Hypochondroplasia

Genetics

-Gene: FGFR3 (Fibroblast growth factor receptor 3; 4p16.3)

-AD

Clinical findings/Dysmorphic features

-Short stature; stocky build; rhizo- or mesomelia; limited elbow extension; brachydactyly; mild joint laxity; macrocephaly; scoliosis; genu varum (O-beine); lumbar lordosis; no trident hand; normal face; adult onset osteoarthritis; mild to moderate ID and/or LD might be present

-Skeletal features very similar to achondroplasia but milder; medical complications common to achondroplasia (spinal stenosis, tibial bowing, obstructive apnea) are less frequent

Etiology

-May approach the prevalence of achondroplasia (i.e., 1 in 15,000 - 40,000 live births)

Pathogenesis

-FGFR3 normally functions as a negative regulator of bone growth

-FGFR3 pathogenic variants --> constitutive activation of the receptor tyrosine kinase (but to lesser degree than these other pathogenic variants)

Genetic testing/diagnosis

-70% are heterozygous for a pathogenic variant in FGFR3; locus heterogeneity

-Targeted mutation analysis: p.Asn540Lys(C1620A) (70%), p.Asn540Lys(C1620G) (30%)