Genetics
In Breast Cancer

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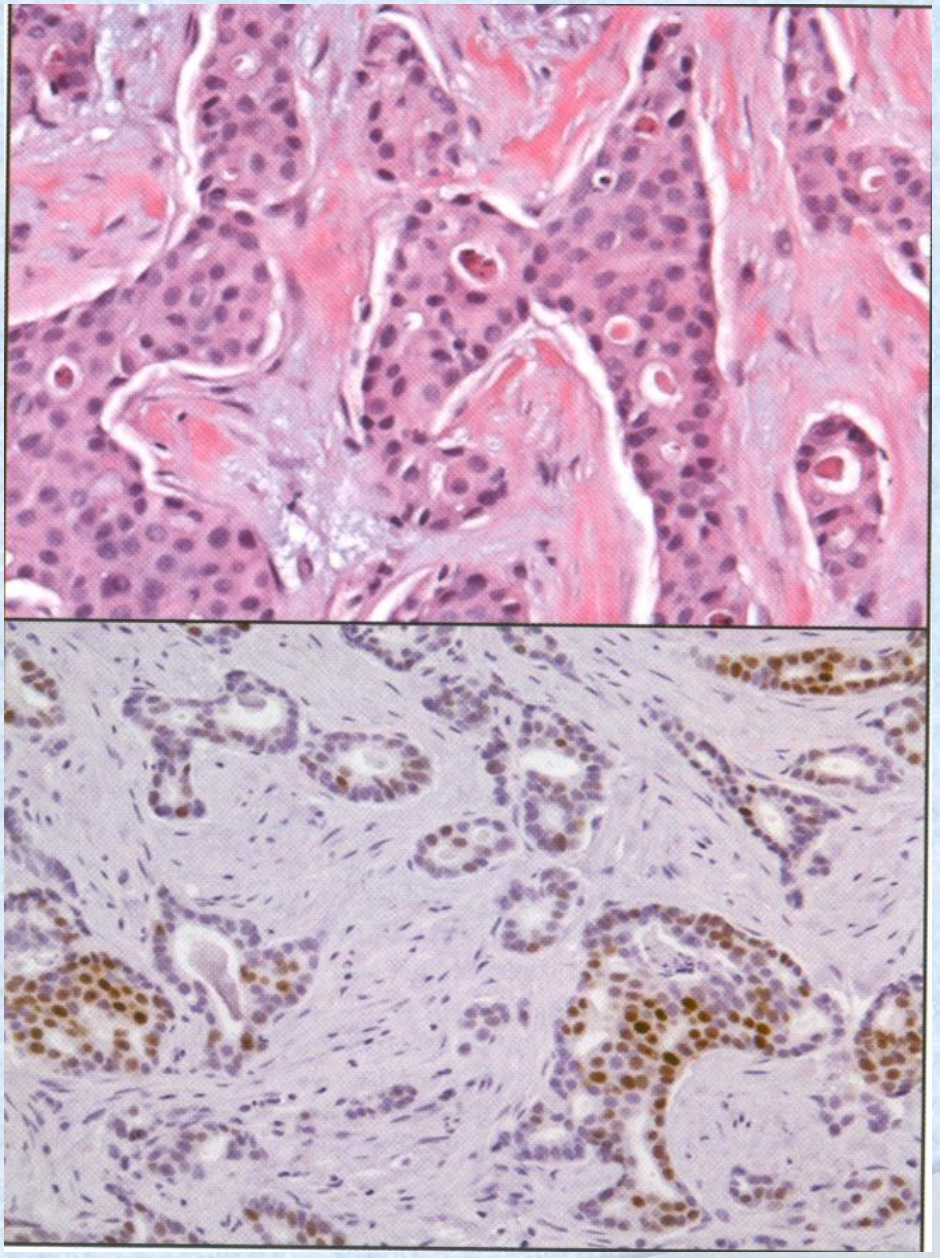
About 5% to 10% of breast cancers are related to specific inherited mutations

BRC A1 and BRC A2 which are mutated in familial breast cancers are involved in DNA repair.

A. BRCAI is located on chromosome 17q 21.3
B. BRCA2 is located on chromosome 13q 12-13.

Most carriers of those mutant genes will develop breast cancer by the age of 70 years, as compared with only 7% of women who do not carry a mutation.

60% to 70% of breast carcinomas express estrogen receptors (ERs) and progesterone receptors (PRS).



Immunohistochemistry for the evaluation of estrogen receptor (ER)

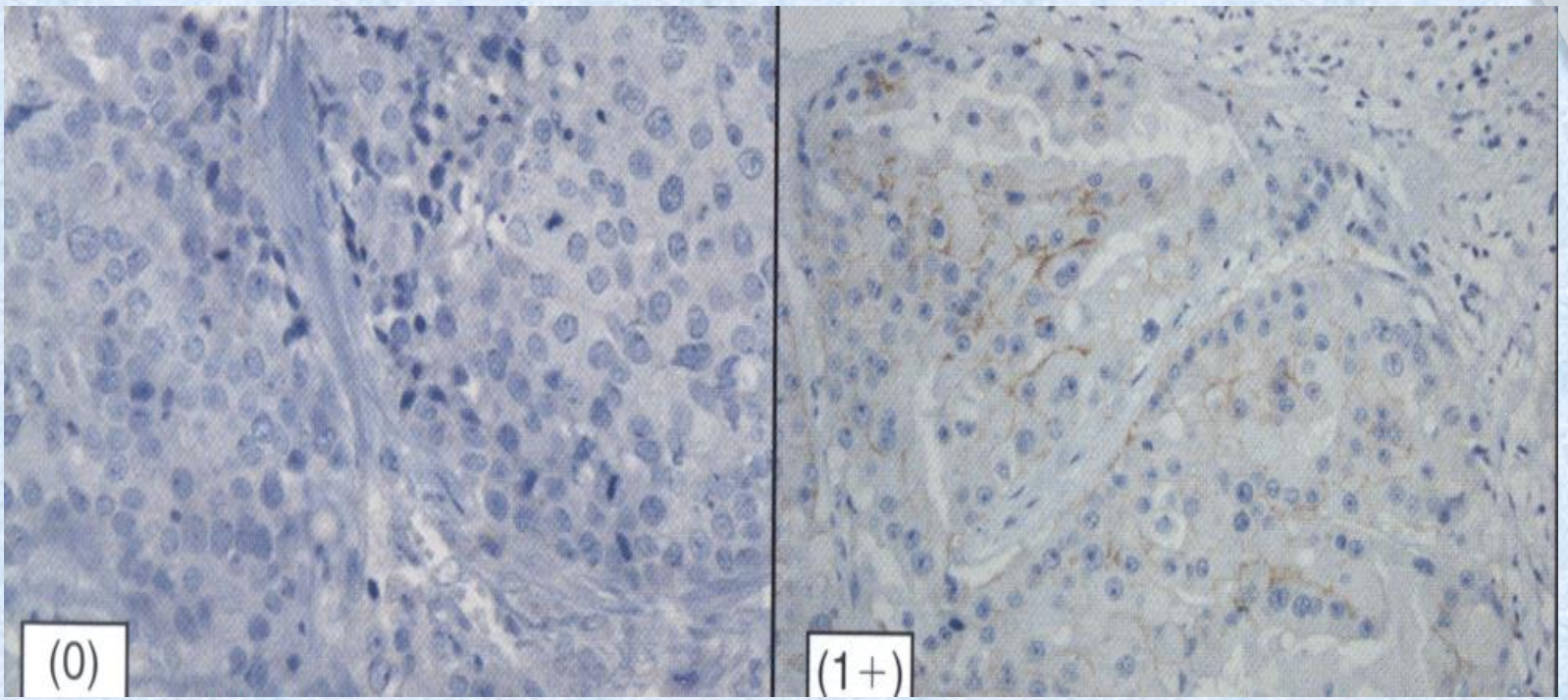
The presence of ERS in breast cancer is a weak prognostic factor, however, it is optimally useful as a predictive factor for the benefit of adjuvant tamoxifen or aromatase inhibitor therapy.

Normal cells have one copy of the HER 2 gene on each chromosome 17 (CHR17) and when this gene is expressed in normal epithelial cells, it is transmits signals regulating cell growth and survival.

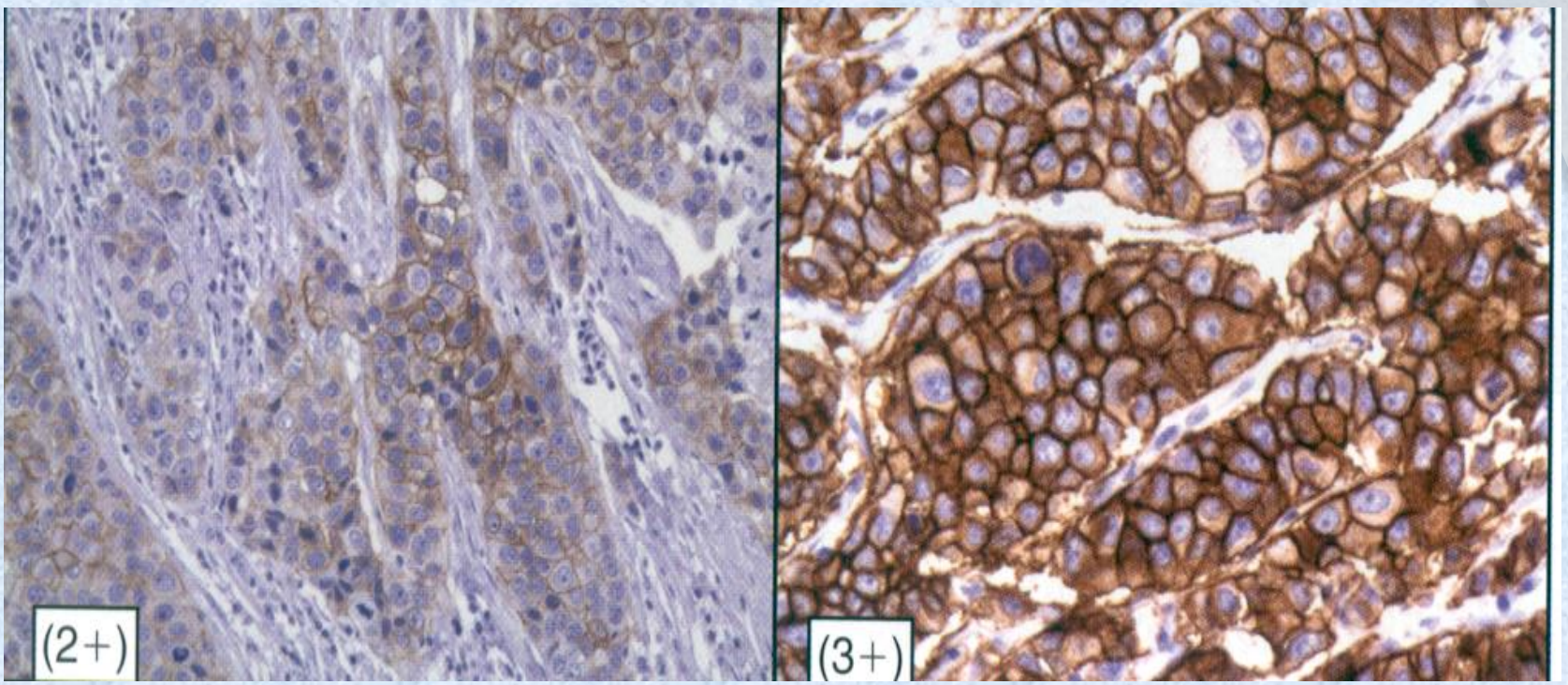
In approximately 15% to 25% of breast cancer, the HER2 gene is found to be amplified 2 fold to greater than 20 folds in each tumour cell nucleus.

As a result, HER2 positive breast cancers tend to be aggressive.

The herceptin molecule (Trastuzumab) has been shown to demonstrate a high specificity and affinity for the HER2 receptor and also acts as a biologic targeted therapeutic agent against HER2 receptors.



Immunohistochemistry (IHC) for the assessment of the level of HER2 protein expression at the tumor cell membrane.



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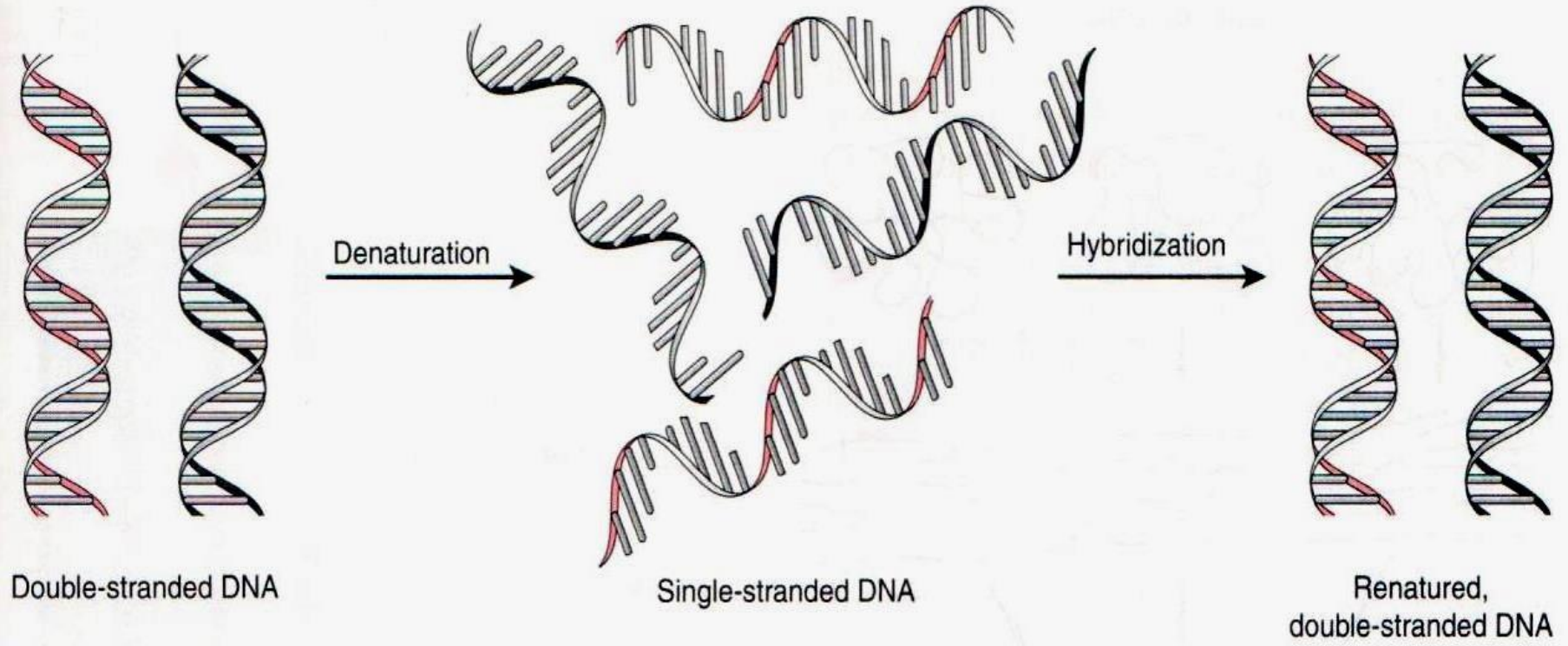
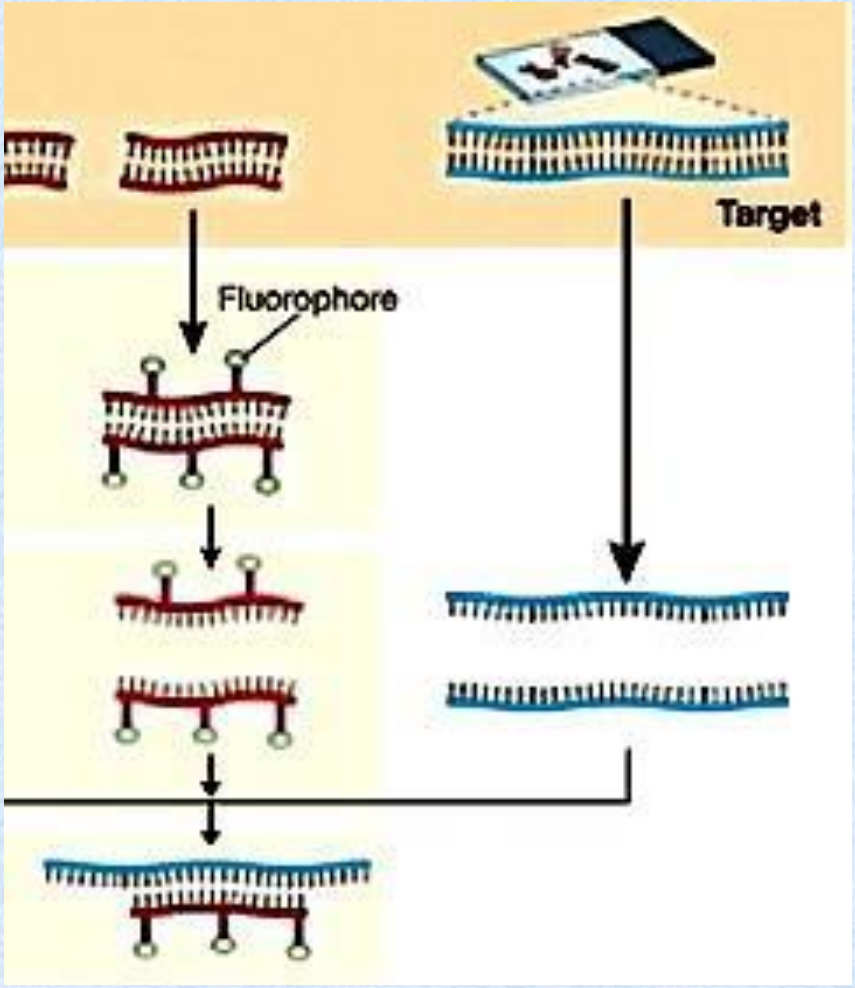
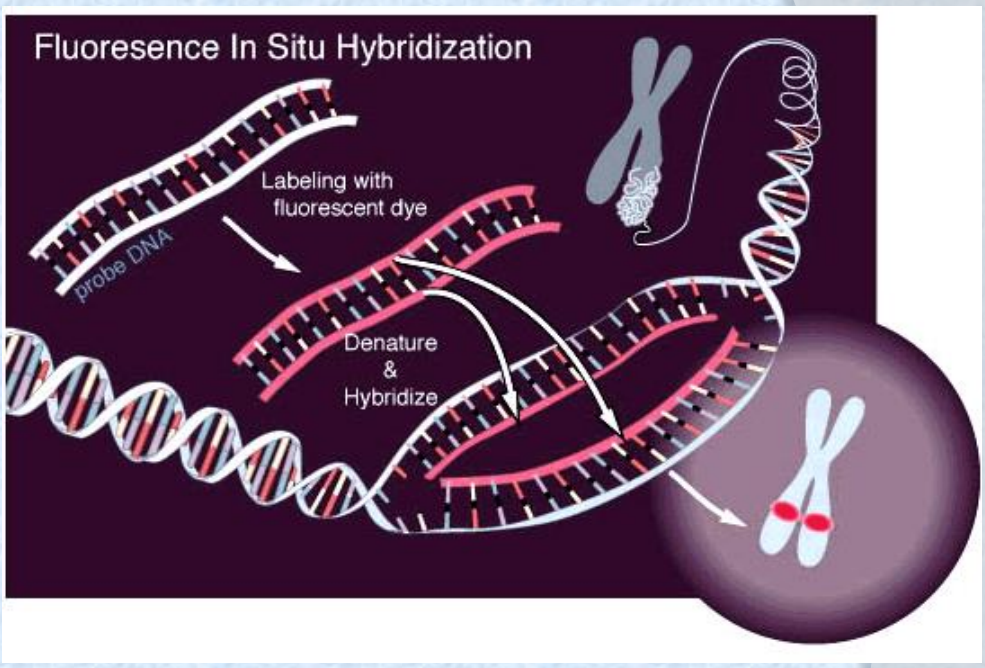


The principle of nucleic acid hybridization. The two complementary strands of a Watson-Crick double helix can be "denatured" by a variety of treatments (such as high temperature, high pH, or very low salt conditions) to yield a collection of single-stranded DNA molecules. Under conditions that favor formation of renatured double-stranded DNA, complementary strands will "hybridize" to each other, but not to other fragments of DNA that have a different nucleotide sequence.





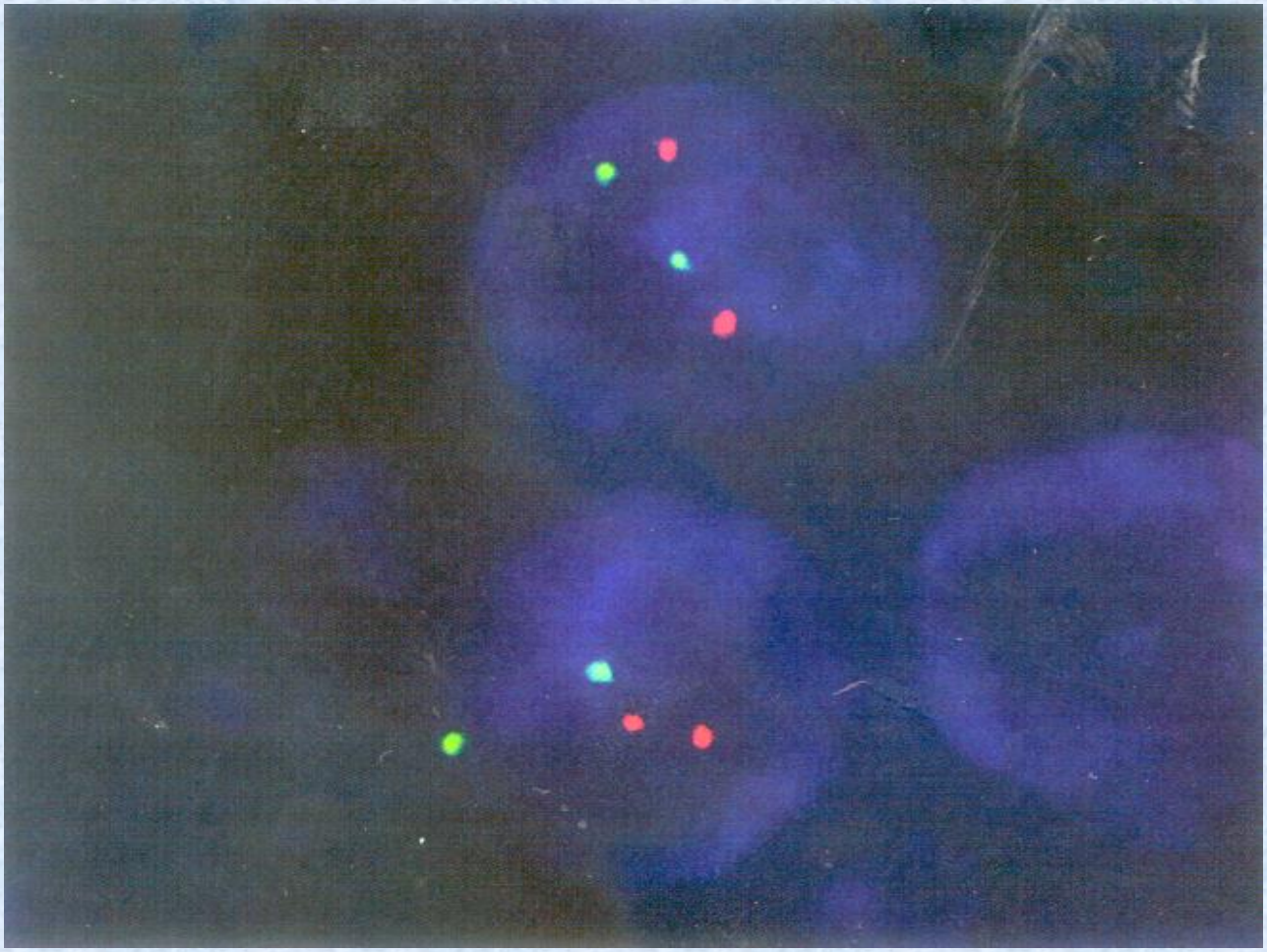
Schematic illustration of FISH technique

Principles of hybridisation

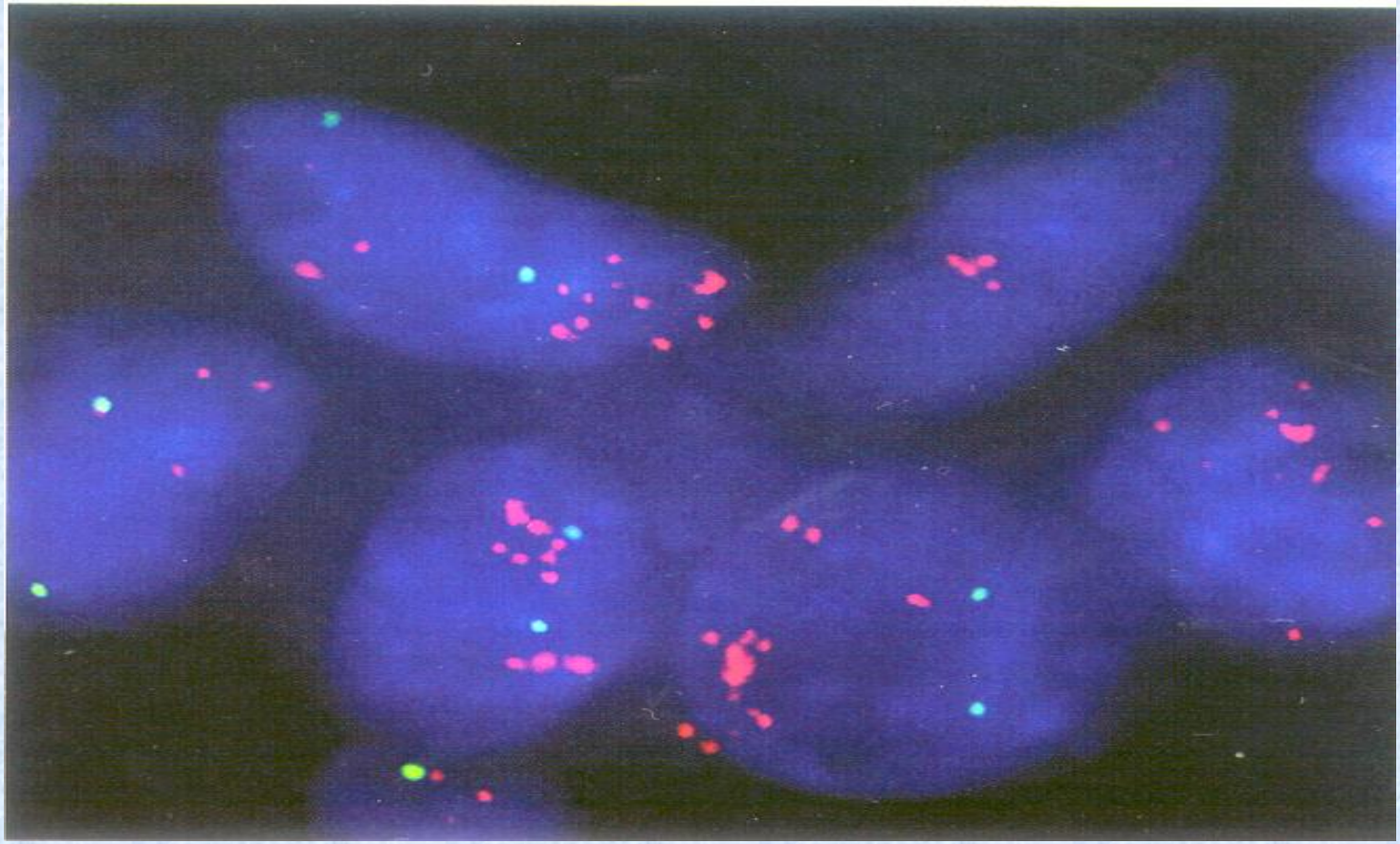
* DNA is double standed.
* Bonds between complementary bases hold strands together (Cytosine ⟷ Guanine; Adenine ⟷ thymine).
* Heat/alkalinise DNA – separation of strands ('denaturation') occurs.
* Cool separated strands – *complementary* double strands re-form.
* Labelled complementary single-strand DNA can identify a DNA sequence (e.g. a gene) in intact cells or disrupted cell preparations.

Immunophenotyping as a Surrogate for Molecular Category Using Estrogen Receptor, Progesterone Receptor and HER2 Status

	Molecular Category			
	Luminal A	Luminal B	HER2	Basal-like*
ER	+	+	−	−
PR	+	+	−	−
HER2	−	+	+	−



Fluorescence in situ hybridization image.



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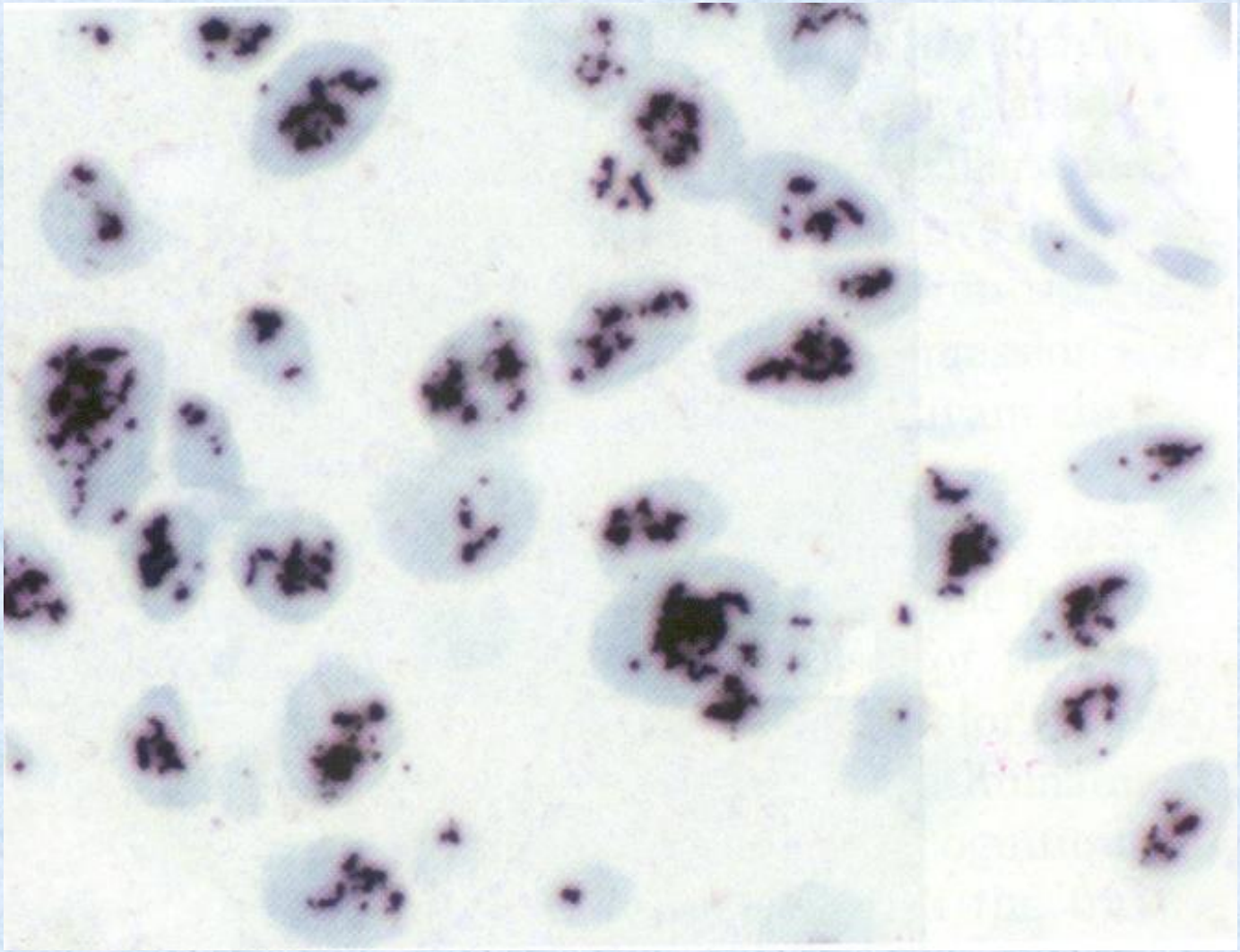
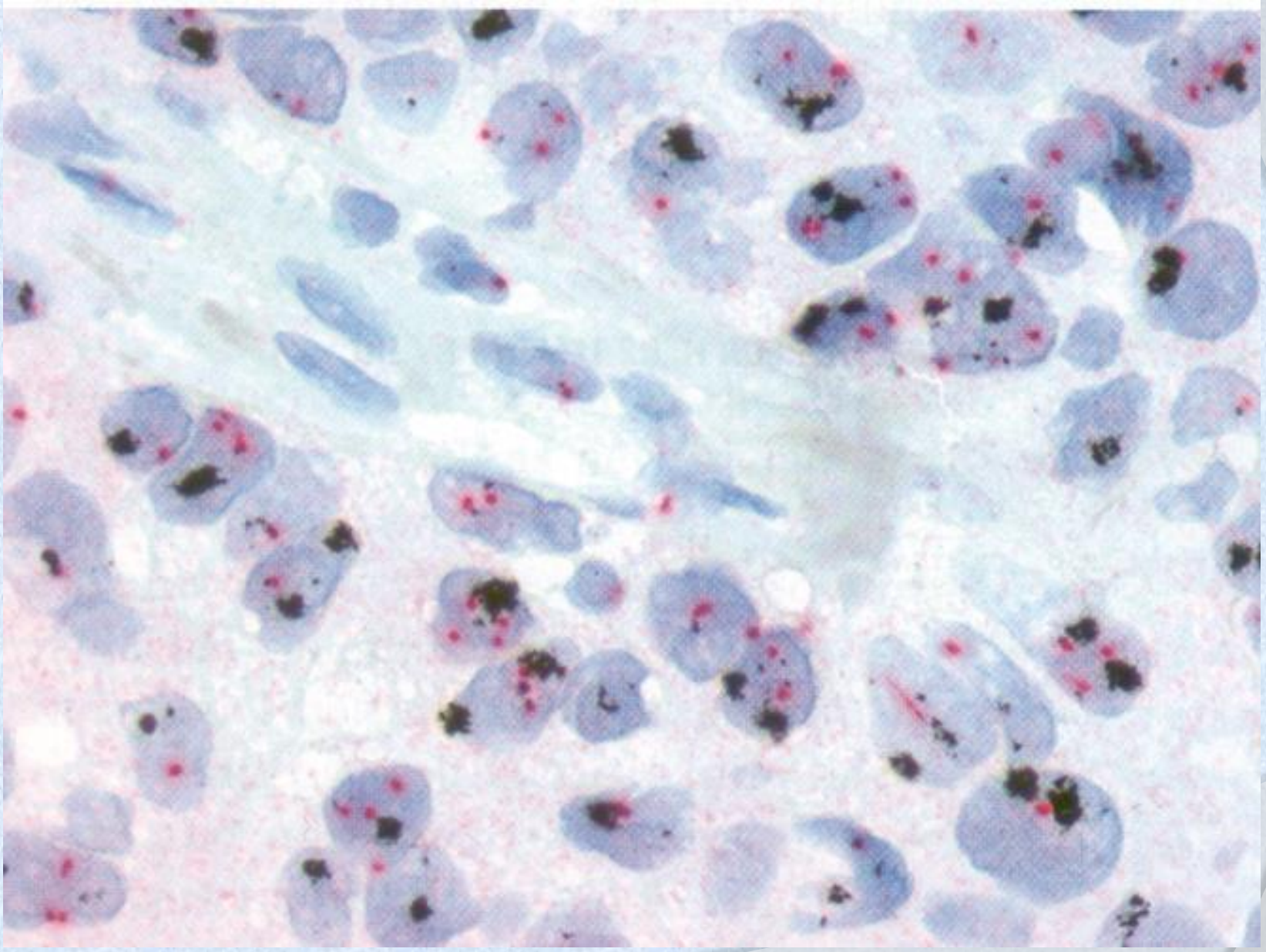
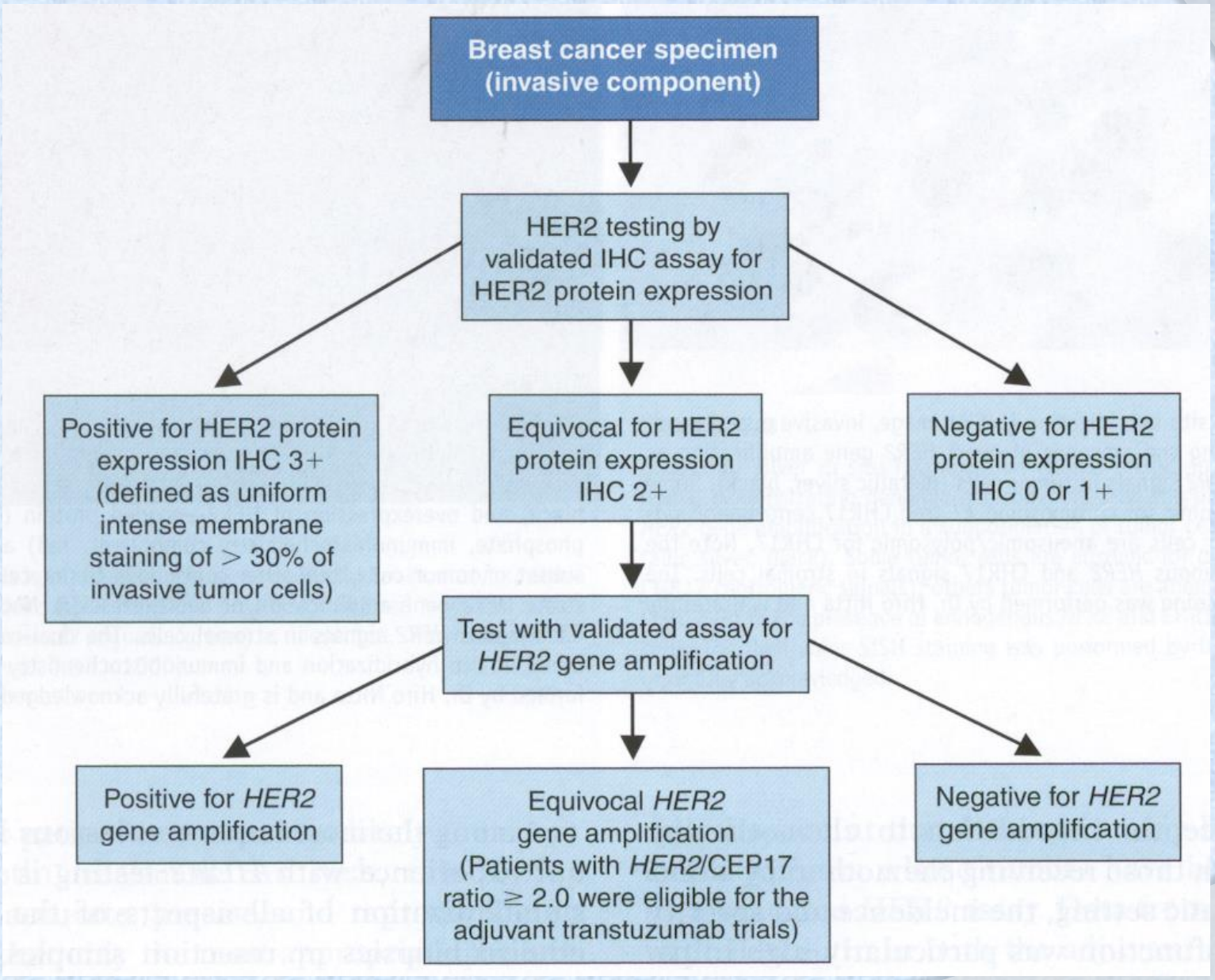


Silver in situ hybridization image.



Dual-color silver in situ hybridization (SISH) image.



ASCO/CAP guideline recommendations for the optimal algorithm for HER2 testing by IHC