Oculocutaneous albinism

Genetics

-TYR (null variants cause OCA1A, pathogenic variants cause OCA1B)

-OCA2 (only gene known to cause OCA2, AR; in PWS/AS region)

-TYRP1 (causes OCA3, AR)

-SLC45A2 (only gene to cause OCA4, AR)

-GPR143 (causes X-linked ocular albinism)

Clinical findings/Dysmorphic features

-OCA1A (no melanin synthesis): nystagmus, reduced iris pigment, foveal hypoplasia, reduced visual acuity, strabismus, white hair and skin, translucent iris

-OCA1B (some melanin synthesis): milder eye and skin manifestation than OCA1

-OCA2: ocular problems same as OCA1 but better vision, range of skin and eye pigmentation from minimal to near normal

-OCA3: gene product necessary to synthesize black/brown eumelanin but not reddish pheomelanin --> phenotype for OCA3 is a milder OCA, reddish pigment in hair and skin

-OCA4: very similar to OCA2

-X-linked OCA: minor skin manifestations; congenital and persistent visual impairment in affected males

Etiology

-OCA1: 1:40,000

-Carrier frequency for OCA1 is approximately 1 in 100

Pathogenesis

-Tyrosinase is the key enzyme, catalyzing several steps in melanin synthesis, including the essential first and second steps: the hydroxylation of tyrosine to L-DOPA and the oxidation of L-DOPA to DOPA quinone

-Most variants of TYR are missense variants that produce enzyme with no catalytic activity

Genetic testing/diagnosis

-Sequencing of TYR for OCA1A and OCA1B, Deletion/Duplication analysis (<1%)