

## Achondroplasia

- The most common form of short limbed dwarfism in humans.
- Characterized by impaired ability to form bone from cartilage.
- Inherited as an autosomal dominant disorder with full penetrance.
- Occurs as a result of mutations in the Fibroblast Growth Factor Receptor 3 (*FGFR3*) gene located on chromosome 4p16.3.
- More than 98% of achondroplasia patients carry a G380R substitution, resulting from G to A point mutation in the *FGFR3* gene. In about 1% of patients the G380R substitution is due to a G to C point mutation.
- Homozygous achondroplasia is a neonatal lethal condition.
- Material: Blood, DNA.
- Method: Restriction Enzyme (RE)-PCR.
- Turnaround time: 3-4 weeks.

## B-Thalassemia

- Blood disorder that reduces the production of Hemoglobin; low levels of oxygen in the body.
- Affected individuals have a shortage of red blood cells (anemia); pale skin, fatigue and more serious complications.
- Classified into two types depending on the severity of symptoms: thalassemia major and thalassemia intermedia. Thalassemia major is more severe.
- Inherited as autosomal recessive and more than 250 mutations in the *HBB* gene, located on chromosome 11p15.5, have been found to cause the disease.
- Material: Blood, DNA.
- Method: Mutational Screen.
- Turnaround time: 3-4 weeks.

## Cystic Fibrosis

- Recessive multi-system genetic disease characterized by abnormal transport of chloride and sodium across epithelium, leading to thick, viscous secretions in the lungs, pancreas, liver, and intestine.
- Caused by a mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, located on chromosome 7q31.2.
- The mutation detection rate varies by test method and ethnic background.
- The most common mutation is a three nucleotide deletion that results in a loss of the amino acid phenylalanine (F) at the position 508 on the protein

( $\Delta F508$ ). However, the most common mutation within the Jordanian population is large deletions in exons 2, 17 and 18.

- Material: Blood, DNA
- Method: Mutational Screen.
- Turnaround time: 3-4 weeks.

## Duchenne Muscular Dystrophy (DMD)

- The most severe and prevalent form of Muscular Dystrophy.
- Characterized by rapid progression of muscle degeneration, eventually leading to loss of ambulation and death.
- Inherited as X-Linked recessive due to mutation in the *DMD* gene, located on chromosome Xp21.2.
- The gene codes for the protein Dystrophin, an important structural component within muscle tissue. Mutations in *DMD* generally result in a disturbance of the open reading frame during Dystrophin protein production. This leads to the synthesis of a truncated, degraded or complete absence of the protein.
- Approximately 65% of the mutations in the *DMD* gene are the most common intragenic deletions. Point mutations, insertion and nucleotide changes together account for 25-30% and duplications account for 5-10%.
- Material: Blood, DNA.
- Method: Deletions Screen.
- Turnaround time: 3-4 weeks.

## Familial Mediterranean Fever (FMF)

- Heredity periodic fever syndrome, characterized by recurrent attacks of fever and inflammation in the peritoneum, synovium, or pleura. The symptoms and severity vary among affected individuals. Amyloidosis, which can lead to renal failure, is the most severe complication.
- *MEFV*, located on chromosome 16p13.3, is the only gene currently known to be associated with FMF. This gene encodes a protein, known as pyrin or marenostrin that is an important modulator of innate immunity.
- Homozygous or compound heterozygous mutations in the *MEFV* gene result in classic FMF which shows autosomal recessive inheritance.
- Several studies on Middle Eastern populations have identified the most common mutations within the *MEFV* gene in FMF patients.
- Material: Blood, DNA.
- Method: Mutational Screen.
- Turnaround time: 3-4 weeks.

## Fragile-X Syndrome

- The most common inherited cause of mental impairment.
- Aside from intellectual disability, prominent characteristics of the syndrome include an elongated face, large or protruding ears, flat feet, larger testes (macroorchidism), and low muscle tone. Behavioral characteristics include attention deficit disorders, speech disturbances, hand biting, hand flapping, autistic behaviors, poor eye contact, and unusual responses to various touches, auditory or visual stimuli.
- The syndrome is associated with the expansion of a single trinucleotide gene sequence (CGG) in *FMR1*, located on chromosome Xq26-q28.
- Only 25% of POI cases have premutation in *FMR1* gene.
- Material: Blood, DNA.
- Method: Expand Long Template PCR.
- Turnaround time: 3-4 weeks.

## Hereditary Hemochromatosis

- Autosomal recessive disorder of iron metabolism causing iron overload, organ failure, and malignancy.
- Results from defects in the *HFE* gene located on chromosome 6p21.3. The *HFE* gene encodes a membrane protein that functions to regulate iron absorption by regulating the interaction of the transferrin receptor with transferrin.
- The most common *HFE* gene mutation in patients with HH is C282Y, followed by H63D.
- Up to 90% of HH patients are either homozygotes (C282Y/C282Y) or compound heterozygotes (C282Y/H63D), with the proportion varying depending on the population studied.
- Material: Blood, DNA.
- Method: RE-PCR.
- Turnaround time: 3-4 weeks.

## Sanjad Sakati Syndrome

- Also called Hypoparathyroidism-Retardation-Dysmorphism (HRD).
- Autosomal Recessive disorder found exclusively in people of Arabian origin.

- It comprises of congenital hypoparathyroidism, severe growth retardation, low IQ and typical facial features.
- The molecular pathology of this syndrome was shown to be mainly due to a deletion of 12 bp (155-166del) in exon 3 of the *TBCE* gene located on chromosome 1q42.3.
- Material: Blood, DNA.
- Method: Standard PCR.
- Turnaround time: 3-4 weeks.

## Sex Determining Region (*SRY*)

- *SRY* gene, located on chromosome Yp11.3, is crucial for male sex determination.
- Deletions of *SRY* can cause 46, XY Disorders of Sex Development (46, XY DSD) or 46, XY Complete Gonadal Dysgenesis (CGD).
- Material: Blood, DNA.
- Method: Standard PCR.
- Turnaround time: 3-4 weeks.

## Spinal Muscular Atrophy (*SMA*)

- Neuromuscular disease characterized by degeneration of motor neurons, resulting in progressive muscular atrophy and weakness.
- Patients with *SMA* have been classified into three types, on the basis of age of onset and clinical severity: type I is the most severe, type II is the intermediate, and type III is the mildest form.
- Inherited as autosomal recessive and caused by mutations in the survival motor neuron gene (*SMN*) located on chromosome 5q13.
- The *SMN* gene is found in telomeric (*SMNt*) and centromeric (*SMNc*) copies, which are nearly identical and differ in exons 7 and 8 by only two base pairs. The telomeric (*SMN1*) is the *SMA*-determining gene, whereas *SMN2* is a modifying factor.
- Homozygous deletion of Exon7 in *SMN1* gene is found in 95% of *SMA* patients. Small mutations are found in the other 5%.
- Material: Blood, DNA.
- Method: RE-PCR.
- Turnaround time: 3-4 weeks.

## Thrombophilia markers (Coagulation factors)

- Factor V is a protein of the coagulation system that functions as a cofactor.
- The gene for factor V (*F5*) is located on chromosome 1q23.
- The most common mutation is R506Q.
- Factor V Leiden is associated with an increased risk of pregnancy loss.
- Thrombin (activated Factor II) is a coagulation protein, a serine protease that catalyses many reactions in the coagulation cascade.
- The Thrombin (prothrombin) gene, *F2*, is located on chromosome 11p11.
- The most common mutation is G20210A, leading to an abundance of prothrombin and causing prothrombin thrombophilia.
- Methylene tetrahydrofolate reductase (MTHFR) is an enzyme required for the multistep process that converts the amino acid homocysteine to methionine.
- The enzyme is coded by the gene *MTHFR* located on chromosome 1p36.3.
- The C677T variant in *MTHFR* has been associated with an increased risk of cardiovascular disease and certain birth defects.
- These factors have the dominant pattern of inheritance.
- Material: Blood, DNA.
- Method: Allele Specific-PCR, RE-PCR and Real-Time PCR.
- Turnaround time: 3-4 weeks.

## Y-chromosome microdeletion

- Y-chromosome Microdeletions are most commonly detected with spermatogenic failure in infertile men.
- Normally there are no physical symptoms to Y-chromosome deletions and the resulting infertility is diagnosed in otherwise healthy males.
- Diagnosed patients usually carry one or more of common deletions identified within azoospermia factor regions (AZFa, AZFb and AZFc) on the Y chromosome.
- Material: Blood, DNA.
- Method: Standard PCR.
- Turnaround time: 3-4 weeks.