Background
The ZytoLight® SPEC CCND1 Break Apart/2q11/CEN 6 Quadruple Color Probe is designed for an accurate identification of renal cell carcinoma (RCC) subtypes by the simultaneous detection of rearrangements affecting the CCND1 (cyclin D1, a.k.a. PRAD1) gene in 11q13.3 and enumeration of chromosomes 2 and 6 in tumor cells. Clear cell RCC (ccRCC), papillary RCC (pRCC), chromophobe RCC (chRCC), and renal oncocytomas (ROs) are the most frequent renal cell tumor subtypes. Patients with ccRCC have a poorer prognosis than patients with pRCC and chRCC. 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/polyomly 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 chRCC, whereas ROs often show rearrangements involving 11q13.3 or losses of chromosomes 1, 14, and sex chromosomes.

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

Probe Description
The SPEC CCND1 Break Apart/2q11/ CEN 6 Quadruple Color Probe is a mixture of a green and a red fluorochrome directly labeled probe hybridizing proximal and distal to the breakpoint on 11q13.3, respectively, a gold fluorochrome directly labeled CEN 6 probe specific for the alpha satellite centromeric region of chromosome 6 (D6Z1), and a blue fluorochrome directly labeled SPEC 2q11 probe. The SPEC 2q11 probe is specific for the AFF3 (AF4/FMR2 family, member 3) gene region in 2q11.2. Due to cross-hybridizations of chromosome 2 alpha satellites to other centromeric regions, probes specific for 2q11 are frequently used for chromosome 2 copy number detection.

References
Results

In a normal interphase nucleus, two red/green fusion signals, two blue, and two gold signals are expected. In a cell with translocation of the CCND1 gene locus, a signal pattern consisting of one red/green fusion signal, one red, and a separate green signal indicates one normal CCND1 locus and one CCND1 locus affected by an 11q13.3 translocation. In cells with aneuploidy of chromosome 2 or 6, more or less signals of the respective color will be visible.

Renal cell carcinoma tissue section with translocation affecting the 11q13.3 locus as indicated by one non-rearranged red/green fusion signal, one red signal, and one separate green signal indicating the translocation.

Renal cell carcinoma tissue section with monosomy of chromosome 2 and 6 as indicated by one blue and one gold signal 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.