Background
The ZytoLight® SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe is designed for an accurate identification of renal cell carcinoma (RCC) subtypes by the simultaneous detection of VHL gene status and enumeration of chromosomes 1, 7, and 17 in tumor cells.

Clear cell RCC (ccRCC), papillary RCC (pRCC), chromophobe RCC (chrRCC) and renal oncocytomas (ROs) are the most frequent renal cell tumor subtypes. Patients with ccRCC have a poorer prognosis than patients with pRCC and chrRCC. RO is considered to be a benign neoplasm. The differentiation between RCC types may sometimes be difficult on histopathological features alone. However, the different subtypes of kidney tumors are characterized by distinct genetic patterns.

Chromosome 3p deletion, including deletion of the tumor suppressor gene VHL (von Hippel-Lindau) in 3p25.3, is the most typical genetic abnormality in ccRCC. pRCC is characterized by trisomy/polysomy of chromosomes 7 and 17. Combined losses of chromosomes 1, 2, 6, 10, 13, 17, and 21 (with 1, 2, 6, and 17 being affected most frequently) are the most common changes in chrRCC, whereas ROs often show rearrangements involving 11q13.3 harboring the CCND1 gene or losses of chromosomes 1, 14, and sex chromosomes.

Consequently, the ZytoLight® SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe is designed to differentiate between ccRCC, pRCC, and some chrRCC tumors and should be used in combination with the ZytoLight® SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe which helps to especially differentiate between chrRCC and ROs.

Probe Description
The SPEC VHL/1p12/CEN 7/17 Quadruple Color Probe is a mixture of a green fluorochrome direct labeled SPEC VHL probe spanning the VHL gene at 3p25.3, a gold fluorochrome direct labeled CEN 7 probe specific for the alpha satellite centromeric region of chromosome 7 (D7Z1), a blue fluorochrome direct labeled CEN 17 probe specific for the alpha satellite centromeric region of chromosome 17 (D17Z1), and a red fluorochrome direct labeled SPEC 1p12 hybridizing in close proximity to the centromere of chromosome 1 at the chromosomal region 1p12.

Due to cross-hybridizations of chromosome 1 alpha satellites to other centromeric regions, probes specific for 1p12 are frequently used for chromosome 1 copy number detection.

References
Results
In a normal interphase nucleus, two green, two red, two gold, and two blue signals are expected. In a cell with deletion affecting the VHL gene, a reduced number of green signals will be observed. In cells with aneusomy of chromosome 1, 7, or 17, more or less signals of the respective color will be visible.

Renal cell carcinoma tissue section with deletion of the VHL gene as indicated by one green signal in each nucleus.

Renal cell carcinoma tissue section with polysomy of the chromosome 7 and 17 as indicated by multiple gold and/or blue signals in each nucleus.

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.