LAD with RAC2 deficiency

GENERAL INFORMATION

Description:

Defects in RAC2 are the cause of neutrophil immunodeficiency syndrome, that clinically resembles LAD1. Rac2 is part of the NADPH oxidase complex. Rac2 is necessary for the regulation of the actin cytoskeleton (chemotaxis and degranulation) and NADPH oxidase (superoxide production) function.

Alternative names:

- LAD caused by Rac2 deficiency
- Neutrophil immunodeficiency syndrome

Classification:

- Defects of phagocyte function
  - Leukocyte adhesion defects

Inheritance:

Autosomal dominant

OMIM:

- #608203 Neutrophil immunodeficiency syndrome
- *602049 Ras-related C3 botulinum toxin substrate 2; RAC2

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Leukocyte adhesion deficiency I

Incidence:

Incidence is not known yet.

CLINICAL INFORMATION

Description:

Patients with neutrophil immunodeficiency syndrome presented severe bacterial infections and poor wound healing, delayed umbilical cord separation, perirectal abscesses, failure to heal surgical wounds, and absent pus at sites of infection in the setting of neutrophilia. Patient shows leukocytosis and neutrophilia, normal levels of serum immunoglobulins, normal complement activity (CH50 and C3), and low-normal numbers of total T and B cells, as well as T-cell subsets for his age. Neutrophils exhibit decreased chemotaxis, polarization, azurophilic granule secretion, and superoxide anion production.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Leukocyte adhesion deficiency, ORPHANET
- Leukocyte adhesion deficiency, eMedicine

Therapeutic options:

- Bone marrow transplantation has been curative.
- Leukocyte adhesion deficiency, eMedicine

Research programs, clinical trials:

- Use of G-CSF to Obtain Blood Cell Precursors, Clinical.Trials.gov
- Posaconazole to Treat Invasive Fungal Infections, Clinical.Trials.gov
- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: RAC2
Alias(es): EN-7, Gx, HSPC022, Ras-related C3 botulinum toxin substrate 2, Ras-related C3 botulinum toxin substrate 3 (rho family, small GTP-binding protein Rac2), Ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2), Rho family, small GTP binding protein Rac2, Small G protein, Ras-related C3 botulinum toxin substrate 2, p21-Rac2, Small G protein

Localization:

Reference sequences:

DNA: M29871 (EMBL) AF498965 (EMBL) Z82188 (EMBL) BC001485 (EMBL) M64595 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** P15153 (SWISSPROT)

Chromosomal Location:

22q12.3-q13.2

Maps:

RAC2 (Map View)

Markers:

STS-AA033975

Variations / Mutations:

- RAC2base; Mutation registry for Neutrophil immunodeficiency syndrome

Other gene-based resources:

Ensembl: ENSG00000128340, GENATLAS: RAC2, GeneCard: RAC2, UniGene: 517601, Entrez Gene: 5880, euGenes: 5880, GDB: 134411

PROTEIN INFORMATION

Description:

Protein function:

Plasma membrane-associated small GTPase which cycles between an active GTP-bond and inactive GDP-bound state. In active state binds to a variety of effector proteins to regulate cellular responses, such as secretory processes, phagocytose of apoptotic cells and epithelial cell polarization. Seems to be involved in the regulation of the NADPH oxidase.

Subunit:

Interacts with DOCK2, which may activate it.

Subcellular location:

Cytoplasmic; membrane-associated when activated.

Enzyme regulation:

Regulated by guanine nucleotide exchange factors (GEFS) which promote the exchange of bound GDP for free GTP, GTPase activating proteins (gaps) which increase the GTP hydrolysis activity, and GDP dissociation inhibitors which inhibit the dissociation of the nucleotide from the GTPase.

Tissue specificity:

Hematopoietic specific

Similarity:

Belongs to the small GTPase superfamily. Rho family

Structures (PDB):

1DS6 Crystal Structure Of A Rac-Rhogdi Complex

Domains:

Effector region domain: 32-40

Other features:

GTP nucleotide phosphate-binding region: 10-17

GTP nucleotide phosphate-binding region: 57-61

GTP nucleotide phosphate-binding region: 115-118

Other related resourses:

PIR: B34386, InterPro: IPR003578; GTPase_Rho, InterPro: IPR001806; Ras_trnsfrmng, InterPro: IPR005225; Small_GTP, Pfam: PF00071; ras

Expression pattern for human:

Tissue	Exp. (%)	Clones
periph blood	72.49	1:19
nasopharyngeal carcinoma	2.11	1:654
invasive tumor (cell line)	1.81	1:761
primary B-cells from tonsils (cell line)	1.71	20:16102
lymphoma, follicular mixed small and large cell	1.46	9:8495
leukocyte	1.25	8:8838
T cells (Jurkat cell line)	1.15	2:2387
lung focal fibrosis	1.06	3:3912
natural killer cells, cell line	1.01	4:5480
lymphoma, cell line	0.96	21:30144
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Animal models:

Mouse:

MGD: ; Rac2

OTHER RESOURCES

Societies:

General:

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