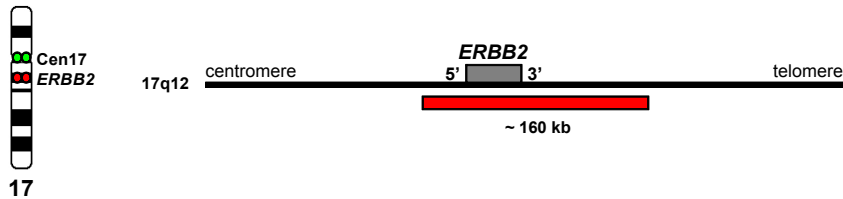


Intended Use

The ready-to-use *ERBB2* and Cen17 DNA-FISH Probe is designed to detect the amplification of the *ERBB2* gene (also named *HER2/neu*) on chromosome 17q12 relative to the control Cen17 by fluorescence in situ hybridization (FISH) in formalin-fixed, paraffin-embedded (FFPE) breast cancer tissue. Overexpression of the *ERBB2* gene occurs in 25-30% of human breast carcinomas, and approximately 90-95% of these cases result directly from gene amplification (1, 2). Patients showing such a rearrangement are at high-risk for relapse, and lower overall survival (2-4). Amplification of the *ERBB2* gene predicts a favorable response to certain chemotherapy regimens and selective monoclonal antibody therapy with trastuzumab (Herceptin®) (1-6). Amplification of the *ERBB2* gene is also seen in other solid tumors including gastric, esophageal, gynecologic, bladder, and non-small cell lung cancer, and correlates with a poor prognosis (1, 7).



The ideogram of chromosome 17 illustrates the respective locations of the hybridizations. The directly labeled Cen17 probe (green) hybridizes to the satellite DNA at 17p11.1-q11. The directly labeled *ERBB2* probe (red) spans the entire gene as indicated on the above schematic. The horizontal red bar indicates the region covered by the probe (approximate to scale, NCBI Build 36.1/Hg18/2006).

Signal Interpretation

In normal diploid metaphase chromosomes and interphase nuclei the probes generate two green and two red signals corresponding to the two normal chromosomes 17 (Figure 1). In cells with amplification or copy number increases, the number of red (*ERBB2*) signals is increased relative to the number of control Cen17 (green) signals (Figure 2). Amplification may also be present in the form of an hsr (homogenously staining region), observed as a brightly fluorescing mass of red signal. An *ERBB2*:Cen17 ratio of 2.2 or more is defined as amplification; ratios in the range 1.8 to 2.2 are considered borderline and should be subjected to discussion between the pathologist and the clinician (6).

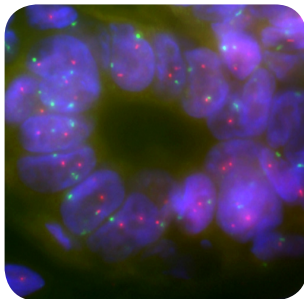


Figure 1: Normal diploid metaphase and interphase nucleus, each with two red (*ERBB2*) and two green (Cen17) signals.

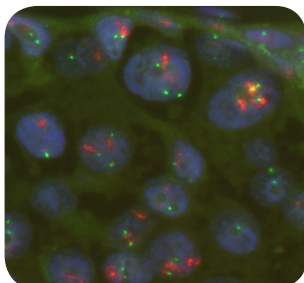


Figure 2: Interphase nuclei from paraffin sections of breast cancer specimens with 5-6 red (*ERBB2*) and, with hsr signal pattern of red (*ERBB2*, arrows). Signals of the Cen17 control are green in color.

Filter Requirements for Fluorescence Microscopy

Fluorophore	Excitation max	Emission max
Green	496 nm	520 nm
Red	580 nm	603 nm
DAPI	360 nm	460 nm

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