# ZytoLight® SPEC EML4 Dual Color Break Apart Probe

CE IVD

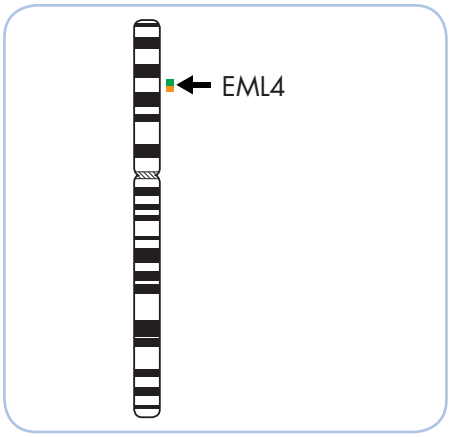
## Background

The ZytoLight® SPEC EML4 Dual Color Break Apart Probe is designed to detect rearrangements involving the chromosomal region 2p21 harboring the EML4 (echinoderm microtubule-associated protein-like 4, a.k.a. ROPP120) gene. Inversions in the short arm of chromosome 2 [inv(2)(p21p23)] have been frequently detected in non-small cell lung cancer (NSCLC) and lead to the formation of EML4-ALK fusion transcripts. A few reports also identified these fusion transcripts in breast, gastric, and colorectal cancers. The fusion genes comprise variably truncated N-terminal portions of the EML4 gene and the intracellular signaling domain of the receptor tyrosine kinase ALK (anaplastic lymphoma receptor tyrosine kinase, a.k.a. CD246). It was found that EML4 mediates ligand-independent dimerization of ALK, resulting in constitutive kinase activity. EML4-ALK was shown to possess transforming activity *in vitro* and *in vivo*. The EML4-ALK fusion transcript is found in about 5% of NSCLC, predominantly adenocarcinomas, and is considered to be mutually exclusive to EGFR or KRAS mutations. The detection of the inversion by Fluorescence *in situ* Hybridization might represent a valuable tool to identify a subpopulation of NSCLC likely to respond to ALK kinase targeting therapies.
The SPEC EML4 Dual Color Break Apart Probe can be used to subsequently confirm EML4-ALK inversion if an ALK Break Apart Probe has been used for initial diagnosis.

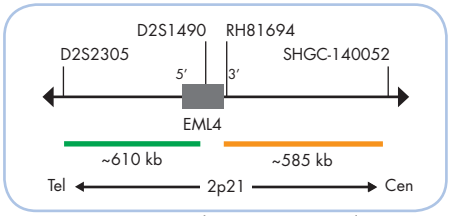
**References**
Choi YL, et al. (2008) Cancer Res 69: 4971-6.
Inamura K, et al. (2009) Mod Pathol 22: 508-15.
Lin E, et al. (2009) Mol Cancer Res 7: 1466-76.
Perner S, et al. (2008) Neoplasia 10: 298-302.
Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
Soda M, et al. (2007) Nature 448: 561-6.
Shaw AT, et al. (2009) J Clin Oncol 27: 4247-53.

## Probe Description

The SPEC EML4 Dual Color Break Apart Probe is a mixture of two direct labeled probes hybridizing to the 2p21 band. The orange fluorochrome direct labeled probe hybridizes proximal, the green fluorochrome direct labeled probe hybridizes distal to the EML4 gene breakpoint region at 2p21.



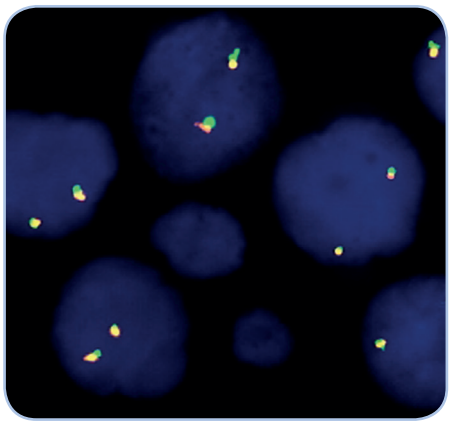

*Ideogram of chromosome 2 indicating the hybridization locations.*



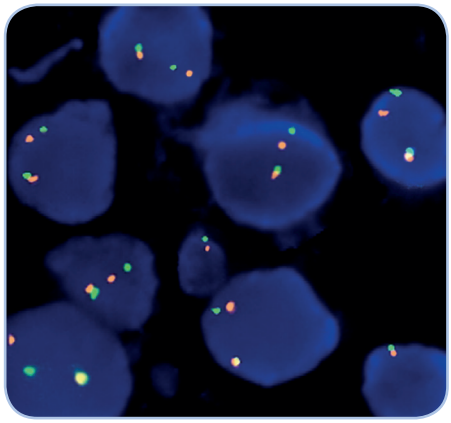

*SPEC EML4 Probe map (not to scale).*

## Results

In an interphase nucleus of a normal cell lacking an inversion involving the 2p21 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 2p21 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 2p21 locus and one 2p21 locus affected by an inversion or translocation.



*SPEC EML4 Dual Color Break Apart Probe hybridized to normal interphase cells as indicated by two orange/green fusion signals per nucleus.*



*NSCLC tissue section with inversion affecting the EML4 locus at 2p21 as indicated by one orange/green fusion (non-rearranged) signal, one green signal, and one separate orange signal indicating the translocation.*

| Prod. No. | Product | Label | Tests* (Volume) |
|---|---|---|---|
| Z-2136-50 | ZytoLight SPEC EML4 Dual Color Break Apart Probe CE IVD | ●/● | 5 (50 µl) |
| **Related Products** | | | |
| Z-2028-5 | ZytoLight FISH-Tissue Implementation Kit CE IVD<br>Incl. Heat Pretreatment Solution Citric, 150 ml; Pepsin Solution, 1ml; Wash Buffer SSC, 150 ml; 25x Wash Buffer A, 50 ml; DAPI/DuraTect-Solution, 0.2 ml | | 5 |

** 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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