ZytoLight® SPEC DiGeorge/Phelan McDermid Dual Color Probe

Intended Purpose

The ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe is designed to detect deletions affecting the chromosomal regions 22q11.21 harboring the HIRA (a.k.a. TUPLE1) gene and 22q13.33 harboring the SHANK3 (a.k.a. prosap2) gene, respectively.

The 22q11.2 deletion syndrome (22q11.2DS), also known as velocardiofacial syndrome (VCFS) and DiGeorge syndrome, is a genetic disorder caused by hemizygous microdeletions on chromosome 22q11.2, with population prevalence of about 1 to 4,000 births. The characteristic phenotype of 22q11.2DS includes cardiac defects, velopharyngeal insufficiency, immune deficiency due to thymic aplasia, growth restriction, and deficits in cognitive abilities.

The 22q11.2 deletion usually occurs by meiotic non-allelic homologous recombination events between low copy repeats on chromosome 22q11.2 termed LCR22. There are eight LCR22s that span the 22q11.2 region termed LCR22A through LCR22H. The majority (90%) of 22q11.2DS patients show a recurrent 3 Mb deletion between LCR22A and LCR22D harboring the HIRA gene.

The 22q13.3 deletion syndrome (Phelan-McDermid syndrome) typically results from deletions of 100 kb to 9 Mb involving the distal long arm of chromosome 22. Almost all of these deletions include the gene SHANK3 that encodes a scaffold protein in the postsynaptic densities of excitatory synapses, connecting membrane-bound receptors to the actin cytoskeleton. This syndrome is characterized by neurological deficits, which include global developmental delay, moderate to severe intellectual impairment, absent or severely delayed speech, and neonatal hypotonia.

References

Burnside RD (2015) Cytogenet Genome Res 146: 89-99.
Morrow BE, *et al.* (2018) Am J Med Genet A 176: 2070-81.
Phelan K & McDermid HE (2012) Mol Syndromol 2: 186-201.
Scambler PJ, *et al.* (1991) Genomics 10: 201-6.
Watt JL, *et al.* (1985) J Med Genet 22: 283-7.

Probe Description

The ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10 ng/µl), which target sequences mapping in 22q11.21* (chr22:19,191,435-19,506,869) harboring the HIRA gene region (see Fig. 1).
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 22q13.33* (chr22:50,924,766-51,188,029) harboring the SHANK3 gene region (see Fig. 1).
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

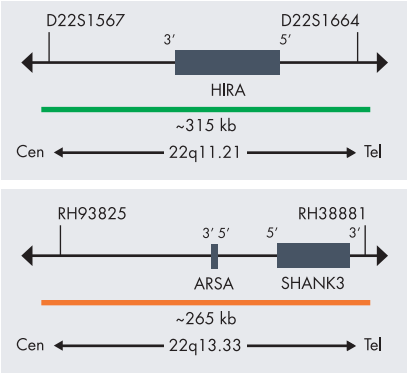


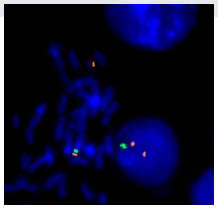
Fig. 1: Top: SPEC HIRA Probe map; Bottom: SPEC SHANK3 Probe map (not to scale)

Ideogram of chromosome 22 indicating the hybridization locations

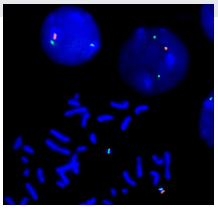
Results

Normal situation: In interphases of normal cells or cells without a deletion involving the respective gene regions, two green and two orange signals appear.

Aberrant situation: In a cell with deletions affecting the HIRA gene region, a reduced number of green signals will be observed. Deletions affecting only parts of the HIRA gene region might result in a normal signal pattern with green signals of reduced size. In a cell with deletions affecting the SHANK3 gene region, a reduced number of orange signals will be observed. Deletions affecting only parts of the SHANK3 gene region might result in a normal signal pattern with orange signals of reduced size



Lymphocytes and metaphase chromosomes from a DiGeorge syndrome case showing a HIRA deletion as indicated by the loss of one green signal.*



Lymphocytes and metaphase chromosomes from a Phelan-McDermid syndrome case showing a SHANK3 deletion as indicated by the loss of one orange signal. **

Labels	Chromosome	Reg. Status	Tests	Order No.
● | ●	22	CE/IVD	5 (50 µl)	**Z-2299-50**

*Kindly provided by Dr. Liehr, Jena, Germany.

**Kindly provided by Dr. Kazmierczak, Bremen, Germany.