Osteopetrosis

Precision Panel

Overview

Osteopetrosis, also known as “marble bone disease ”, is a term referred to a group of skeletal disease that are characterized by a generalized increase in bone density due to a defective bone resorption by osteoclasts, the cells in charge of this function in bone tissue. Consequently, bone modelling and remodelling are impaired. The defect in bone turnover characteristically results in skeletal fragility despite increased bone mass, and it may also cause hematopoietic insufficiency, disturbed tooth eruption, nerve entrapment syndrome and growth impairment. Three forms of osteopetrosis can be distinguished based on the pattern of inheritance: autosomal recessive, autosomal dominant and X-linked.

The Igenomix Osteopetrosis Precision Panel can be used to make a directed and accurate differential diagnosis of bone fragility 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.

Indications

The Igenomix Osteopetrosis Precision Panel is indicated for those patients with a suspected clinical diagnosis of osteogenesis imperfecta presenting with the following manifestations:

- Nasal stuffiness
- Neuropathies
- Deafness
- Short stature
- Frontal bossing
- Large head
- Hydrocephalus
- Osteomyelitis
- Bone fragility and fractures
- Anemia
- Easy bruising and bleeding
- Recurring infections
- Sleep apnea
- Blindness
- Delayed dentition

Clinical Utility

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, encompassing physical rehabilitation and surgical procedures, management of hearing and dental abnormalities, as well as drugs, such as vitamin D or gamma interferon.
- Prenatal detection of osteopetrosis for a directed obstetric and perinatal treatment of affected infants.
- Combining phenotypic and genotypic data to improve diagnostic rate of these patients in the target population as well as identification of mutations associated with unique disease complications.
- Risk assessment of asymptomatic family members according to the mode of inheritance.

Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
AMER1	Osteopathia Striata With Cranial Sclerosis Syndrome	X,XD,G	99.45%	NA of NA
ANKH	Chondrocalcinosis, Autosomal Dominant Craniometaphyseal Dysplasia, Calcium Pyrophosphate Deposition	AD	100%	19 of 19
CA2	Osteopetrosis With Renal Tubular Acidosis, Autosomal Recessive Osteopetrosis	AR	100%	36 of 36
CLCN7	Albers-Schonberg Osteopetrosis, Autosomal Recessive Malignant Osteopetrosis, Hypopigmentation, Organomegaly, And Delayed Myelination And Development, Intermediate Autosomal Dominant Osteopetrosis, Autosomal Recessive Osteopetrosis	AD,AR	99.85%	109 of 111
CSF1R	Brain Abnormalities, Neurodegeneration, And Dysosteosclerosis, Familial Progressive Subcortical Gliosis	AD,AR	100%	122 of 124
CTSK	Pycnodysostosis	AR	99.97%	59 of 59
DLX3	Amelogenesis Imperfecta Type IV, Tricho-Dento-Osseous Syndrome	AD	100%	10 of 10
FERMT3	Leukocyte Adhesion Deficiency Type III	AR	100%	17 of 17
GJA1	Alopecia Congenita With Keratosis Palmoplantaris, Atrioventricular Septal Defect, Autosomal Dominant Palmoplantar Keratoderma And Congenital Alopecia, Craniometaphyseal Dysplasia, Erythrokeratodermia Variabilis, Hypoplastic Left Heart Syndrome, Oculodentodigital Dysplasia, Syndactyly Type 3	AD,AR,MU,O	100%	119 of 119
IKBKG	Ectodermal Dysplasia And Immunodeficiency, Incontinentia Pigmenti	X,XR,XD,G	38.16%	NA of NA
LEMD3	12q14 Microdeletion Syndrome, Buschke-Ollendorff Syndrome, Isolated Osteopoikilosis, Melorheostosis With Osteopoikilosis	AD	99.06%	30 of 33
LRP4	Cenani-Lenz Syndactyly Syndrome, Congenital Myasthenic Syndrome, Sclerosteosis	AD,AR	100%	32 of 32
LRP5	Autosomal Dominant Endosteal Hyperostosis, Exudative Vitreoretinopathy, Hyperostosis Corticalis Generalisata, Autosomal Dominant Osteopetrosis, Osteoporosis-Pseudoglioma Syndrome, Osteosclerosis-Developmental Delay-Craniosynostosis Syndrome, Polycystic Liver Disease With Or Without Kidney Cysts, Retinopathy Of Prematurity, Van Buchem Disease Type 2	AD,AR	98.12%	265 of 269
LRRK1	Osteosclerotic Metaphyseal Displasia, Albers-Schonberg Osteopetrosis		99.66%	6 of 6
MITF	Coloboma, Osteopetrosis, Microphthalmia, Macrocephaly, Albinism, And Deafness, Familial Melanoma Cutaneous Malignant, Tietz Syndrome, Waardenburg Syndrome Type 2, Waardenburg-Shah Syndrome	AD,AR	100%	72 of 72
OSTM1	Infantile Osteopetrosis With Neuroaxonal Dysplasia, Autosomal Recessive Osteopetrosis, Autosomal Recessive	AR	100%	8 of 9
PLEKHM1	Intermediate Osteopetrosis,o Autosomal Dominant Osteopetrosis, Autosomal Recessive Osteopetrosis	AD,AR	99.97%	4 of 4
PTDSS1	Lenz-Majewski Hyperostotic Dwarfism	AD	100%	7 of 7
PTH1R	Blomstrand Lethal Chondrodysplasia, Dental Noneruption, Eiken Skeletal Dysplasia, Metaphyseal Chondrodysplasia, Jansen Type, Ollier Disease	AD,AR	100%	48 of 48
RELA	Ependymoma, Chronic Mucocutaneous Ulceration	AD	99.83%	3 of 3

SLC29A3	Dysosteosclerosis, Histiocytosis-Lymphadenopathy Plus Syndrome	AR	100%	32 of 32
SLCO2A1	Primary Autosomal Recessive Hypertrophic Osteoarthropathy, Pachydermoperiostosis	AR	99.98%	82 of 82
SNX10	Autosomal Recessive Malignant Osteopetrosis	AR	100%	14 of 14
SOST	Autosomal Dominant Craniodiaphyseal Dysplasia, Hyperostosis Corticalis Generalisata, Sclerosteosis	AD,AR	99.87%	14 of 14
TBXT	Neural Tube Defects, Sacral Agenesis With Vertebral Anomalies	AD,AR	99.91%	NA of NA
TCIRG1	Autosomal Dominant Severe Congenital Neutropenia, Autosomal Recessive Malignant Osteopetrosis, Dysosteosclerosis, Intermediate Osteopetrosis, Autosomal Recessive Osteopetrosis	AR	100%	140 of 146
TGFB1	Camurati-Engelmann Disease, Cystic Fibrosis, Inflammatory Bowel Disease, Immunodeficiency, And Encephalopathy	AD,AR	99.75%	24 of 24
TNFRSF11A	Dysosteosclerosis, Juvenile Paget Disease, Autosomal Recessive Osteopetrosis, Paget Disease Of Bone, Polyostotic Osteolytic Dysplasia, Hereditary Expansile	AD,AR	96.37%	17 of 22
TNFRSF11B	Familial Calcium Pyrophosphate Deposition, Juvenile Paget Disease Of The Bone	AR	99.98%	16 of 16
TNFSF11	Autosomal Recessive Malignant Osteopetrosis	AR	99.84%	4 of 4
TRAF6	Autosomal Dominant Hypohidrotic Ectodermal Dysplasia		99.89%	1 of 1
USB1	Dyskeratosis Congenita, Poikiloderma With Neutropenia	AR	100%	24 of 24

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology

Contact us

Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

References

1. Palagano, E., Menale, C., Sobacchi, C. *et al.* Genetics of Osteopetrosis. *Curr Osteoporos Rep* 16, 13–25 (2018). https://doi.org/10.1007/s11914-018-0415-2
2. Wu, C. C., Econs, M. J., DiMeglio, L. A., Insogna, K. L., Levine, M. A., Orchard, P. J., Miller, W. P., Petryk, A., Rush, E. T., Shoback, D. M., Ward, L. M., & Polgreen, L. E. (2017). Diagnosis and Management of Osteopetrosis: Consensus Guidelines From the Osteopetrosis Working Group. *The Journal of clinical endocrinology and metabolism*, *102*(9), 3111–3123. https://doi.org/10.1210/jc.2017-01127
3. Stark, Z., & Savarirayan, R. (2009). Osteopetrosis. *Orphanet journal of rare diseases*, *4*, 5. https://doi.org/10.1186/1750-1172-4-5
4. Del Fattore, A., Cappariello, A., & Teti, A. (2008). Genetics, pathogenesis and complications of osteopetrosis. *Bone*, *42*(1), 19–29. https://doi.org/10.1016/j.bone.2007.08.029
5. Stark, Z., & Savarirayan, R. (2009). Osteopetrosis. *Orphanet Journal Of Rare Diseases*, *4*(1). doi: 10.1186/1750-1172-4-5
6. Tolar, J., Teitelbaum, S., & Orchard, P. (2004). Osteopetrosis. *New England Journal Of Medicine*, *351*(27), 2839-2849. doi: 10.1056/nejmra040952