

## ZytoDot® 2C SPEC CDK4/CEN 12 Probe

### Background

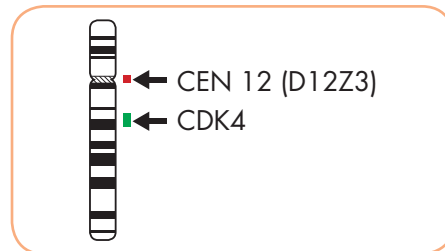
The ZytoDot® 2C SPEC CDK4/CEN 12 Probe is designed for the detection of CDK4 gene amplifications. The cyclin-dependent kinase 4 (CDK4) gene is located in the chromosomal region 12q14.1, ~10 Mb centromeric to the murine double minute (MDM2) gene and is frequently coamplified with MDM2 in different malignancies.

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-, G2-, 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.

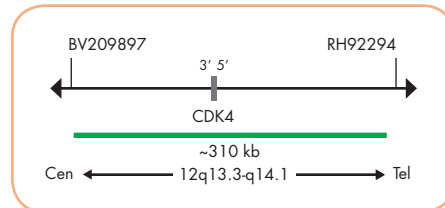
Although MDM2/CDK4 coamplification is not restricted to atypical lipomatous tumors/well-differentiated liposarcomas (ALT/WDLPS) and dedifferentiated liposarcomas (DDLPS), its detection is a strong criterion for distinguishing these tumor types from other undifferentiated sarcomas and even from carcinomas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

### Probe Description

The ZytoDot® 2C SPEC CDK4/CEN 12 Probe is a mixture of a Digoxigenin-labeled probe specific for the chromosomal region 12q13.3-q14.1 harboring the CDK4 gene and a Dinitrophenyl-labeled CEN 12 probe specific for the alpha satellite centromeric region of chromosome 12 (D12Z3).



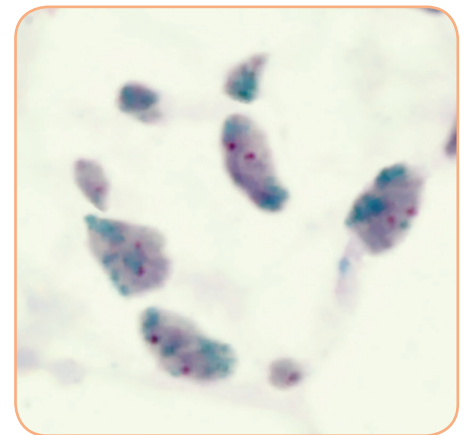
Ideogram of chromosome 12 indicating the hybridization locations.



SPEC CDK4 Probe map (not to scale).

### Results

In a normal interphase nucleus, using the ZytoDot® 2C CISH Implementation Kit, two green (CDK4) and two red (CEN 12) signals are expected. In a cell with amplification of the CDK4 gene locus or polysomy of chromosome 12, multiple copies of the green signal or green signal clusters will be observed.



Liposarcoma tissue section with CDK4 amplification as indicated by large green clusters.

### References

- Binh MB, et al. (2005) Am J Surg Pathol 29: 1340-7.
- Fischer U, et al. (2010) Int J Cancer 126: 2594-602.
- Lee SE, et al. (2014) Histol Histopathol 29: 127-38.
- Lopes MA, et al. (2001) Oral Oncol 37: 566-71.
- Mejia-Guerrero S, et al. (2010) Genes Chromosomes Cancer 49: 518-25.
- Sirvent A, et al. (2007) Am J Surg Pathol 31: 1476-89.
- Wunder JS, et al. (1999) Oncogene 18: 783-8.

Prod. No.	Product	Label	Tests* (Volume)
C-3062-400	ZytoDot 2C SPEC CDK4/CEN 12 Probe CE IVD	Digoxigenin/DNP	40 (400 µl)
<b>Related Products</b>			
C-3044-40	ZytoDot 2C CISH Implementation Kit CE IVD		40
Incl. Heat Pretreatment Solution EDTA, 500 ml; Pepsin Solution, 4ml; Wash Buffer SSC, 500 ml; 20x Wash Buffer TBS, 2x 50 ml; Anti-DIG/DNP-Mix, 4 ml; HRP/AP-Polymer-Mix, 4 ml; AP-Red Solution A, 0.4 ml; AP-Red Solution B, 15 ml; HRP-Green Solution A, 0.8 ml; HRP-Green Solution B, 15 ml; Nuclear Blue Solution, 20 ml; Mounting Solution (alcoholic), 4 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.