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**

<table>
<thead>
<tr>
<th>Reason for referral</th>
<th>Chromosome 22 dosage</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>None detected</td>
<td>This result does not support a diagnosis of 22q11.2 deletion syndrome</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Deletion detected</td>
<td>This result supports a diagnosis of 22q11.2 deletion syndrome</td>
</tr>
</tbody>
</table>

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.