Familial Dysautonomia

Genetics

-IKBKAP/ELP1 (IkappaB kinase complex-associated protein/Elongator complex protein 1, 9q31)

-AR

Clinical findings/Dysmorphic features

-Debilitating/weakening disease present from birth

-Affects development and survival of sensory, sympathetic, parasympathetic neurons --> neuronal degeneration progresses throughout life

-Gastrointestinal dysfunction, vomiting crises, recurrent pneumonia, altered sensitivity to pain and temperature perception, cardiovascular instability

Etiology

-Incidence among AJ is 1:3,700 live births (corresponds to a carrier frequency of 1:36)

Pathogenesis

-ELP1: part of the human elongator complex --> creating a permissive chromatin structure for efficient mRNA elongation during transcription

-Predominant splice donor site variant c.2204+6T>C --> expression of ELP1 in a tissue-specific manner (brain expresses mutated ELP1; lymphoblasts and fibroblasts express wild type ELP1)

-p.Arg696Pro disrupts phosphorylation site

Genetic testing/diagnosis

-Diagnosis by molecular genetic testing of ELP1 (IKBKAP)

-2 variants account for > 99% of mutated alleles in AJ (c.2204+6T>C and p.Arg696Pro)

-8 month old with absent tearing, autonomic neuropathy, episodic vomiting, feeding disorder, and absent fungiform papillae