GEISINGER IHC

Stains are a good thing ... **Quality** stains are our thing.

Vol. I, Issue 2 • Summer 2013 **NEWS**

In this issue:

Guest Lecture Series:

Geisinger Medical Laboratories (GML) is pleased to announce its upcoming guest lectures. Three well-known speakers will be giving presentations on the following dates. All lectures will take place in the Henry Hood Center for Health Research (HHCHR) on the campus of Geisinger Medical Center in Danville, Pennsylvania. Lecture times are 9 a.m. to 1:30 p.m. Lunch will be provided. If you are interested in attending one or more of the presentations, please contact Melissa Erb at (570) 214-9781 for registration information. Limited seating available.

September 6, 2013
Dr. Philip Cagle
Lung Pathology and Molecular Testing
Intermediate Room #4

September 13, 2013
Dr. Jennifer Hunt
Molecular Diagnostics in Anatomic Pathology
Executive Conference Room

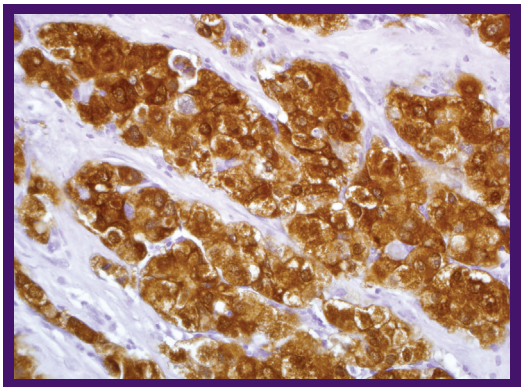
October 4, 2013
Dr. Stuart Schnitt
Diagnostic Problems in Breast Pathology
Intermediate Room #1

Antibody Updates

Arginase-1 for HCC

Arginase catalyzes the hydrolysis of arginine to ornithine and urea. Arginase-1 (Arg-1) is a cytosolic enzyme expressed predominantly in the liver as a component of the urea cycle.

Arg-1 is a sensitive and specific marker for the distinction of liver metastases from hepatocellular carcinoma (HCC). We recently performed immunohistochemical evaluation of Arg-1(Epitomics, clone EPR6672, 1:1000 dilution), hepatocyte paraffin-1 (HepPar-1), and glypican-3 on 1,240 surgical specimens and 62 liver fine-needle aspiration specimens (29 HCCs, 28 metastatic tumors, and 5 benign liver cases). The staining results on tissue microarray sections showed that 2.7% and 3.1% of nonhepatic tumor cases were positive for HepPar-1 and glypican-3, respectively; none was positive for Arg-1. For fine-needle aspiration specimens, 19 HCCs were positive for all 3 markers; 9 were positive for 1 or 2 markers; and only 1 case was negative for all 3 markers. These data demonstrate that Arg-1 is the most specific marker in differentiating a non-HCC from HCC. We recommend using 3 markers as a panel in distinguishing HCC from metastatic carcinoma.



Arginase-1 in hepatocellular carcinoma

References:

Timek DT, Shi J, Liu H, Lin F. Arginase-1, HepPar-1, and Glypican-3 are the most effective panel of markers in distinguishing hepatocellular carcinoma from metastatic tumor on fine-needle aspiration specimens. Am J Clin Pathol. 2012 Aug;138(2):203-10.

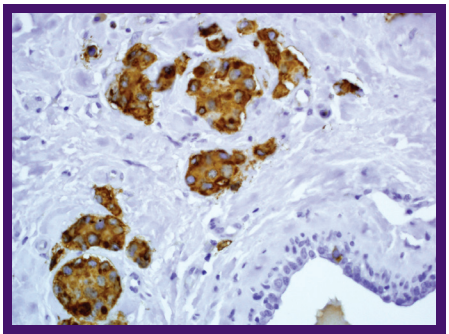
Yan BC, Gong C, Song J, Krausz T, Tretiakova M, Hyjek E, Al-Ahmadie H, Alves V, Xiao SY, Anders RA, Hart JA. Arginase-1: a new immunohistochemical marker of hepatocytes and hepatocellular neoplasms. Am J Surg Pathol. 2010 Aug;34(8):1147-54.

(continued on page 2)

Antibody Updates *(continued from page 1)*

TFF1 for breast carcinoma

Trefoil factor 1 (TFF1) is a member of trefoil family. TFF1 is usually expressed in normal breast ductal epithelium and gastric mucosal epithelial cells, goblet cells and small intestinal epithelial cells. Our recent study showed TFF1 (Epitomics, clone EP47, 1:100 dilution) was frequently expressed in both breast ductal and lobular carcinomas and much less frequently expressed in other carcinomas, including lung adenocarcinoma, endometrial adenocarcinoma and ovarian serious carcinoma, as summarized in the table below.



TFF1 in breast carcinoma

Antibody	Lung ADC	Breast DCA	Breast LCA	OSC	EADC
TFF1	5/111 (5%)	68/95 (72%)	41/47 (87%)	0/41 (0)	4/58 (7%)

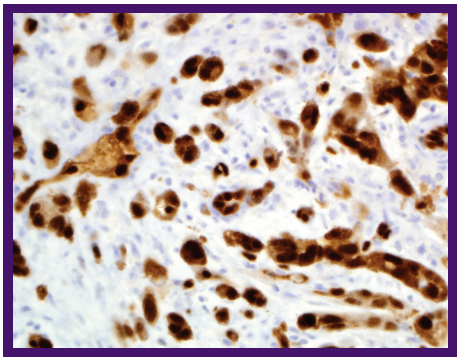
Note: ADC – adenocarcinoma; DCA – ductal carcinoma; LCA – lobular carcinoma; OSC – ovarian serous carcinoma; EADC – endometrial adenocarcinoma

References: F Lin, JW Prichard, M Zhang, H Liu. Identification of an Effective Immunohistochemical Panel in Distinction of Breast Carcinoma from Ovarian Serous Carcinoma [USCAP Abstract #1186]. Mod. Pathol. 2012; 25 (S2):283A.

H Liu, H Yin, H Wang, F Lin. Re-Evaluation of Immunohistochemical Markers in Endometrial Carcinoma [USCAP Abstract #1189]. Mod. Pathol. 2012; 25 (S2):283A

F Lin, S Zhu, H Deng, H Liu. Identification of an Effective Immunohistochemical Panel in Distinction of Breast Carcinoma from Lung Adenocarcinoma [USCAP Abstract #2012]. Mod. Pathol. 2012; 25 (S2):482A.

ERG for vascular tumors and prostatic adenocarcinoma



ERG in angiosarcoma

The transmembrane protease serine 2-E twenty-six related gene (TMPRSS2-ERG) fusion leading to ERG overexpression was found to be highly specific for and detected in approximately 50% of prostate cancers (ranging from 35-70%). Overexpression of ERG has also been suggested by some investigators to correlate with the poor prognosis of prostatic adenocarcinoma with Gleason score of 6 (3+3).

At GML, immunohistochemical stain for ERG (Epitomics, clone EPR3864, 1:100 dilution) was performed on TMA sections of normal tissues (N=456) and carcinomas (N=1,130) from various organs, including 90 cases of low- to intermediate-grade (L-MG) and 36 cases of high-grade (HG) prostatic adenocarcinomas, respectively. ERG expression was detected in 44% (40/90) of L-MG prostatic adenocarcinomas and 25% (8/36) of HG prostatic adenocarcinomas.

In addition, ERG has been demonstrated to be a highly sensitive and specific marker for both benign and malignant vascular tumors.

Reference: Liu H, Shi J, Wilkerson M, Yang XJ, Lin F. Immunohistochemical evaluation of ERG expression in various benign and malignant tissues. Ann Clin Lab Sci. 2013;43(1):3-9.

Immunohistochemical Panel Updates

Legend: + greater than 75% of cases positive; – less than 5% of cases positive; +/– 50-75% of cases positive

Lung adenocarcinoma vs. endometrial adenocarcinoma

Antibody	Lung adenocarcinoma	Endometrial adenocarcinoma
Napsin A	+	–
TTF-1	+	–
ER	–	+
PAX8	–	+
Vimentin	–	+
CEA	+	–

Approximately 5% of endometrial adenocarcinomas may be positive for TTF1, 10% positive for CEA, and 10% negative for vimentin.

Urothelial carcinoma vs. papillary renal cell carcinoma

Antibody	Urothelial carcinoma	Papillary renal cell carcinoma
GATA3	+	–
p63	+	–
Uroplakin II	+/-	–
CK903	+	–
RCC	–	+
PAX8	–	+
CD10	–	+

Select Abstracts from the 2013 USCAP Meeting
Part 2 of 2

SATB2:

- SATB2 is a specific marker of osteoblastic differentiation in mesenchymal tumors, both osteosarcomas and sarcomas with heterologous differentiation (Abstract #33).
- SATB2 shows excellent sensitivity and specificity for colon adenocarcinoma. When utilized in double stain, SATB2 and CK20 are the most specific combination for colon adenocarcinoma (Abstract #721).
- SATB2 is a highly sensitive marker for hindgut (distant 1/3 transverse colon to rectosigmoid) well-differentiated neuroendocrine tumors (WDNETs) and is much more sensitive than CDX2 (Abstract # 682).

ALK:

- The majority of angiomatoid fibrous histiocytoma (AFH) cases studied were positive for ALK IHC with at least one antibody. AFH with positive ALK IHC showed no *ALK* gene rearrangement by FISH (0/8) while 67% of inflammatory myofibroblastic tumors (IMTs) were ALK-positive by IHC. Of these, *ALK* gene rearrangement was demonstrated by FISH in 9/10 IMTs. The results indicate that ALK expression in AFH is common, particularly with the D5F3 and 5A4 clones, and is a potential source of diagnostic confusion in IMT (Abstract #28).
- ALK protein expression was detected by immunostain using a monoclonal antibody (Cell Signaling Technology) in 36 cases (5 *ALK*-rearranged adenocarcinomas, 19 NSCLCs with increased *ALK* copy numbers, and 12 normal *ALK* NSCLCs). The study indicates that immunohistochemical staining for ALK could be used as a surrogate assay to screen *ALK*-rearranged adenocarcinoma for targeted therapy (Abstract #1933).

Uroplakin II:

- The monoclonal mouse anti-UPII antibody [BC21] demonstrated superior sensitivity in UC of the bladder when compared to monoclonal mouse UPIII [BC17] (Abstract #901).

MUC4:

- MUC4 is a sensitive and reliable immunohistochemical marker for distinguishing low-grade fibromyxoid sarcoma (LGFMS) from non-LGFMS tumors other than synovial sarcoma (Abstract #59).

INI1:

- 50% of extraskeletal myxoid chondrosarcoma (ESMC) cases showed variable loss of INI1 expression (Abstract #75).
- 40% of myoepithelial tumors are INI1-deficient (Abstract #65).

Vimentin:

- Vimentin was negative in 98% (38/39) of primary ovarian endometrioid carcinomas, whether or not they were associated with an endometrial tumor. In contrast, 84% of primary endometrial carcinomas were vimentin-positive (Abstract #1127).

D2-40, p16 and caludin-4 for mesothelioma:

- D2-40 is a good marker for mesothelioma, negative in lung adenocarcinoma, and can be focally positive in squamous cell carcinoma (Abstract#1883)
- p16 deletion by FISH in mesothelioma, especially in sarcomatoid mesothelioma (Abstract#1888)
- Claudin-4 expresses in 100% of lung adenocarcinomas and is negative in 100% of mesotheliomas (Abstract #1926).

CD34 and SMA:

- CD34 and a-SMA can distinguish verrucous hyperplasia from verrucous carcinoma, with verrucous CA positive for SMA and negative for CD34; in contrast, the stroma of verrucous hyperplasia is positive for CD34 and negative for SMA (Abstract #1296).

Napsin A:

- In addition to the expression of napsin A (polyclonal antibody) in lung adenocarcinoma, papillary renal cell carcinoma, clear cell renal cell carcinoma, and upper GI adenocarcinoma, napsin A expression has been reported in anaplastic (32%), poorly differentiated (13%) and micropapillary pattern (50%) thyroid carcinomas (Abstract 541).

For additional information about these and other USCAP abstracts, refer to Mod Pathol. 2013;26(S2) or visit nature.com/modpathol/journal/v26/n2s/index.html.

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NEWS

Look Inside for:

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