Myeloperoxidase deficiency

GENERAL INFORMATION

Description:

Myeloperoxidase (MPO) deficiency is a common inherited disorder linked to increased susceptibility to infection and malignancy. Myeloperoxidase (MPO) enzyme is expressed in the azurophilic granules of neutrophils and in the lysosomes of monocytes. Its major role is to aid in microbial killing. MPO deficiency can be divided into two subgroups: primary (congenital) and secondary (acquired). Primary MPO deficiency has a genetic origin, present varying degree of severity in more than one family member, and involves both the neutrophil and monocyte lineages.

Alternative names:

- MPO deficiency
- Alius-Grignashi-Anomaly
- Grignashi anomaly

Classification:

- Defects of phagocyte function

Inheritance:

Autosomal recesseive

OMIM:

- #254600 Myeloperoxidase deficiency
- *606989 Myeloperoxidase, MPO

Cross references:

Incidence:

1:2000

CLINICAL INFORMATION

Description:

Most patients with myeloperoxidase deficiency are asymptomatic and the condition is usually undiagnosed. Patients have recurrent infections, particularly candidal and an increased incidence of malignancy. Visceral infections with Candida are most of the time associated with diabetus mellitus. Patients can present also an increased number of blood eosinophils.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Myeloperoxidase deficiency, ORPHANET
- Myeloperoxidase deficiency, eMedicine

Therapeutic options:

- Maintenance antibiotic therapy is not recommended if myeloperoxidase deficient subjects do not suffer from infections. Patients affected also by diabetus mellitus, with a high tendency to localized and systemic infections need a prompt and prolonged therapy with antibiotics. In case of infections with resistant micro-organisms or species of fungi, parenteral antibiotics are beneficial.
- Myeloperoxidase deficiency, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.

GENE INFORMATION

Names:

HUGO name: MPO
Alias(es): Myeloperoxidase, Myeloperoxidase precursor

Localization:

Reference sequences:

DNA: M17176 (EMBL) X15377 (EMBL) A08802 (EMBL) , **cDNA:** M19507 (EMBL) X04876 (EMBL) J02694 (EMBL) S56200 (EMBL) , **Protein:** P05164 (SWISSPROT) Other Sequences

Chromosomal Location:

17q23.1

Maps:

MPO (Map View)

Variations / Mutations:

- MPObase; Mutation registry for Myeloperoxidase deficiency

Other gene-based resources:

Ensembl: ENSG00000005381, GENATLAS: MPO, GeneCard: MPO, UniGene: 458272, Entrez Gene: 4353, euGenes: 4353, GDB: 120192

PROTEIN INFORMATION

Description:

Protein function:

Part of the host defense system of polymorphonuclear leukocytes. It is responsible for microbicidal activity against a wide range of organisms. In the stimulated PMN, MPO catalyzes the production of hypohalous acids, primarily hypochlorous acid in physiologic situations, and other toxic intermediates that greatly enhance PMN microbicidal activity.

Catalytic activity:

Cl(-) + h(2)o(2) = hocl + 2 h(2)o

Subunit:

Tetramer of two light chains and two heavy chains.

Cofactor:

Binds 1 heme B (iron-protoporphyrin IX) group covalently and 1 calcium ion per heterodimer.

Structures (PDB):

1MHL Crystal Structure Of Human Myeloperoxidase Isoform C Crystallized In Space Group P2(1) At pH 5.5 and 20 Deg C
1CXP Cryogenic Crystal Structure Of Human Myeloperoxidase Isoform C
1D2V Crystal Structure Of Bromide-Bound Human Myeloperoxidase Isoform C At pH 5.5
1D5L Crystal Structure Of Cyanide-Bound Human Myeloperoxidase Isoform C At pH 5.5
1D7W Crystal Structure Of Human Myeloperoxidase Isoform C Complexed With Cyanide and Bromide At pH 4.0
1DNU Structural Analyses Of Human Myeloperoxidase-Thiocyanate Complex
1DNW Human Myeloperoxidase-Cyanide-Thiocyanate Complex

Other features:

Signal peptide: 1-48

Propeptide: 49-164

Myeloperoxidase: 165-745

89 kda myeloperoxidase: 49-745

84 kda myeloperoxidase: 155-745

Myeloperoxidase light chain: 165-278

Myeloperoxidase heavy chain: 279-745

Calcium-binding region: 262

Calcium-binding region: 334

Calcium-binding region Via carbonyl oxygen: 336

Calcium-binding region: 338

Calcium-binding region: 340

Protoheme ix (covalent) binding site: 260

Protoheme ix (covalent) binding site: 408

Protoheme ix (covalent) binding site: 409

Iron (protoheme ix axial ligand) binding site: 502

Disulfide bond interchain: 319

Disulfide bonds: 167-180, 281-291, 285-309, 387-398, 606-663, 704-730
N-linked (glcnac...) glycosylation sites: 355, 391, 483
Other related resourses:

PIR: OPHUM, InterPro: IPR002007; Anim_peroxidase, InterPro: IPR002016; Peroxidase, Pfam: PF03098; An_peroxidase, PROSITE: PS00435; PEROXIDASE_1, PROSITE: PS00436; PEROXIDASE_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
whole blood	75.26	23:2445
leukopheresis	10.53	6:4557
cord blood	6.19	6:7759
thymus, pooled	2.52	1:3169
rpe and choroid	1.51	2:10565
pool, liver+spleen	0.91	7:61327
bone marrow	0.81	2:19854
bone	0.64	1:12499
unclassified	0.62	4:51898
pool, lung+testis+B-cell	0.57	4:55714

OTHER RESOURCES

Societies:

General:

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