ZytoLight® Bladder Cancer Quadruple Color Probe

Intended Purpose

The ZytoLight Bladder Cancer Quadruple Color Probe is designed to detect CDKN2A (a.k.a. p16) deletions and aneuploidy of chromosomes 3, 7, and 17 in cytology specimens of tumors, e.g., in urine samples from patients with hematuria suspected of having bladder cancer (BC).

Moreover, it has been shown that the detection of CDKN2A deletions and/or aneusomies of chromosomes 3, 7, and/or 17 may be used for the surveillance of patients with a history of bladder cancer to early detect possible tumor recurrence.

BC represents the ninth most common cancer worldwide. About 430,000 new BC cases and 165,000 BC deaths occurred in 2012. Most of these tumors are non-invasive, well-differentiated, papillary tumors (pTa, low grade) and can be cured by endoscopic transurethral resection.

However, up to 70% of pTa and superficially invasive (pT1) tumors recur and of these, 15-30% are characterized by tumor progression. Therefore, a long-term follow-up of patients with BC is necessary.

The two standard methods used in the follow-up are either invasive (cystoscopy) or have a low sensitivity (cytology). BC cells are characterized by typical cytogenetic changes. Homozygous deletion of the CDKN2A gene at 9p21.3 and polysomy of chromosomes 3, 7, and/or 17 are common abnormalities observed in urothelial cell carcinoma, all of which can be detected by FISH. FISH on cells from urine has been shown to be highly sensitive and specific for detection of tumor cells in urine.

References

Antoni S, *et al.* (2017) Eur Urol 71: 96-108.
Dimashkieh H, *et al.* (2013) Cancer Cytopathol 121: 591-7.
Junker K, *et al.* (2006) Cytogenet Genome Res 114: 279-83.
Placer J, *et al.* (2002) Eur Urol 42: 547-52.

Probe Description

The ZytoLight Bladder Cancer Quadruple Color Probe is composed of:

- ZyGold (excitation 532 nm/emission 553 nm) labeled polynucleotides (~5,5 ng/µl), which target sequences mapping in 9p21.3* (chr9:21,742,619-22,056,863) harboring the CDKN2A gene region (see Fig. 1).
- ZyRed (excitation 580 nm/emission 599 nm) labeled polynucleotides (~0.5 ng/µl), which target sequences mapping in 3p11.1-q11.1 specific for the alpha satellite centromeric region D3Z1 of chromosome 3.
- ZyGreen (excitation 503 nm/emission 528 nm) labeled polynucleotides (~4,5 ng/µl), which target sequences mapping in 7p11.1-q11.1 specific for the alpha satellite centromeric region D7Z1 of chromosome 7.
- ZyBlue (excitation 418 nm/emission 467 nm) labeled polynucleotides (~12,0 ng/µl), which target sequences mapping in 17p11.1-q11.1 specific for the alpha satellite centromeric region D17Z1 of chromosome 17.
- Formamide based hybridization buffer

* according to Human Genome Assembly GRCh37/hg19

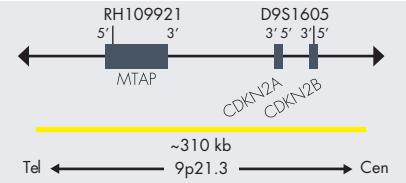
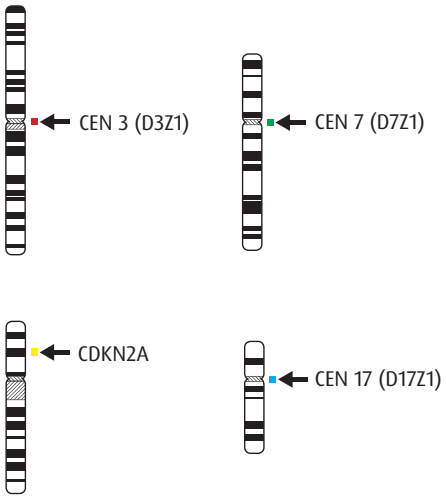


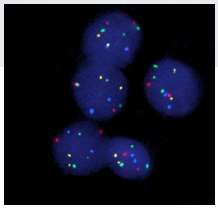
Fig. 1: SPEC CDKN2A Probe map (not to scale)



Ideograms of chromosome 3, 7, 9 and 17 indicating the hybridization locations

Results

Normal situation: In interphases of normal cells or cells without a deletion involving the CDKN2A gene region, two gold, two red, two green, and two blue signals are expected.
Aberrant situation: In a cell with deletion of the CDKN2A gene region, a reduced number of gold signals will be observed. Deletions affecting only parts of the CDKN2A gene region might result in a normal signal pattern with gold signals of reduced size. In cells with aneusomy of chromosomes 3, 7, or 17, more or less signals of the respective color will be visible.



Interphase tumor cells with trisomy of chromosome 7 as indicated by three green signals in each nucleus.

Labels	Chromosome	Reg. Status	Tests	Order No.
	3, 7, 9, 17	CE/IVD	5 (50 µl)	**Z-2305-50**
			20 (200 µl)	**Z-2305-200**