WHITEPAPER

Meeting the Mark on Multiplex: Breast Cocktail

BIOCARE MEDICAL

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Studies show multiplex immunohistochemical (IHC) stains, like Biocare Medical's breast cocktail, may help with improving diagnostic concordance rates and in reducing overdiagnosis and misclassification of atypical ductal hyperplasia lesions.[1]

What is in Biocare's signature cocktail that gives it an advantage over single antibody breast markers?

Biocare's breast cocktail (CK 5/14 + P63 + CK 7/18) is comprised of mouse monoclonal anti-CK5, anti-CK14, and anti-p63 antibodies and rabbit monoclonal anti-CK7 and anti-CK18 antibodies. CK5 and CK14 are high molecular weight keratins expressed in the cytoplasm of basal cell and myoepithelium of breast tissues.[1-4] p63 is a transcription factor present in the nuclei of myoepithelial cells.[1,4] CK7 and CK18 are low molecular weight cytokeratins expressed in luminal cells of breast tissues.[1-3] Using innovative multiplex detection systems, such as Biocare's Mach 2 Double Stain 2 polymer, the cocktailed antibodies can be targeted and labeled simultaneously with two separate enzymes. With this polymer, the high molecular weight keratins and p63 mouse antibodies are labeled with an HRP enzyme and visualized with DAB, while the rabbit antibodies are labeled with an AP enzyme and visualized with a Fast Red chromogen. Usual ductal hyperplasia is associated with basal cell expression, intermixed with cells expressing the keratins of luminal cells. When examined microscopically, a cocktail-stained lesion exhibiting usual hyperplasia will demonstrate brown basal cells, intermixed with red luminal cells. Most atypical ductal hyperplasia and low-grade ductal carcinoma in situ cases are basal marker negative and luminal marker positive, exhibiting mostly red stained luminal cells. This cocktail may also identify micro-invasive breast carcinomas and aid in the identification of tumors with a basal phenotype, which were negative for ER/PR and c-erbB-2 and showed expression of CK5/p63 and/or CK14.[5]

The application of multiplex stains, like Biocare's breast cocktail, may be particularly beneficial to cases where tissue is limited, as many phenotypes can be observed on a single tissue section. Utilizing IHC in combination with hematoxylin and eosin (H&E), has been shown to significantly increase inter-observer agreement amongst pathologists, compared to H&E alone.[1] This improvement in diagnostic concordance may help reduce unnecessary surgical operations, improving patient care worldwide.

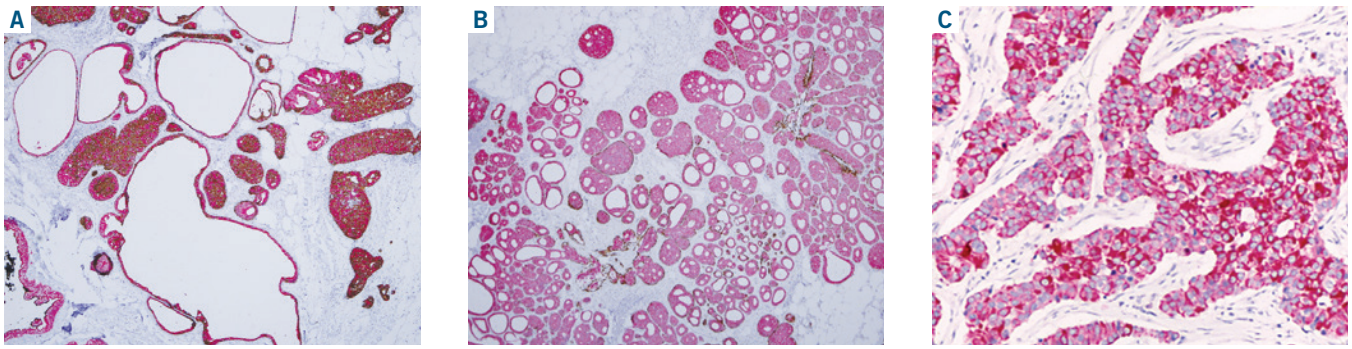
Interested in distinguishing your antibody menu with Biocare's Breast cocktail (CK 5/14 + P63 + CK 7/18)?

Available as a standard predilute (in both 6 ml and 25 ml sizes) and a Ventana formatted prediluted version (Biocare Ultraline™ offering), this cocktail can be used both manually and on most automated IHC instrumentation. For more information, please call 1-800-799-9499 or visit our website: https://biocare.net/product/ck514-p63-ck718/.

Components of Biocare's breast cocktail (CK 5/14 + P63 + CK 7/18)

Antibody	anti-CK5	anti-CK14	anti-p63	anti-CK7	anti-CK18
Clone	XM26	LL002	4A4	BC1	EP30
Source	Mouse Monoclonal	Mouse Monoclonal	Mouse Monoclonal	Rabbit Monoclonal	Rabbit Monoclonal
Isotype	IgG1/kappa	IgG3	IgG2a/kappa	IgG	IgG
Epitope/Antigen	CK5	CK14	p63	CK7	CK18
Cellular Localization	Cytoplasmic	Cytoplasmic	Nuclear	Cytoplasmic	Cytoplasmic
Cell Type	Progenitor cells Myoepithelial/ luminal Basal phenotype	Progenitor cells Myoepithelial/ luminal Basal phenotype	Basal Myoepithelium Basal phenotype	Normal breast cells Glandular epithelium Luminal epithelium	Normal breast cells Glandular epithelium Luminal epithelium

Antibody Cocktail Images



A. Breast lesion stained with Biocare's breast cocktail showing usual hyperplasia.[5]

B. Breast lesion stained with Biocare's breast cocktail showing atypical ductal hyperplasia.[5]

C. Invasive breast cancer stained with Biocare's breast cocktail- CK7/18 staining only.[5]

1. Jain, R., Mehta, R., Dimitrov, R. *et al.* Atypical ductal hyperplasia: interobserver and intraobserver variability. Mod Pathol 24, 917–923 (2011). https://doi.org/10.1038/modpathol.2011.66

2. Hicks DG. Appl Immunohistochem Mol Morph. 2011 Dec; 19(6):501-05.

3. Tacha DE, *et al*. Mod Pathol. 2009 Jan; 22(Suppl 1s):388A.

4. Moriya T, *et al.* Med Mol Morphol. 2006 Mar; 39(1):8-13.

5. Tacha D, *et al.* A Rapid Double Immunostaining Technique with a Single Cocktail of CK5, CK14, p63, CK7 and CK18 Distinguishes Between Hyperplasia of the Usual Type, Atypical Hyperplasia, Microinvasive and Basal Phenotype Breast Cancers. USCAP. John B. Hynes Convention Center Boston, Massachusetts. 2009 March. Poster Presentation.