Waardenburg syndrome

Genetics

-PAX3 (WS1/WS3)/ MITF, SOX10, SNAI2 (WS2)/ EDNRB, EDN3, SOX10 (WS4)

-AD

Clinical findings/Dysmorphic features

-Four types:

-WS1: SNHL (~60%), heterochromic irides (~30%), white forelock (~50%), early graying (~40%), leukoderma (also known as Vitiligo: loss of skin pigmentation; (~30%)), dystrophia canthorum (lateral displacement of the inner canthi), neural tube defect

-WS2: like WS1 without dystrophia canthorum

-WS3: like WS1 + limb hypoplasia or contracture, carpal bone fusion (middle hand), syndactyly

-WS4: Pigmentary abnormalities, hearing loss, Hirschsprung disease

Etiology

- 1:20,000 to 1:40,000

-Approximately 3% of congenitally deaf children

Pathogenesis

-Haploinsufficiency --> PAX3 is a homeobox TF involved in melanocyte development

Genetic testing/diagnosis

-WS1: PAX3 sequencing --> 90%; Del/Dup --> 6%

Others

-Hearing aids or cochlear implants

-Folic acid supplementation of pregnancies at risk for WS1 related neural tube defect