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Gene Section
Short Communication

TYRP1 (tyrosinase-related protein 1)

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Abstract

TYRP1 gene, having a chromosomal location of 9p23, encodes a melanosomal enzyme belonging to the tyrosinase family. TYRP1 catalyses oxidation of 5,6-dihydroxyindole-2-carboxylic acid (DHICA) into indole-5,6-quinone-2-carboxylic acid. TYRP1 is also thought to play a role in stabilizing tyrosinase and modulates its catalytic activity, in maintenance of melanosome structure, affecting melanocyte proliferation and melanocyte cell death. Defects in this gene cause oculocutaneous albinism type III; OCA III (also known as rufous oculocutaneous albinism).

Keywords
TYRP1, albinism, OCA III

Identity

Other names: CATB, TRP1, CAS2, TYRP 3, TRP 3, EC 1.14.18.1, b-PROTEIN

HGNC (Hugo): TYRP1

Location: 9p23

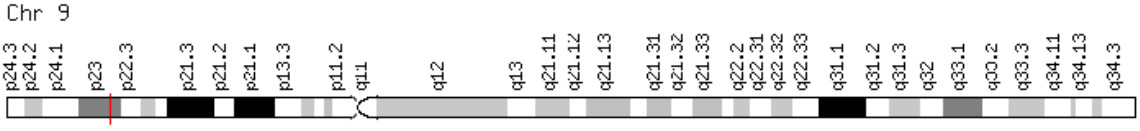
DNA/RNA

Description

In Chromosome 9, the 24,852 bases long gene starts from12,685,439 bp from pter and ends at 12,710,290 bp from pter; Orientation: Plus strand. The gene contains 8 exons and spans ~24.8 kb of the genome.

Transcription

The gene encodes a 2876 bp mRNA. This gene has been reported to have 7 transcripts (splice variants) of which 3 have been found to be protein coding (http://asia.ensembl.org/Homo_sapiens/Gene/Summary?g=ENSG00000107165;r=9:12685439-12710290). Microphthalmia-associated transcription factor (MITF) stimulates melanin synthesis by up-regulating expression of TYRP1 acting as a transcription factor.



Cytogenetic band showing TYRP1 locus (Ref: http://www.genecards.org/cgi-bin/carddisp.pl?gene=TYRP1)

Protein

Description

The gene encodes a protein, containing 537 amino acids, of molecular mass 60724 Da; it is an enzyme needing Cu++ as cofactor (binds 2 copper ions per subunit).

Expression

TYRP1 is mainly expressed in two cell types: (a) Melanocytes that are derived from neural crest cells colonizing within iris, cochlea, skin and choroids, and (b) Retinal pigment epithelial (RPE) cells that are derived from the optic cup. It has also been reported to be expressed in heart and ear (http://genatlas.medecine.univ-paris5.fr/fiche.php?symbol=TYRP1). Interestingly, expression of the gene in the following tissue types are evident by its existence in the corresponding cDNA libraries: brain, cerebrum, ear, embryonic tissue, eye, fetus, gastrointestinal tract, heart, kidney, mammary gland, nervous, retina, skin, stem cell and stomach (http://cgap.nci.nih.gov/Genes/GeneInfo?ORG=Hs LLNO=7306).

Localisation

TYRP1 is a melanosomal membrane protein.

Function

TYRP1 acts a 5,6-dihydroxyindole-2-carboxylic acid (DHICA) oxidase converting DHICA to Indole 5,6-quinone carboxylic acid in the melanin biosynthesis pathway. It is also involved in maintaining the stability of tyrosinase protein, modulating its catalytic activity in eumelanin synthesis, in maintenance of melanosome structure and affects melanocyte proliferation and cell death.

Homology

Interspecies: Homolog to murine brown locus. Intraspecies : Homolog to tyrosinase family of proteins comprising of TYR, TYRP1 and DCT (TYRP2)

Mutations

Germinal

A small number of mutations in the TYRP1 gene have been found to cause oculocutaneous albinism III. Seventeen mutations have been reported in Albinism Database (http://www.ifpcs.org/albinism/oca3mut.html). It is to be noted that Albinism Database has been updated till 2009. OCA3 has been described primarily in dark-skinned people from Southern Africa. Affected individuals have reddish-brown skin, ginger or red hair, and hazel or brown irises. OCA3 or Rufous oculocutaneous albinism has been estimated to affect 1:8500 individuals in Africa; however, it is very rare in any other populations as per published literature.

Somatic

Somatic mutations in TYRP1 have been identified in different cancers (https://dcc.icgc.org/genes/ENSG00000107165, http://cancer.sanger.ac.uk/cosmic/search?q=TYRP1), but no causality has been reported.

Implicated in

Melanoma

TYRP1 expression has been found to be significantly correlated with distant metastasis-free survival (DMFS), overall survival and Breslow thickness in melanoma patients (F Journe et al., 2011). Polymorphisms in 3'UTR of TYRP1 mRNA: rs683 and rs910 have been found to affect TYRP1 mRNA regulation by miR-155 and its subsequent translation into protein (El Hajj P et al., 2015). These SNPs have been hypothesized to render TYRP1 expression nonsusceptible to miR-155 activity and disclose a prognostic value for TYRP1 protein in a subgroup of melanoma patients. TYRP1 SNP rs1408799 has been found to be associated with melanoma risk (OR, 0.77; 95% CI, 0.60-0.98) (Nan H et al., 2009).

References

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