:29369
lung	3.44	10:227901
pancreas	2.32	2:67592
testis	1.46	2:107669
lymph_Node	1.38	2:113869
mixed	1.00	4:314320
uterus	0.61	1:128533
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Animal models:

Mouse:

MGD: ; Gfi1

OTHER RESOURCES

Societies:

General:

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

Disease specific:

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