ZytoLight® SPEC NUTM1 Dual Color Break Apart Probe

CE IVD

Background

The ZytoLight® SPEC NUTM1 Dual Color Break Apart Probe is designed to detect translocations involving the chromosomal region 15q14 harboring the NUTM1 (NUT midline carcinoma family member 1, a.k.a. NUT) gene.

NUT midline carcinoma (NMC) is a rare and aggressive form of squamous cell carcinoma that arises mainly in the head, neck, or mediastinum. NMC is genetically defined by the presence of chromosomal rearrangements involving the NUTM1 gene. Two-thirds of NMCs have t(15;19)(q14;p13.1) fusing the NUTM1 gene to the BRD4 gene. Less commonly, NMC harbors a NUTM1-variant fusion gene involving BRD3 or still-uncharacterized genes. NMCs may be indistinguishable from more common squamous cell carcinomas and are thus an underdiagnosed entity. Therefore, the diagnosis of NMC depends on the confirmation of NUTM1 rearrangement.

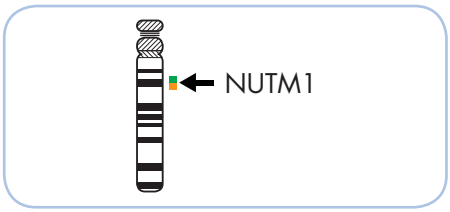
BRD3 and BRD4 belong to the bromo and extra terminal (BET) family of bromodomain proteins. BRD-NUTM1 chimeric oncoproteins repress squamous differentiation, possibly by sequestering histone acetyltransferase activity. Accordingly, histone deacetylase inhibitors or BET inhibitors were shown to reverse the effects of BRD-NUTM1 fusion proteins by inducing terminal differentiation of NMC cells *in vitro* and in xenograft models.

Hence, detection of NUTM1 rearrangements by FISH represents a useful tool in the differential diagnosis of NMC and may be of therapeutic significance.

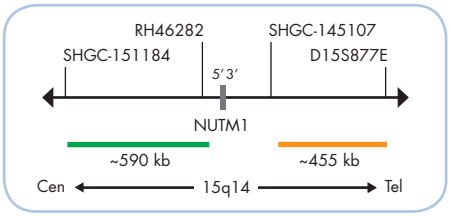
References
French CA (2012) Annu Rev Pathol 7: 247-65.
Kubonishi I, et al. (1991) Cancer Res 51: 3327-8.
Müller S & Knapp S (2014) Med Chem Commun 5: 288-96.

Probe Description

The SPEC NUTM1 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 15q14 band. The green fluorochrome direct labeled probe hybridizes proximal and the orange fluorochrome direct labeled probe hybridizes distal to the NUTM1 gene.



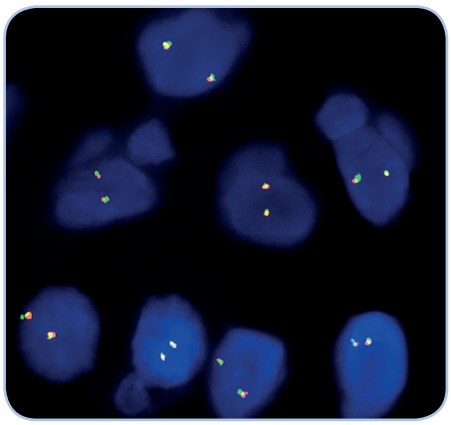
Ideogram of chromosome 15 indicating the hybridization locations.



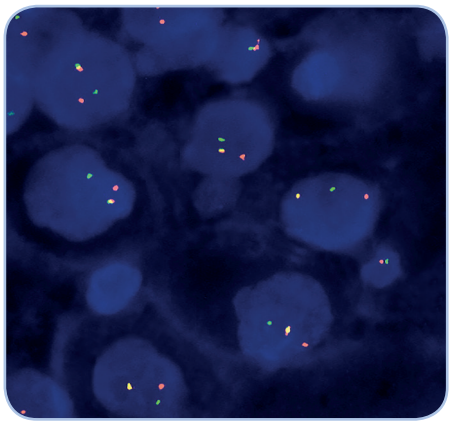
SPEC NUTM1 Probe map (not to scale).

Results

In an interphase nucleus lacking a translocation involving the 15q14 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 15q14 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 15q14 locus and one 15q14 locus affected by a translocation.



SPEC NUTM1 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.



NMC tissue section with translocation of the NUTM1 gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal indicating the translocation.

Prod. No.	Product	Label	Tests* (Volume)
Z-2208-200	ZytoLight SPEC NUTM1 Dual Color Break Apart Probe CE IVD	●/●	20 (200 µl)
Related Products			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit CE IVD Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 500 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraTect-Solution, 0.8 ml		20

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

ZytoLight® FISH probes are direct labeled using the unique ZytoLight® *Direct Label System II* providing improved signal intensity. Advanced specificity of the single copy SPEC probes is obtained by the unique ZytoVision® *Repeat Subtraction Technique.*

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