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22q11.2 Deletion Syndrome

22q11.2 Deletion Syndrome (22q11DS) is one of the most common genetic causes of learning disabilities and mild intellectual disability, with an incidence of 1 per 4,000 live births. Individuals with 22q11DS, also known as DiGeorge syndrome or Velo-Cardio-Facial syndrome, have a number of physical and cognitive clinical features in common, such as congenital heart defects, learning difficulties and characteristic facial features, although not everyone with 22q11DS has all of the features or is affected to the same degree of severity.

Genetics

22q11.2 deletion syndrome is caused by a deletion in a region of chromosome 22, designated 22q11.2. The autosomal dominant condition occurs when a deletion is present on one of two copies of chromosome 22. An individual with a 22q11.2 deletion has a 50% chance of transmitting the chromosome 22 with the deletion to a child. Most patients (~90%) with 22q11DS are new occurrences (deletion is not inherited) while ~10% of individuals with 22q11.2 deletion syndrome have inherited the deletion from a parent.

Approximately 90% of individuals with 22q11DS have a "common" 3 Mb deletion that removes over 40 genes and is detectable with chromosome FISH analysis. The remaining patients include those who have smaller deletions that are nested within the 3 Mb typically deleted region and a few patients with deletions outside of this region. To date no correlation has been found between the size or extent of the deletion and the severity of the clinical phenotype. Molecular testing for 22q11DS involves the determination of the copy number of the genes in the 22q11 region to define the relative start and end point of the deletion (see Figure 1 below).

Test Methods

- Quantitative testing to determine the relative copy numbers of 29 genes in the 22q11-13 region (see Fig.1), using Multiplex Ligation dependent Probe Amplification

Test Sensitivity

Approximately 90% of 22q11DS deletions are due to the common 3Mb deletion, with another 5% of patients having a smaller nested deletion within the 22q11 region. These cases will be detected with MLPA.

Who Should be Tested?

- Individuals clinically suspected of being affected with 22q11DS and negative on FISH analysis
- Individuals with a family history of 22q11DS
- Pregnancies at increased risk of being affected with 22q11DS

Potential Outcomes & Interpretation of Test Results

Reason for referral	Chromosome 22 dosage	Explanation
Diagnosis	None detected	This result does not support a diagnosis of 22q11.2 deletion syndrome
Diagnosis	Deletion detected	This result supports a diagnosis of 22q11.2 deletion syndrome

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/

- DiGeorge # 188400
- Velocardiofacial # 192430

GeneTests online clinical information resource - http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=gr_22q11deletion#gr_22q11deletion

To locate a genetics center near you, visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

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1. Chromosome analysis should be performed on patients clinically suspected of being affected with 22q11.2DS prior to molecular analysis. These studies may identify patients with a translocation involving chromosome 22 and another chromosome.

2. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the diagnosis of 22q11.2DS.

3. The clinical course or severity of symptoms cannot be predicted by molecular analysis.

4. Test results should be interpreted in the context of clinical findings, family history, and other laboratory data.

5. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.

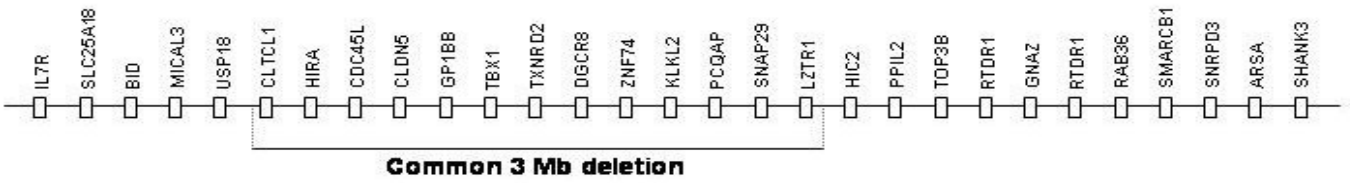

Figure 1. Map of the 29 genes in the 22q11-13 region analyzed with MLPA kit P250. The common 3Mb deletion which extends from the *CLTCL1* gene to the *LZTR1* gene is indicated.