

# ZytoMation® ALK Dual Color Break Apart FISH Probe



## Background

The ZytoMation® ALK Dual Color Break Apart FISH Probe is designed to detect rearrangements involving the chromosomal region 2p23.1-p23.2 harboring the ALK (ALK receptor tyrosine kinase, a.k.a. CD246) gene.

ALK encodes a transmembrane receptor tyrosine kinase. This gene exerts characteristic oncogenic activities through fusion to several gene partners or mutations both in hematopoietic and non-hematopoietic solid tumors.

Translocations affecting the ALK gene locus are frequently found in anaplastic large cell lymphoma (ALCL), an aggressive non-Hodgkin lymphoma arising from T-cells. The most frequent translocation t(2;5) results in a fusion with the NPM1 gene located on chromosome 5q35. This rearrangement results in a NPM1/ALK fusion protein, which is constitutively activated through autophosphorylation, and that in turn mediates malignant cell transformation by activating downstream effectors like e.g. STAT3.

Additionally, inversions affecting the ALK gene located on 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.

ALK kinase targeted therapies may represent a very effective therapeutic strategy in NSCLC patients carrying EML4-ALK rearrangements.

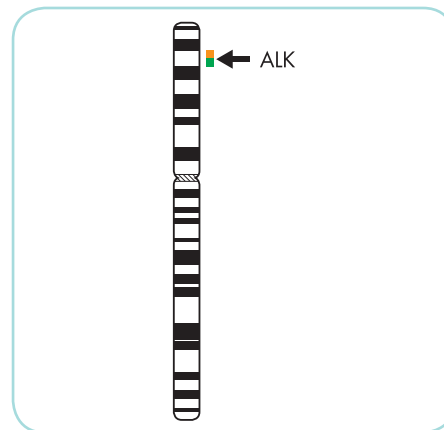
## References

- Inamura K, et al. (2009) Mod Pathol 22: 508-15.
- Koivunen JP, et al. (2008) Clin Cancer Res 14: 4275-83.
- Martelli MP, et al. (2009) Am J Pathol 174: 661-70.
- Palmer RH, et al. (2009) Biochem J 420: 345-61.
- Perner S, et al. (2008) Neoplasia 10: 298-302.
- Rodig SJ, et al. (2009) Clin Cancer Res 15: 5216-23.
- Sasaki T, et al. (2010) Eur J Cancer 46: 1773-80.
- Von Laffert M, et al. (2013) Lung Cancer 81: 200-6.
- Zhang Q, et al. (2007) Nat Med 11: 1341-8

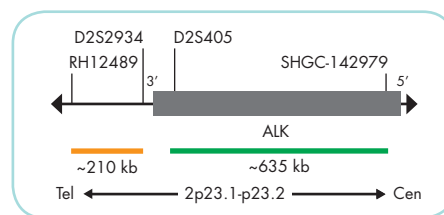
## Probe Description

The ZytoMation® ALK Dual Color Break Apart FISH Probe is composed of:

- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~6.0 ng/µl), which target sequences mapping in 2p23.1-p23.2\*\* (chr2:29,460,144-30,095,822) proximal to the ALK breakpoint region.
- ZyOrange (excitation 547 nm/emission 572 nm) labeled polynucleotides (~4.0 ng/µl), which target sequences mapping in 2p23.2\*\* (chr2:29,174,204-29,383,335) distal to the ALK breakpoint region.
- Formamide based hybridization buffer



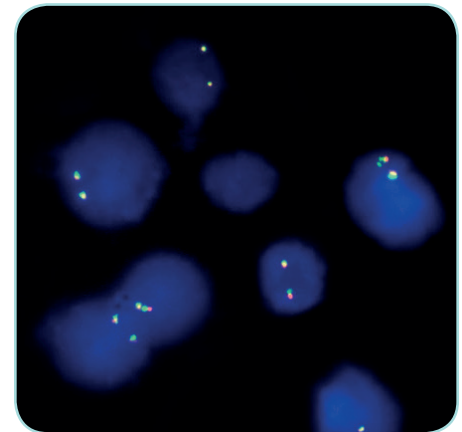
Ideogram of chromosome 2 indicating the hybridization locations.



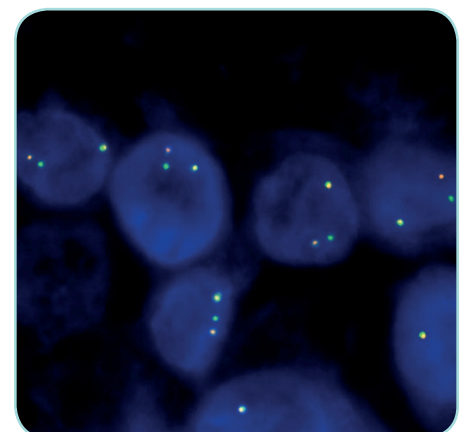
ALK Probe map (not to scale).

## Results

In an interphase nucleus of a normal cell lacking a translocation involving the 2p23.1-p23.2 band, two orange/green fusion signals are expected representing two normal (non-rearranged) 2p23.1-p23.2 loci. A signal pattern consisting of one orange/green fusion signal, one orange signal, and a separate green signal indicates one normal 2p23.1-p23.2 locus and one 2p23.1-p23.2 locus affected by a translocation or inversion. EML4-ALK inversion with deletion of 5'-ALK sequences is indicated by one or multiple isolated orange signals.



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



Lung cancer tissue section with translocation of the ALK gene as indicated by one non-rearranged orange/green fusion signal, one orange and one separate green signal.

Prod. No. Product

Z-2315-5.1ML ZytoMation ALK Dual Color Break Apart FISH Probe CE IVD

Label Tests\* (Volume)

●/● up to 20 (5.1 ml)

\* Using 240 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