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Gene Section
Short Communication

OCA2 (OCA2 melanosomal transmembrane protein)

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Abstract

OCA2 gene (OCA2), having a chromosomal location of 15q12-q13, encodes an integral membrane transporter protein playing a role in regulating the pH of melanosomes.
OCA2 is hypothesized to be involved in the transport of tyrosine, the precursor to melanin synthesis, within the melanocyte. Defects in this gene are the cause of oculocutaneous albinism type II; OCA II.

Keywords: OCA2, albinism, OCA II

Identity

Other names: SHEP1, EYCL2, EYCL3, BOCA, BEY1, BEY2, EYCL, HCL3, PED, BEY, D15S12, PEDH

HGNC (Hugo): OCA2

Location: 15q12

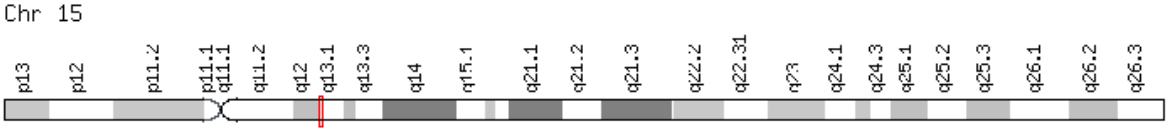
DNA/RNA

Description

In Chromosome: 15, the 344,486 bases long gene starts from 27,754,873 bp from pter and ends at 28,099,358 bp from pter; Orientation: Minus strand. It contains 24 exons and spans ~344.5 kb of the genome.

Transcription

The gene encodes a 3154 bp transcript.
Alternative splicing results in at least two transcript variants.
Variant 2 lacks an alternate in-frame exon in the central coding region, compared to variant 1, resulting in an isoform that is shorter than isoform 1.



Cytogenetic band showing OCA2 locus (Ref: http://www.genecards.org/cgi-bin/carddisp.pl?gene=OCA2&keywords=OCA2)

Protein

Description

The gene encodes a protein containing 838 amino acids with molecular mass of 92850 Da. The OCA2 is thought to be a melanosomal multipass integral membrane protein (with 12 predicted transmembrane domains). OCA2 is characterized by the presence of a conserved consensus acidic dileucine-based sorting motif within the cytoplasmic N-terminal region. A second dileucine signal within this region confers steady-state lysosomal localization in melanocytes. It belongs to the CitM (TC 2.A.11) transporter family.

Expression

Due to its localization in the melanosomal membrane, OCA2 is thought to be expressed in the melanocytes.

Localisation

OCA2 is hypothesized to be present in the melanosomal membrane of the melanocytes.

Function

The precise function of OCA2 has not been elucidated till date. However, the potential functions include: a) normal biogenesis of melanosomes, b) for normal processing and transport of tyrosinase and other melanosomal proteins, and c) maintenance of an acidic pH in melanosomes.

Homology

Its sequence predicts that OCA2 has a homology to a superfamily of permeases. It has been proposed that OCA2 also regulates the post-translational processing of tyrosinase, which catalyzes the rate limiting steps in melanin biosynthesis and is a major determinant of brown and/or blue eye color.

Mutations

Germinal

Mutations in OCA2 are responsible for albinism known also as OCA2. A few OCA2 mutations have been associated also with autosomal recessive ocular albinism. While the degree of cutaneous pigment and iris color may vary, the newborn with OCA2 nearly always have pigmented hair. Nevi and freckles are common. Visual acuity is better than in OCA1 and reaches 3/10. Africans with OCA2 appear with light brown hair and skin, and gray irises. Eighty six mutations in OCA2 have been reported in Albinism Database (http://www.ifpcs.org/albinism/oca2mut.html). It is to be noted that Albinism Database has been updated till 2009.

Somatic

Somatic mutations in OCA2 have been identified in cancers (http://www.cancerindex.org/geneweb/OCA2.htm, http://cancer.sanger.ac.uk/cosmic/search?q=OCA2), but no causality have been reported.

Implicated in

Melanoma

Note

In 2005, Jannot et al reported, based on allelic distribution between cases and controls, that malignant melanoma and OCA2 are associated (p value=0.030 after correction for multiple testing). In 2010 Duffy et al claimed the OCA2 variant Arg419Gln (rs1800407) to be a significant risk factor for cutaneous malignant melanoma based on a genome wide association study (GWAS). In 2011, another GWAS identified a locus at chromosome 15q13.1 (HERC2/OCA2 region) in a discovery cohort of 1804 melanoma cases and 1026 controls, to be associated with melanoma (Amos et al., 2011). Co-segregation analysis in an OCA2 affected pedigree containing individuals diagnosed with both cutaneous and iris melanoma, revealed that OCA2 variants could act as contributors towards melanoma predisposition (Hawkes et al., 2013).

The OCA2 Arg419Gln SNP has also been found to be associated with basal cell carcinoma of skin (OR, 1.50; 95% CI, 1.06-2.13) (Nan et al., 2009)

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