# ZytoLight® SPEC BRAF/CEN 7 Dual Color Probe

## Background

The ZytoLight ® SPEC BRAF/CEN 7 Dual Color Probe is designed for the detection of amplifications involving the chromosomal region 7q34 harboring the BRAF gene (B-Raf proto-oncogene, serine/ threonine kinase). The BRAF gene encodes a protein-serine/threonine kinase that participates in the MAPK cascade, which regulates a large variety of cell processes. Activating mutations in BRAF are found in many tumor types, including malignant melanoma, thyroid, colorectal, and ovarian carcinomas, lung adenocarcinoma, as well as in some sarcomas and gliomas. These mutations lead to constitutive activation of BRAF thereby promoting tumorigenesis.

Copy number gains of mutated and non-mutated BRAF have been identified in malignant melanoma (MM), follicular thyroid tumors, astrocytoma, colorectal, and prostate cancer due to amplification of the gene or polysomy of chromosome 7. These amplifications lead to an overexpression of BRAF and to constitutive activation of the MAPK signaling pathway. Follicular carcinomas with BRAF copy number gain were observed to be more often invasive. Colorectal carcinoma or melanoma patients with BRAF V600E mutation were found to acquire resistance to MEK and BRAF inhibitors through amplification of the mutated BRAF gene.

Hence, detection of BRAF amplifications by Fluorescence *in situ* Hybridization may be of therapeutic relevance for these

# cancer patients.

 References

 Ciampi R, et al. (2005) Endocr Pathol 16: 99-105.

 Corcoron RB, et al. (2010) Sci Signal 3: ra84.

 Dougherty MJ, et al. (2010) Neuro Oncol 12: 621-30.

 Little AS, et al. (2011) Sci Signal 4: ra17.

 Prister S, et al. (2001) Clin Invest 118: 1739-49.

 Ren G, et al. (2012) Genes Chromosomes Cancer 51: 1014-23.

 Roskoski R Jr. (2010) Biochem Biophys Res Commun 399: 313-7.

 Spittle C, et al. (2007) J Mol Diagn 9: 464-71.

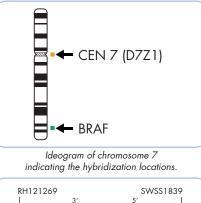
 Tanami H, et al. (2004) Oncogene 23: 8796-804.

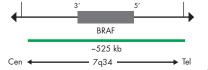
 Villanueva J, et al. (2013) Cell Rep 4: 1090-9.

 Villance-Rayne C, et al. (2006) Hum Pathol 37: 520-7.

#### **Probe Description**

The SPEC BRAF/CEN 7 Dual Color Probe is a mixture of a green fluorochrome direct labeled SPEC BRAF probe specific for the BRAF gene at 7q34 and an orange fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1).



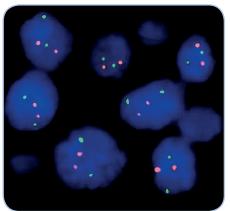


SPEC BRAF Probe map (not to scale).

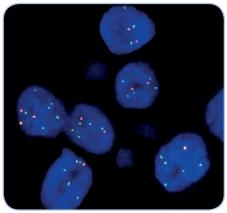
## Results

In a normal interphase nucleus, two orange and two green signals are expected. In a cell with amplification of the BRAF gene locus or polysomy of chromosome 7, multiple copies of the green signal or large green signal clusters will be observed.

Molecular diagnostics simplified



Normal interphase cells, BRAF (green), CEN 7 (orange).



NSCLC tissue section with amplification of the BRAF gene (green).

Prod. No.	Product	Label	Tests* (Volume)
Z-2191-200	ZytoLight SPEC BRAF/CEN 7 Dual Color Probe CE IVD	•/•	20 (200 µl)
Related Products			
Z-2028-20	Zyto <i>Light</i> FISH-Tissue Implementation Kit C € IVD		20
	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		
* 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.

#### ZytoVision GmbH · Fischkai 1 27572 Bremerhaven · Germany www.zytovision.com

65