ALPS type III

GENERAL INFORMATION

Description:

Defects in NRAS are a cause of juvenile myelomonocytic leukemia (JMML) [mim:607785]. JMML is a pediatric myelodysplastic syndrome that constitutes approximately 30% of childhood cases of myelodysplastic syndrome (MDS) and 2% of leukemia. NRAS mutations leads to key features resembling ALPS and hematopoietic malignancies.

Alternative names:

- ALPS3
- NRAS deficiency

Classification:

- Defects in lymphocyte apoptosis
  - Autoimmune lymphoproliferative syndrome

Inheritance:

Autosomal dominant/Autosomal recessive

OMIM:

- *164790 Neuroblastoma ras viral oncogene homolog; NRAS
- #601859 Autoimmune lymphoproliferative syndrome, type I
- #603909 Autoimmune lymphoproliferative syndrome, type II

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Apoptosis mediator APO-1/Fas defects
- IDR factfile for APO-1 ligand/Fas ligand defects
- IDR factfile for Autoimmune lymphoproliferative syndrome type II

Incidence:

Incidence unknown.

CLINICAL INFORMATION

Description:

Patient had lifelong lymphadenopathy and splenomegaly, marked leukocytosis, large non-Hodgkin's B cell lymphoma, positive autoantibodies: direct antiglobulin test, ANA, ACA IgG and IgM, rheumatoid factor.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Autoimmune lymphoproliferative syndrome, ORPHANET
- Lymphoproliferative disorders, eMedicine

Genetic:

- IDdiagnostics

Therapeutic options:

- Immune suppression. In patients with massive lymphoproliferation, chemotherapy with prednisone, cyclophosphamide and vincristine has been unsuccessful. In case of hypersplenism, splenectomy is often performed. Severe autoimmune manifestation can be treated with steroids and cyclophosphamide.
- Lymphoproliferative disorders, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies
- APLSbase, Jennifer Puck, National Human Genome Research Institute

GENE INFORMATION

Names:

HUGO name: NRAS

Localization:

Reference sequences:

DNA: D0125 (IDRefSeq) , **cDNA:** X02751 (EMBL) , **Protein:** P01111 (SWISSPROT) Other Sequences

Chromosomal Location:

1p13.2

Maps:

NRAS (Map View)

Variations / Mutations:

- NRASbase; Mutation registry for ALPS type III

Other gene-based resources:

Ensembl: ENSG00000009307, GENATLAS: NRAS, GeneCard: NRAS, UniGene: 486502, Entrez Gene: 486502, euGenes: 486502, GDB: 486502, HomoloGene: 55661

PROTEIN INFORMATION

Description:

Protein function:

Ras proteins bind gdp/gtp and possess intrinsic gtpase activity

Subcellular location:

Cell membrane; lipid-anchor; cytoplasmic side. Golgi apparatus membrane; lipid-anchor. Note=shuttles between the plasma membrane and the golgi apparatus

Post-translational modification:

Palmitoylated by the zdhhc9-golga7 complex. A continuous cycle of de- and re-palmitoylation regulates rapid exchange between plasma membrane and golgi

Enzyme regulation:

Alternate between an inactive form bound to gdp and an active form bound to gtp. Activated by a guanine nucleotide-exchange factor (gef) and inactivated by a gtpase-activating protein (gap)

Similarity:

Belongs to the small gtpase superfamily. Ras family

Other features:

Gtpase nras: 1-186

Propeptide Removed in mature form: 187-189

GTP nucleotide phosphate-binding region: 10-17

GTP nucleotide phosphate-binding region: 57-61

GTP nucleotide phosphate-binding region: 116-119

Other related resourses:

PIR: TVHURA, PIR: I38149, InterPro: IPR003577; GTPase_Ras, InterPro: IPR013753; Ras, InterPro: IPR015592; Ras_Ras_related, InterPro: IPR001806; Ras_trnsfrmng, InterPro: IPR005225; Small_GTP_bd, Pfam: PF00071; Ras, PRINTS: PR00449; RASTRNSFRMNG, SMART: SM00173; RAS

Expression pattern for human:

Tissue	Exp. (%)	Clones
vascular	8.46	7:47857
lymph_node	7.94	11:80139
uncharacterized_tissue	5.13	19:214464
embryonic_tissue	5.10	4:45419
bladder	4.57	2:25314
bone_marrow	4.29	3:40470
blood	3.63	5:79803
muscle	3.43	6:101253
skin	3.32	10:174239
heart	3.32	4:69792

Animal models:

Mouse:

MGD: ; Nras

OTHER RESOURCES

Societies:

General:

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

Other information sources:

- Immunodeficiencies+ALPS type III