Your solution provider
in the world of genomics

CLINICAL DIAGNOSTICS

PREDICTIVE GENETIC TESTS FOR BONE DISEASES

Personal Genomics

With the collaboration of Bone Clinic and Professor Maria Luisa Brandi, we offer tests for the genetic diagnosis of bone diseases.

Personal Bone Care (BPC), a genetic diagnostic platform covering a broad spectrum of pathologies of mineral and bone metabolism of probable congenital origin, integrates the best of medical specialisation for bone health with the most advanced technology for DNA analysis.

The platform was the result of our interaction with **Bone Clinic** (integrated into the organisational model of Villa Donatello Clinic) led by **Professor Maria Luisa Brandi**, a world-renowned endocrinologist who specialised in bone diseases.

Why testing

Tests are a useful tool to corroborate clinical diagnoses of bone diseases, as well as to define the most suitable therapeutic strategies.

Target patients

The tests are suitable diagnostic tools for patients whose medical history may be consistent with mineral and bone metabolism diseases of genetic aetiology.

What the tests detect

The tests analyse the coding sequence and the related exon/ intron boundary junctions of the genes involved in congenital bone dysplasia, bone mineralisation defects and congenital disorders of the parathyroid glands.

Reliability

99%

The analyses have analytical sensitivity and specificity greater than 99%. The tests detect small sequence variations (single nucleotide changes, insertions/deletions of a few base pairs).

1. Blood sampling
2. DNA extraction and gene sequencing
3. Bioinformatics analysis
4. Reporting and results in 30 working days

PERSONAL BONE DYSPLASIAS
Genetic test for congenital skeletal dysplasia

WHAT IS CONGENITAL SKELETAL DYSPLASIA

Skeletal dysplasias include a series of skeletal abnormalities and malformations of various origins, which can be the expression of rare genetic syndromes. Hereditary/congenital skeletal dysplasia includes approximately 500 different clinical phenotypes and is predominantly caused by recessive genetic defects (both copies of the disease gene must be mutated for the disease to manifest).

These pathologies present a high phenotypic heterogeneity, with different ages of onset: in some cases, the clinical diagnosis can be made in the prenatal phase, other forms of skeletal dysplasia are evident only at birth or, in some cases, manifest themselves in the post-natal period, as well as in infancy and adulthood.

Furthermore, congenital skeletal dysplasias can present in syndromic forms, in which the involvement of other organs is evident and, at times, in these forms, the bone involvement can have incomplete penetrance, and not become manifest in all affected individuals, or do so with varying degrees of severity. Alternatively, congenital skeletal dysplasia is considered isolated when the skeleton is the primary target of the gene defect.

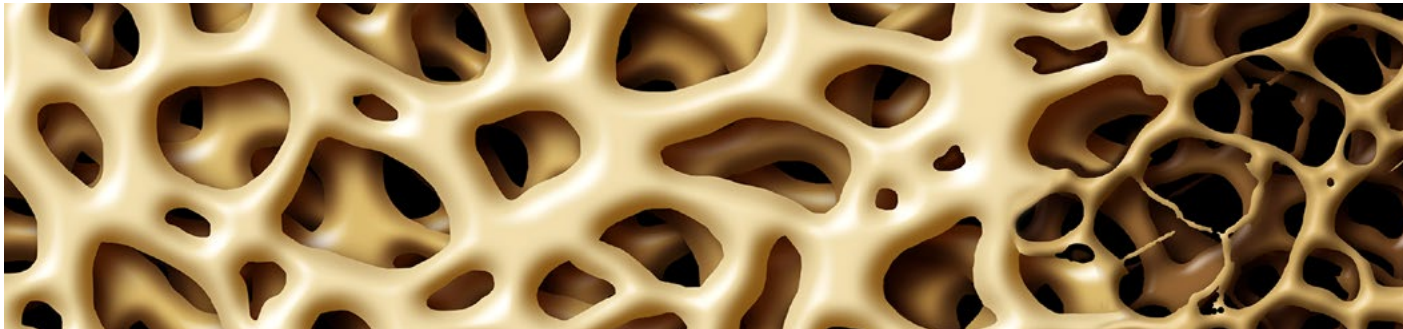
Why testing
The test is a useful tool to corroborate the clinical diagnosis as well as to define the best therapeutic strategies.

What the test detects
The test analyses the entire coding sequence and related exon/intron boundary junctions of 389 different genes that are predominantly involved.

How is testing performed
The genetic test consists in collecting blood, in extracting the genomic DNA and in analysing the entire coding sequence and related exon/intron boundary junctions of the genes under study. The analysis is conducted with NGS technology. On the basis of scientific literature data and the classification stored in databases, only the variations classified as predisposing to the disease will be reported. The test allows detecting small sequence variations (single nucleotide changes and insertions/deletions of a few base pairs).

Reporting times
Results available in 30 working days.

Sensitivity and specificity
Analysis sensitivity and specificity >99%.



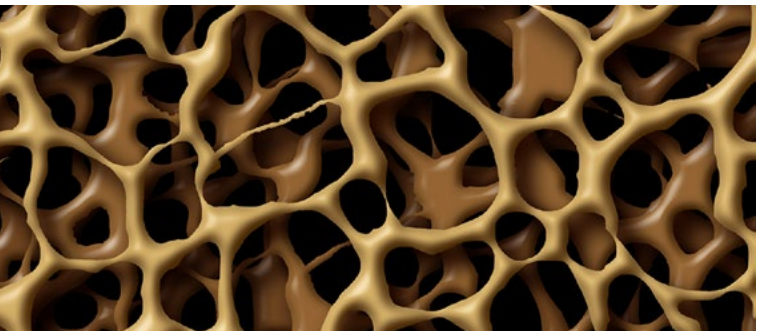
WHAT ARE BONE MINERALISATION DISORDERS

Mineralisation is a biological process consisting in the deposition of calcium phosphate in the extracellular matrix of bones and of all calcified tissues. In addition to its fundamental support function, the mineral component of the bone constitutes the body's main calcium reserve, which is useful for compensating for any imbalances in this vital element.

There are many pathologies linked to the bone mineralisation process:

"Soft bone", called osteomalacia in adults and rickets in children, occurs when mineralisation is reduced or absent. In this case, fragile bones are susceptible to deformations, fractures and pain.

When mineralisation is excessive, it is called bone sclerosis, which rather than giving strength and hardness to the bone, induces a reduction in normal remodelling and damage repair, resulting in structural fragility and increased susceptibility to fractures.



This type of disorders constitute a heterogeneous group of rare inherited diseases caused by gene variants on one or more of the many genes involved in the regulation of calcium homoeostasis. Among the main mineralisation hereditary disorders we find:

Hypophosphatasia: caused by a defect on the ALPL gene that codes for a non-specific tissue alkaline phosphatase enzyme (TNS-ALP), which leads to a reduction in bone mineralisation. The clinical spectrum of the disease is extremely variable. The most severe forms present severe rickets, bone fragility, multiple fractures, osteoarticular pain and even neurological conditions (convulsions, seizures, encephalopathy, insomnia, anxiety, and depression).

Osteogenesis imperfecta: includes a heterogeneous group of genetic diseases characterised by a decrease in mineralised bone mass, with consequent increase in skeletal fragility, and a susceptibility to multiple bone fractures of varying severity.

Disorders of phosphate metabolism: caused by mutations in the genes that code for proteins that lead to a reduction of phosphate, the ion that, with calcium, makes up bone crystal, hydroxy phosphite; in these disorders, there is a reduced generalised bone mineralisation (rickets), bone deformations, fragility fractures, short stature and tooth loss. In addition, there are also mutations on genes that induce an increase in phosphate in the blood, and are responsible for congenital hyperphosphatemic familial tumoral calcinosis, which occurs with the deposition of calcium phosphate crystals in skin, muscles, tendons and ligaments.

Why testing
The test is a useful tool to corroborate the clinical diagnosis as well as to define the best therapeutic strategies.

What the test detects
The test analyses the entire coding sequence and related exon/intron boundary junctions of 76 different genes that are predominantly involved.

How is testing performed
The genetic test consists in collecting blood, in extracting the genomic DNA and in analysing the entire coding sequence and related exon/intron boundary junctions of the genes under study.
The analysis is conducted with NGS technology.
On the basis of scientific literature data and the classification stored in databases, only the variations classified as predisposing to the disease will be reported. The test allows detecting small sequence variations (single nucleotide changes and insertions/deletions of a few base pairs).

Reporting times
Results available in 30 working days.

Sensitivity and specificity
Analysis sensitivity and specificity >99%.

WHAT ARE CONGENITAL PARATHYROID DISORDERS

The parathyroid glands are 4 small endocrine glands, located in the neck, behind the thyroid, whose function is to regulate the correct level of calcium
in the blood, through the synthesis and release of parathyroid hormone (parathyroid hormone; PTH). Both an increase (hypercalcaemia) a reduction (hypercalcaemia) in the circulating levels of calcium cause severe functional alterations. Dysfunctions of the parathyroid glands may be responsible for persistent alterations in the levels of blood calcium, resulting from an excessive release of parathyroid hormone (hyperparathyroidism) or a reduced/absent synthesis of parathyroid hormone (hypoparathyroidism), which lead, respectively, to hypercalcaemia and hypocalcaemia.

Hyperparathyroidism is a pathological condition defined as an excess of parathyroid hormone levels in the blood (> 65 pg/ml or > 7.6 pmol/L), resulting in increased blood calcium levels and, in most cases, persistent hypercalcaemia.
The genetic causes of the various inherited forms of hyperparathyroidism are largely known, and include a number of genes involved in regulating the growth and function of parathyroid cells.
The genetic approach allows a differential diagnosis, and thus, clinical surveillance and the most appropriate therapeutic choice, enabling, for example, the early identification of the risk of malignant carcinoma, which occurs frequently in a specific subgroup of clinical manifestations.

Hypoparathyroidism is a pathological condition defined by a partial or total deficit of parathyroid hormone secretion, which leads to hypocalcaemia. The most severe manifestations which occur with varying degrees of intensity are:
1) neuromuscular and neuromotor symptoms (muscle pain, cramps, spasms and paraesthesia),
2) neurocognitive and neuropsychiatric symptoms (difficulty concentrating, depression and anxiety),
3) cardiovascular symptoms (hypotension, myocardial contractility deficit with reduced cardiac output, bradycardia, arrhythmias, increased ischemic heart disease and mortality from cardiovascular complications), and, 4) nephrolithiasis and kidney stones.

When a genetic form of hypoparathyroidism is suspected, patients and family members can undergo genetic testing. Genetic tests help to confirm the clinical diagnosis, to guide in the choice of the most appropriate treatment, to identify family members who are carriers of the mutation and those who do not carry the gene defect and, therefore, are not at risk of developing the disease.

Why testing

The test is a useful tool to corroborate the clinical diagnosis as well as to define the best therapeutic strategies.

What the test detects

The test analyses the entire coding sequence and related exon/intron boundary junctions of 32 different genes that are predominantly involved.

How is testing performed

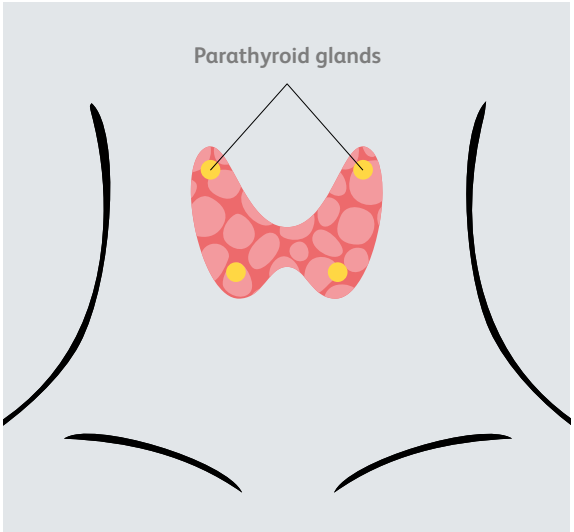
The genetic test consists in collecting blood, in extracting the genomic DNA and in analysing the entire coding sequence and related exon/intron boundary junctions of the genes under study.
The analysis is conducted with NGS technology.
On the basis of scientific literature data and the classification in databases, only those variations classified as predisposing to the disease are reported.
The test allows detecting small sequence variations (single nucleotide changes and insertions/deletions of a few base pairs).

Reporting times

Results available in 30 working days.

Sensitivity and specificity

Analysis sensitivity and specificity >99%.



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