

## ZytoLight® SPEC CDK4/CEN 12 Dual Color Probe

### Background

The ZytoLight® SPEC CDK4/CEN 12 Dual Color Probe is designed for the detection of CDK4 gene amplifications. The cyclin-dependent kinase 4 (CDK4) gene is located in the chromosomal region 12q14.1, ~10 Mb centromeric to the murine double minute (MDM2) gene and is frequently coamplified with MDM2 in different malignancies.

In a complex with cyclin D1 (CCND1), the CDK4 encoded serine/threonine kinase phosphorylates the retinoblastoma protein 1 (RB1) which in turn leads to the release of the E2F transcription factor and subsequently to an upregulation of genes which are required for progression through the S-, G<sub>2</sub>-, and M-phases of the cell cycle. Due to amplification of the respective chromosomal region, CDK4 is overexpressed in many human tumors such as soft tissue sarcomas, osteosarcomas (OS), and gliomas. In glioblastomas, the lack of amplification of several genes like CDK4 was recognized to be associated with a longer survival time. In OS, coamplification of MDM2 and CDK4, located in two discontinuous regions, occurs frequently in parosteal OS and less often in classical high-grade OS.

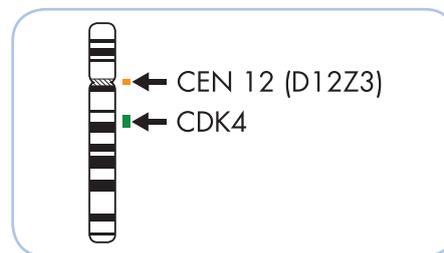
Although MDM2/CDK4 coamplification is not restricted to atypical lipomatous tumors/well-differentiated liposarcomas (ALT/WDLPS) and dedifferentiated liposarcomas (DDLPS), its detection is a strong criterion for distinguishing these tumor types from other undifferentiated sarcomas and even from carcinomas and lymphomas.

### References

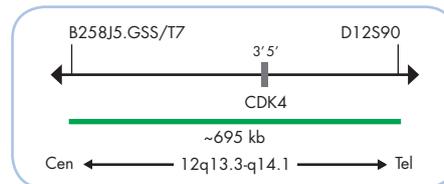
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 Fischer U, et al. (2010) *Int J Cancer* 126: 2594-602.  
 Lopes MA, et al. (2001) *Oral Oncol* 37: 566-71.  
 Mejia-Guerrero S, et al. (2010) *Genes Chromosomes Cancer* 49: 518-25.  
 Sirvent N, et al. (2007) *Am J Surg Pathol* 31: 1476-89.  
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### Probe Description

The SPEC CDK4/CEN 12 Dual Color Probe is a mixture of an orange fluorochrome direct labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3) and a green fluorochrome direct labeled SPEC CDK4 probe specific for the chromosomal region 12q13.3-q14.1 harboring the CDK4 gene.



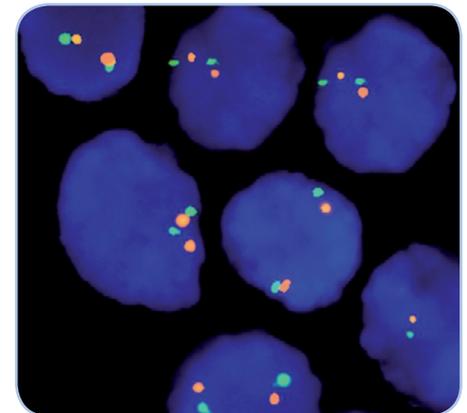
Ideogram of chromosome 12 indicating the hybridization locations.



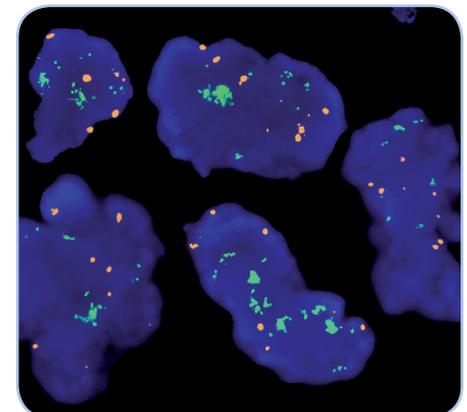
SPEC CDK4 Probe map (not to scale).

### Results

In a normal interphase nucleus two orange and two green signals are expected. Nuclei with amplification of the CDK4 gene locus 12q13.3-q14.1, or polysomy of chromosome 12 will show multiple copies of the green signal or large green signal clusters.



SPEC CDK4/CEN 12 Dual Color Probe hybridized to normal interphase cells as indicated by two orange and two green signals in each nucleus.



Liposarcoma tissue section, CDK4 signal cluster (green), CEN 12 (orange).

Prod. No.	Product	Label	Tests* (Volume)
Z-2103-200	ZytoLight SPEC CDK4/CEN 12 Dual Color Probe <b>CE IVD</b>	●/●	20 (200 µl)
<b>Related Products</b>			
Z-2028-20	ZytoLight FISH-Tissue Implementation Kit <b>CE IVD</b> Incl. Heat Pretreatment Solution Citric, 500 ml; Pepsin Solution, 4 ml; Wash Buffer SSC, 500 ml; 25x Wash Buffer A, 100 ml; DAPI/DuraText-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.