ZytoLight® SPEC DiGeorge/Phelan McDermid Dual Color Probe

CE IVD

Background

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.

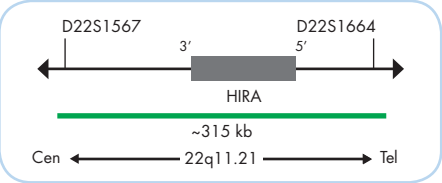
The 22q13.3 deletion syndrome (Phelan-McDermid syndrome) typically results from deletions of 100 kb to 9 Mb involving the distal long arm of chromosome 22. Almost all of these deletions include the gene SHANK3 that encodes a scaffold protein in the postsynaptic densities of excitatory synapses, connecting 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.

Probe Description

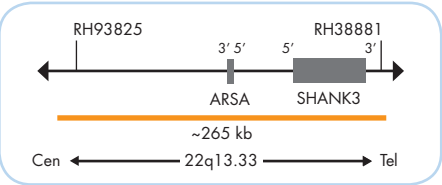
The ZytoLight® SPEC DiGeorge/Phelan McDermid Dual Color Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~10.0 ng/µl),which target sequences mapping in 22q11.21** (chr22:19,191,435-19,506,869) harboring the HIRA gene region.
- 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.
- Formamide based hybridization buffer

Ideogram of chromosome 22 indicating the hybridization locations.



SPEC HIRA Probe map (not to scale).

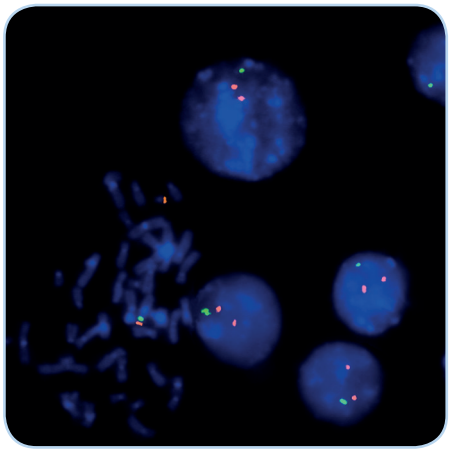


SPEC SHANK3 Probe map (not to scale).

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.

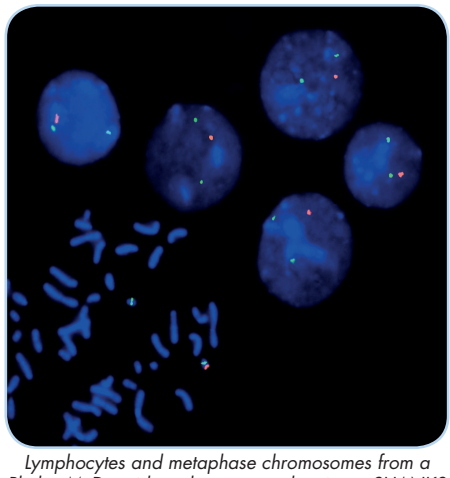
Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with deletion of the HIRA gene locus, a reduced number of green signals will be observed. In a cell with deletion of the SHANK3 gene locus, a reduced number of orange signals will be observed.



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

Kindly provided by Dr. Liehr, Jena, Germany.



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

Kindly provided by Dr. Kazmierczak, Bremen, Germany.

Prod. No.	Product	Label	Tests* (Volume)
Z-2299-50	ZytoLight SPEC DiGeorge/Phelan McDermid Dual Color Probe CE IVD	●/●	5 (50 µl)
Related Products			
Z-2099-20	ZytoLight FISH-Cytology Implementation Kit CE IVD Incl. Cytology Pepsin Solution, 4 ml; 20x Wash Buffer TBS, 50 ml; 10x $MgCl_2$, 50 ml; 10x PBS, 50 ml; Cytology Stringency Wash Buffer SSC, 500 ml; Cytology Wash Buffer SSC, 500 ml; DAPI/DuraTect-Solution, 0.8 ml		20

** Using 10 µl probe solution per test. IVD labeled products are only available in certain countries. All other countries research use only! Please contact your local dealer for more information.*

***According to Human Genome Assembly GRCh37/hg19*