Kabuki syndrome

Genetics

-KMT2D (75%, AD; MLL2), KDM6A (3-5%, XLR; Lysine-specific demethylase 6A)

Clinical findings/Dysmorphic features

-Facial: long palpebral fissures with eversion of the lateral third of the lower eyelid; arched and broad eyebrows; short columella with depressed nasal tip; large, prominent, cupped ears

-Fetal finger pads; mild to moderate ID (IQ<80); joint laxity; high palate; hypotonia; short stature; CHD; CL/P; scoliosis; renal anomalies; hearing loss; speech delay

Etiology

-Approx. 1:32,000 – 1:86,000

Pathogenesis

-KDM6A and KMT2D part of ASCOM complex --> removes repressive epigenetic marks and deposit activating methylation marks on chromatin

Genetic testing/diagnosis

-Diagnosis of KS in a proband with a history of infantile hypotonia, DD, and/or ID AND one or both of the following:

1) typical dysmorphic features (long palpebral fissures with eversion of the lateral third of the lower eyelid, and ≥2 of the following: arched/broad eyebrows with lateral third displaying notching/sparseness; short columella with depressed nasal tip; large, prominent, cupped ears; persistent fingertip pads)

2) heterozygous variant in KMT2D or heterozygous or hemizygous pathogenic variant in KDM6A

-KMT2D (99% sequencing); KDM6A (80% sequencing, 20% InDel)

Others

-Risk for immunodeficiency