Igenomix®

Achondroplasia And Hypochondroplasia

Precision Panel
Skeletal

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Definition

The Igenomix Achondroplasia Precision Panel can be used to make a directed and accurate differential diagnosis of disproportionately short stature ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Overview

Achondroplasia is the most common cause of disproportionate short stature. Affected individuals have rhizomelic shortening of the limbs, macrocephaly, and characteristic facial features with frontal bossing and midface retrusion.
They affect the skull, spine, and extremities in varying degrees. The characteristic feature of achondroplasia is a disproportionately short stature (dwarfism). The short stature mainly results from shortening of the limbs with proximal segments affected disproportionally, a phenotype referred as rhizomelia.
Achondroplasia is the most common type of short-limb disproportionate dwarfism. More than 95% of patients have the same point mutation in the gene for fibroblast growth factor receptor 3 (FGFR3) which is inherited in an autosomal dominant pattern.

Specialties involved

Skeletal

Indications and Clinical Utility

The Igenomix Achondroplasia Precision Panel is indicated for those patients with a suspected clinical diagnosis of achondroplasia presenting with the following manifestations:
- Disproportionate short stature
- Macrocephaly with frontal bossing
- Prominent mandible
- Shortening of the arms with redundant skin folds
- Limitation of elbow extension
- Delayed gross motor development
- Brachydactyly
- Exaggerated lumbar lordosis
- Thoracolumbar kyphosis

The clinical utility of this panel is:
- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.
- Early initiation of treatment with a multidisciplinary team that includes supportive treatment in the form of medical care, early surgical care, rehabilitation and physical therapy.
- Prenatal detection of achondroplasia for a directed obstetric and perinatal treatment of affected infants.
- Risk assessment of asymptomatic family members according to the mode of inheritance.

Diagnostic Yield

Next Generation Sequencing provides a high sensitivity to identify DNA sequence mutations in the coding regions of the genes included in the panel according to de DP20 coverage (see list of genes), including intronic boundaries.
This test has limited sensitivity to detect variants in some genes due to the presence of pseudogenes, regions of high homology, repeat expansions or small deletions or duplications (i.e. 1-2 exons)

Related Genes

Gene	OMIM Diseases	Inheritance
B3GALT6	· Spondyloepimetaphyseal dysplasia with joint laxity · Spondyloepimetaphyseal dysplasia with joint laxity	AR
COL10A1	· Metaphyseal chondrodysplasia, schmid type · Metaphyseal chondrodysplasia, schmid type	AD
FGFR3	· Achondroplasia · Achondroplasia · Achondroplasia, severe, with developmental delay and acanthosis nigricans;Saddan · Camptodactyly-tall stature-scoliosis-hearing loss syndrome · Camptodactyly, tall stature, and hearing loss syndrome · Crouzon syndrome with acanthosis nigricans; can · Crouzon syndrome-acanthosis nigricans syndrome · Hypochondroplasia · Hypochondroplasia · Muenke syndrome · Muenke syndrome · Saethre-chotzen syndrome · Severe achondroplasia-developmental delay-acanthosis nigricans syndrome · Thanatophoric dysplasia type 1 · Thanatophoric dysplasia type 2 · Thanatophoric dysplasia, type i · Thanatophoric dysplasia, type ii	AD, AR
GNAS	· Pseudohypoparathyroidism type 1a · Pseudohypoparathyroidism type 1b · Pseudohypoparathyroidism type 1c · Pseudohypoparathyroidism, type ib · Pseudohypoparathyroidism, type ic; php1c · Pseudopseudohypoparathyroidism · Pseudopseudohypoparathyroidism; pphp	AD
PTH1R	· Metaphyseal chondrodysplasia, jansen type	AD, AR
SHOX	· Langer mesomelic dysplasia · Langer mesomelic dysplasia · Leri-weill dyschondrosteosis · Léri-weill dyschondrosteosis	AD, AR, X, G

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