BIOCARE MEDICAL

Multiplex IHC

Solving complex clinical problems & simplifying interpretation

- The most advanced multiplex technology available for any IHC laboratory
- Increase predictive value by combining highly sensitive & highly specific antibodies on one slide
- Conserve precious patient tissue, reduce labor + reagent costs by ≥ 50%

Simplify & Enhance

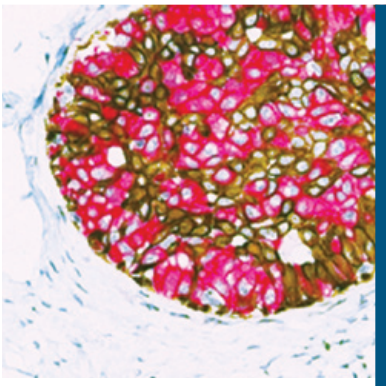
- **Allows for differentiation of CIS from benign lesions (breast, prostate & bladder)**
- **Simultaneously test for morphology distinct markers > superior diagnostic data**
- **Eliminate multiple slides to evaluate antigen ratios such as Kappa:Lambda**

ADH-5™ (CK5/14 + p63 + CK7/18)

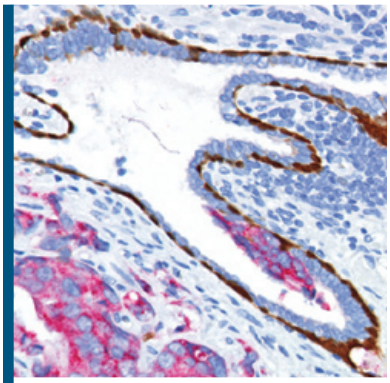
Simplifying interpretation of five challenging breast diseases in one easy test

ADH-5 simplifies interpretation and helps with diagnostic challenges such as differentiation of atypical ductal hyperplasia from hyperplasia of the usual type, identifying microinvasion and invasive ductal carcinoma, and distinguishing basal phenotypes in triple negatives, by simultaneously testing for 5 key markers of breast disease in one simple procedure. This powerful Multiplex IHC is composed of CK5/14 + p63 + CK7/18 antibodies: invasive vs. noninvasive breast lesions are easily distinguished by presence/absence of myoepithelium (CK5/14 and/or p63, DAB) and glandular staining with CK7/18 (Fast Red). Luminal or cytoplasmic staining may also be observed with CK5/14 luminal staining and/or CK7/18 (bimodal staining). For pure basal-phenotype classification, CK5/14 and in some cases of p63 (DAB) is observed. Breast cancer with bimodal and/or basal-like staining is associated with poor prognosis.

- Five complex clinical problems, one simple solution
- One Multiplex IHC replaces five individual antibody stains



Hyperplasia of the usual type: p63 staining basal myoepithelium (DAB), CK5/14 (DAB) and CK7/18 (FR) staining luminal epithelium.



Prostate cancer and prostatic intraepithelial neoplasia stained with PIN-4, CK5/14, p63 (DAB), P504S (FR).

PIN-4™ (CK5/14 + p63 + P504S)

Multiplex IHC for differentiation of PIN vs. prostate carcinoma

PIN-4 is used for the rapid differentiation of high grade prostatic intraepithelial neoplasia (PIN) from invasive carcinoma of the prostate and benign prostatic lesions, especially in difficult cases or cases with limited tissues. This simultaneous Multiplex IHC achieves a very high level of sensitivity and specificity via a combination of four morphologically distinct markers for prostate malignancy. HMW CK (CK5 + CK14) stains basal cells of normal and benign prostate. p63 is used as a differential marker for benign and malignant prostate tumors, as it is detected in basal cells, but is negative in malignant tumors. P504S is expressed in prostatic adenocarcinoma, but not in benign prostatic tissue. It is also expressed in premalignant lesions of the prostate: high-grade PIN and atypical adenomatous hyperplasia.

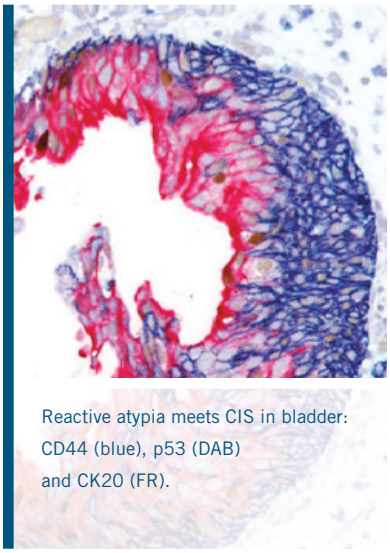
- Simplifies PIN diagnosis and differentiates carcinoma
- Decreases interpretation time by consolidating positive & negative markers

*A two-component version (IVD, ASR) can also be purchased:

Prostate Cocktail-2X (CK5 + CK14 + p63) Cat. No. PM 364 AAK, HK, JJK (IVD) / p504S-2X Cat. No. PP 365 AA, H, JJ (ASR)

Multiplex IHC

- **Combine up to 5 morphologically distinct markers for malignancy**
- **Rapid four-step automated procedure with convenient ready-to-use reagents**
- **A single Multiplex IHC can replace up to 5 single Ab stains; reducing labor + reagent costs by 50%**



Reactive atypia meets CIS in bladder: CD44 (blue), p53 (DAB) and CK20 (FR).

Uro-3 Triple Stain™ (CD44 + p53 with CK20)

Differentiating urothelial carcinoma *in situ* (CIS) from reactive atypia in bladder

In normal urothelium, the superficial umbrella cell layer shows reactivity for CK20 (FR) only; CD44 (Blue) staining is limited to the basal and parabasal urothelial cells and p53 (DAB) nuclear staining is absent or focal. For reactive atypia or marked atypia, CD44 (blue) shows increased reactivity in all layers of the urothelium and is often absent in neoplastic cells. In cases of CIS, diffuse, strong cytoplasmic reactivity for CK20 (FR) and nuclear reactivity for p53 (DAB) is observed throughout the urothelium.

- Differentiate urothelial CIS from reactive atypia
- Differentiate CIS via strong reactivity for CK20 and p53
- CD44 is overexpressed in reactive atypia of the urothelium

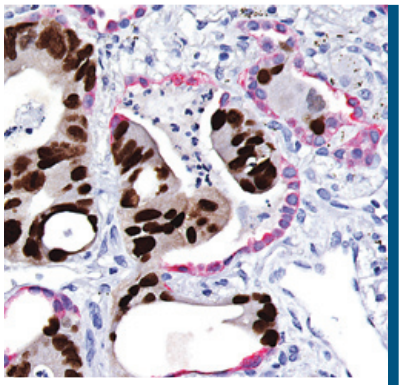
CDX2 + CK7

Multiplex IHC - Differentiation with Distinction

CDX2 is a homeobox gene that encodes an intestine-specific transcription factor. It is expressed in the nuclei of epithelial cells throughout the intestine, from duodenum to rectum. The CDX2 protein is expressed in primary and metastatic colorectal carcinomas, and has been observed in intestinal metaplasia of the stomach and intestinal-type gastric cancer. It is not expressed in the normal gastric mucosa. Studies have shown CDX2 to be a superior marker compared to CK20, and can be substituted in a panel of antibodies where CK20 is being used.

CK7 is a basic cytokeratin expressed in epithelial cells of ovary, lung and breast, but not of colon or gastrointestinal tract. CK7 is often used in conjunction with CK20 in distinguishing pulmonary, ovarian and breast carcinomas (CK7+) from colon carcinomas (CK7-). CDX2 + CK7 and TIF-1 is a common panel used to differentiate primary lung cancers from metastatic colon cancers.

- CDX2 + CK7 distinguishes colon carcinoma from ovarian, lung or breast carcinomas

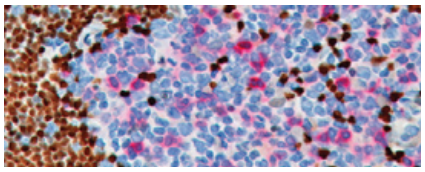


Colon cancer stained with CDX2 (DAB) metastasized into lung tissue stained with CK7 (FR).

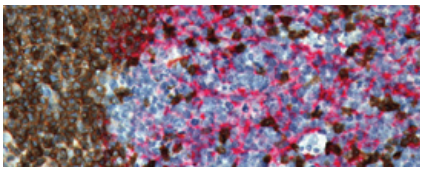
*Tissue Stained by Deb Van Eyck, Waukesha Memorial Hospital.

Multiplex IHC Tests

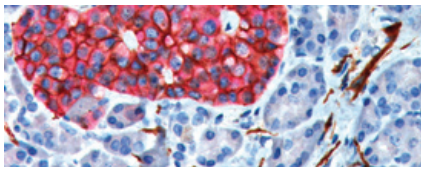
Simplify interpretation and increase laboratory productivity, while dramatically decreasing reagent and labor cost.



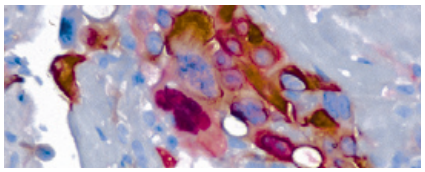
CD10 + Cyclin D1 staining mantle cell lymphoma



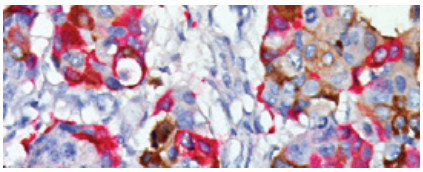
CD23 + CD5 staining mantle cell lymphoma



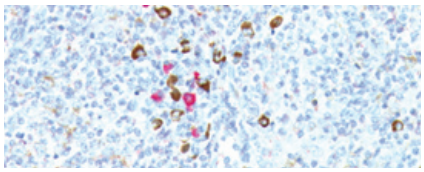
CD56 + Synaptophysin staining pancreas



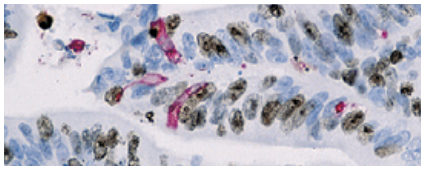
CK5/6 + Calretinin staining mesothelioma



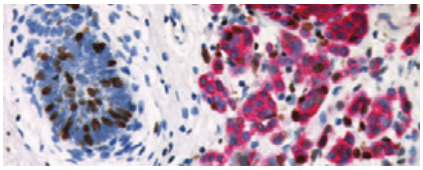
GCDFP-15 + Mammaglobin staining breast cancer



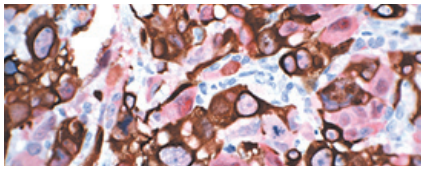
Kappa + Lambda staining neoplastic lymphoma



Ki-67 + Caspase-3 staining colon cancer



Pan Melanoma + Ki-67 staining melanoma



Pan Melanoma + S100 staining melanoma

Ordering Information

Product Name	Clinical Utility	Cat. No.
ADH-5™	Used to differentiate 5 phenotypes of breast cancer i.e. distinguish ADH from typical hyperplasia	PM 360DS
CD10 + Cyclin D1	Used as a panel for mantle cell lymphoma: Cyclin D1 (+) in mantle cell CD10 (-)	PM 314DS
CD23 + CD5	Used as a panel for mantle cell lymphoma: CD5 (+) in mantle cell CD23 (-)	PM 315DS
CD56 + Synaptophysin	Neuroendocrine neoplasms (eg. pheochromocytoma and pancreatic islet cell neoplasms)	PPM 316DS
CDX2 + CK7	Differentiation between colon, breast, and lung carcinoma for tumors of unknown origin	PM 367DS
CK5/6 + Calretinin	Identification of mesothelioma (positive for both markers)	PM 246DS
GCDFP-15 + Mammaglobin	Metastatic tumors expressing GCDFP-15 + Mammaglobin confirm tissue of unknown origin as breast	PM 317DS
HMW CK + LMW CK	Used for differentiation between squamous cell carcinoma and adenocarcinoma	PM 245DS
Kappa + Lambda	Identification of monoclonality in lymphomas, myelomas, and plasmacytomas	PPM 214DS
Ki-67 + Caspase-3	Evaluation of cell proliferation (Ki-67) and cell death (Caspase-3)	PPM 240DS
L26 + CD3	Differentiation between B-Cell (CD20) and T-Cell (CD3) lymphomas	PM 237DS
Pan Melanoma + Ki-67	Distinguishes melanocytic nevi that mimic melanoma	PM 362DS
Pan Melanoma + S100	Evaluation of suspected malignant melanomas	PPM 213DS
PIN-4™	Differentiation between benign prostate lesions, high-grade PIN, and invasive prostate carcinomas	PPM 225DS or PM 364, PP 365
Uro-3 Triple Stain™	Differentiate urothelial reactive atypia from CIS in bladder	PM 370TS

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