Immunodeficiency, centromere instability and facial abnormalities syndrome (ICF)

GENERAL INFORMATION

Description:

Defects in DNMT3B are a cause of immunodeficiency-centromeric instability-facial anomalies syndrome. ICF is a rare autosomal recessive disorder characterized by a variable immunodeficiency, mild facial anomalies, and centromeric heterochromatin instability involving chromosomes 1, 9, and 16. ICF is biochemically characterized by hypomethylation of CpG sites in some regions of heterochromatin.

Alternative names:

- ICF
- ICF syndrome

Classification:

- DNA breakage associated syndromes

Inheritance:

Autosomal recessive

OMIM:

- #242860 Immunodeficiency, centromere instability and facial abnormalities syndrome (ICF)
- *602900 DNA methyltransferase 3b; DNMT3B

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Nijmegen-breakage syndrome
- IDR factfile for Bloom syndrome
- IDR factfile for Ataxia-telengiectasia

Incidence:

1:200,000

CLINICAL INFORMATION

Description:

Features of this disease include severe immunodeficiency with an absence or profound reduction in at least two immunoglobulin isotypes which cause most ICF patients to succumb to infectious diseases before adulthood.
In some cases patients can have impaired cellular immunity, neurologic and intestinal dysfunction, peculiar facial features, and delayed developmental milestones. Affected individuals usually suffer from severe respiratory tract infections, and often do not survive into adulthood. Mild facial anomalies include hypertelorism, low-set ears, epicanthal folds and macroglossia.

Diagnosis:

Diagnostic laboratories:

Clinical:

- ICF syndrome, ORPHANET

Therapeutic options:

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Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: DNMT3B
Alias(es): ICF, M.HsaIIIB, DNA (cytosine-5-)-methyltransferase 3 beta, DNA MTase HsaIIIB, DNA methyltransferase HsaIIIB, DNA (cytosine-5)-methyltransferase 3B, EC 2.1.1.37, Dnmt3b

Localization:

Reference sequences:

DNA: AL035071 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** Q9UBC3 (SWISSPROT) Other Sequences

Chromosomal Location:

20q11.2

Maps:

DNMT3B (Map View)

Markers:

D20S1126

Variations / Mutations:

- DNMT3Bbase; Mutation registry for ICF syndrome

Other gene-based resources:

Ensembl: ENSG00000088305, GENATLAS: DNMT3B, GeneCard: DNMT3B, UniGene: 251673, Entrez Gene: 1789, euGenes: 1789, GDB: 9862955

PROTEIN INFORMATION

Description:

Protein function:

Required for genome wide de novo methylation and is essential for development. Isoforms 4 and 5 are probably not functional due to the deletion of two conserved methyltransferase motifs.

Catalytic activity:

S-adenosyl-l-methionine + DNA = s-adenosyl-l-homocysteine + DNA containing 5-methylcytosine

Subunit:

Interacts with ubl1 and ube2i9.

Subcellular location:

Nuclear

Post-translational modification:

Sumoylated

Tissue specificity:

Ubiquitous; highly expressed in fetal liver, heart, kidney, placenta, and at lower levels in spleen, colon, brain, liver, small intestine, lung, peripheral blood mononuclear cells, and skeletal muscle. Isoform 1 is expressed in all tissues except brain, skeletal muscle and PBMC, 3 is ubiquitous, 4 is expresed in all tissues except brain, skeletal muscle, lung and prostate and 5 is detectable only in testis and at very low level in brain and prostate.

Similarity:

Belongs to the C5-methyltransferase family.

Domains:

PWWP domain: 225-283

Other features:

Zinc finger region Add-type: 435-527

Other related resourses:

InterPro: IPR001525; C5_DNA_meth, InterPro: IPR011011; FYVE_PHD_ZnF, InterPro: IPR000313; PWWP, Pfam: PF00145; DNA_methylase, Pfam: PF00855; PWWP, SMART: SM00293; PWWP, PROSITE: PS00094; C5_MTASE_1, PROSITE: PS00095; C5_MTASE_2, PROSITE: PS50812; PWWP

Expression pattern for human:

Tissue	Exp. (%)	Clones
embryonic stem cells	85.79	14:4820
ovary	2.89	7:71634
placenta	2.28	11:142648
peripheral_nervous_system	1.41	1:21019
skin	1.18	6:150171
bone_marrow	1.01	1:29369
other	0.98	14:423795
cervix	0.90	1:32826
brain	0.65	7:319574
bone	0.58	1:51252
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Animal models:

Mouse:

MGD: ; Dnmt3b

OTHER RESOURCES

Societies:

General:

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