WHAT IS HYPOCHONDROPLASIA?

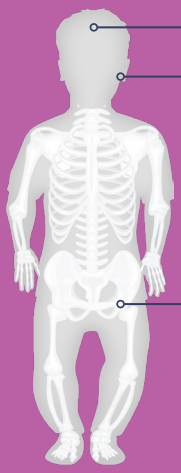
Hypochondroplasia
is a **RARE,** autosomal dominant **skeletal dysplasia**[1]

Estimated prevalence of 1 in 15,000–40,000[1-3]
(estimates vary and the condition is often underdiagnosed)

Associated with impaired QOL,
most notably in physical and social domains

CLINICAL FEATURES[3]

- Short stature
- Stocky build
- Macrocephaly
- Joint laxity
- Rhizomelia or mesomelia
- Broad, short hands and feet
- Limited elbow extension



MULTISYSTEM COMPLICATIONS[4,5]

Neurological
Neurological disorders (eg epilepsy)
Neurocognitive issues
Intellectual disability
Hydrocephalus

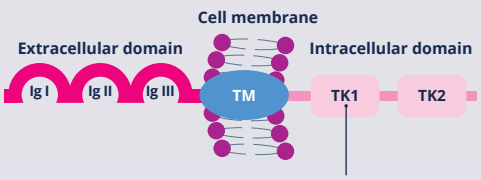
Otolaryngologic
Otitis media
Conductive hearing loss
Obstructive sleep apnea

Skeletal
Genu varum
Scoliosis
Lumbar lordosis
Spinal stenosis

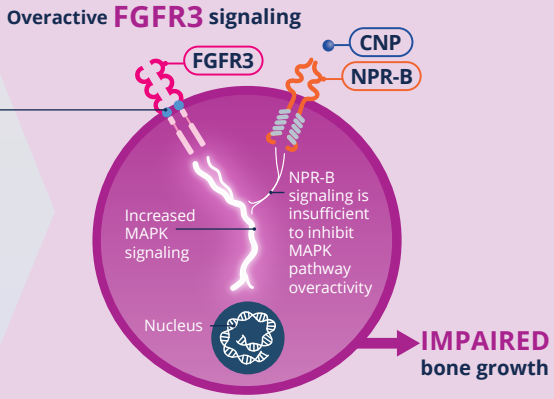
Individuals may present with highly variable features and complications.

PATHOPHYSIOLOGY[6-9]

Hypochondroplasia is caused by gain-of-function variants in *FGFR3* that lead to an imbalance between the FGF/FGFR3 and CNP/NPR-B signaling pathways[6,7]



Asn540Lys (N540K mutation) can be found in **~70%** of individuals with hypochondroplasia[7,8]



IgI, IgII, IgIII, immunoglobulin-like domains; TK, tyrosine kinase domains; TM, transmembrane domain

DIAGNOSIS

GENETIC TESTING for pathogenic *FGFR3* VARIANTS[3]

Help shorten the diagnostic journey with no-cost gene panel testing

CLINICAL and RADIOLOGIC evaluation[3]

DIAGNOSTIC CHALLENGES[3,7]

- Heterogeneous presentations
- Delayed recognition
- Subtle clinical features
- Lack of consensus on diagnostic criteria
- Overlap with other skeletal conditions

BIOMARIN

CNP, C-type natriuretic peptide; FGFR3, gene encoding fibroblast growth factor receptor 3; FGFR3, fibroblast growth factor receptor 3; MAPK, mitogen-activated protein kinase; NPR-B, natriuretic peptide factor receptor-B

References: 1. Dauber A et al. *EClinicalMedicine* 2024;71:102591; **2.** Rangos N et al. *Horm Res Paediatr.* 2023;96(suppl 3):1–399; **3.** Bober MB et al. *GeneReviews.* May 7, 2020; **4.** Linnankivi T et al. *Am J Med Genet A.* 2012; 158A:3119–3125; **5.** Doherty M et al. *J Rare Dis Res Treat.* 2017;2:25–32; **6.** Foldynova-Trantirkova et al. *Hum Mutat.* 2012;33(1):29–41; **7.** Kim et al. *Ann Pediatr Endocrinol Metab.* 2022;27(2):90–97; **8.** Sun et al. *BMC Med Genomics.* 2021;14(1):261. **9.** Ornitz DM, et al. *Dev Dyn.* 2017;246(4):291-309.

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