Loeys-Dietz Syndrome (LDS)

Genetics

-TGFBR2 (55-60%), TGFBR1 (20-25%), TGFB2 (5-10%), SMAD3 (5-10%), SMAD2 (1-5%), TGFB3 (1-5%), deletions and duplications are rare

-AD

Clinical findings/Dysmorphic features

-Vascular findings: cerebral, thoracic, abdominal arterial aneurysms and/or dissections

-Skeletal manifestations: pectus excavatum or pectus carinatum, scoliosis, joint laxity, arachnodactyly, talipes equinovarus (clubfoot)

-75% have LDS type I with craniofacial manifestations (ocular hypertelorism, bifid uvula/cleft palate, craniosynostosis)

-25% have LDS type II with cutaneous manifestations (velvety and translucent skin; easy bruising; widened, atrophic scars)

Etiology

-Not known

Pathogenesis

-Increased TGFβ signaling in the vasculature of persons with LDS

-SMAD3, TGFB2, TGFB3 --> predicted loss of function variants somehow still increase TGFβ-signaling in aortic walls of affected individuals

Genetic testing/diagnosis

-Gene Panel