GEISINGER IHC

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

Vol. I, Issue 4 • Winter 2014 **NEWS**

In this issue:

Geisinger IHC Antibody Updates

Carbonic anhydrase IX (CA IX)

Carbonic anhydrase IX (CA IX) is a membrane isoenzyme and hence imparts a membrane-predominant staining pattern in immunohistochemistry. Studies have shown that staining for CA IX is positive in 85 to 100% of clear cell renal cell carcinomas (CRCCs) and essentially negative in other renal cell carcinoma subtypes.[1-3] However, the data on its reactivity in other tissue types and tumors are inconsistent. We immunohistochemically evaluated CA IX expression on 1551 cases of tumors and normal tissues from various organs. There was overexpression of CA IX in CRCC (88%, 68/77). Twenty-six of 29 (90%) intrahepatic cholangiocarcinomas (ICCs) were positive. In contrast, only 5 of 34 (15%) hepatocellular carcinomas (HCCs) were focally positive. No staining was seen in chromophobe renal cell carcinoma (ChRCC), oncocytoma, seminoma, or carcinomas of the breast, thyroid, or prostate. All normal renal tubules showed no staining. These data demonstrate the diagnostic utility of CA IX in 1) differentiating CRCC from ChRCC and oncocytomas; 2) distinguishing low-grade CRCC from normal renal tubules in small samples; 3) separating ICC from HCC; and 4) identifying metastatic CRCC from other metastases with clear cell features.[4] Expression of CA IX in a case of ICC, CRCC and normal kidney is shown in Figure 1, Figure 2, and Figure 3, respectively.

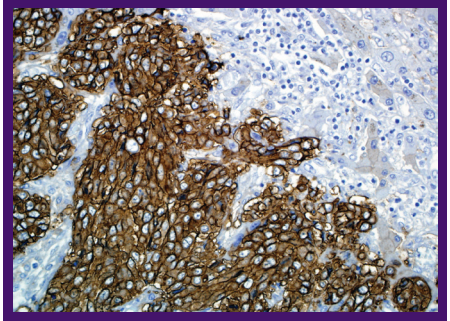

Figure 1: CA IX expression in ICC

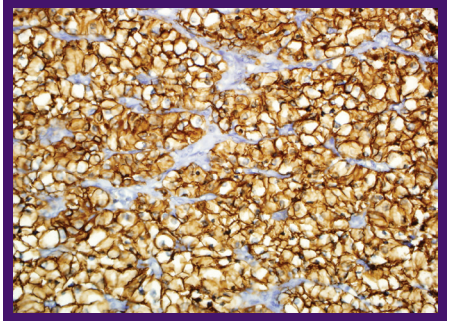

Figure 2: CA IX expression in CRCC

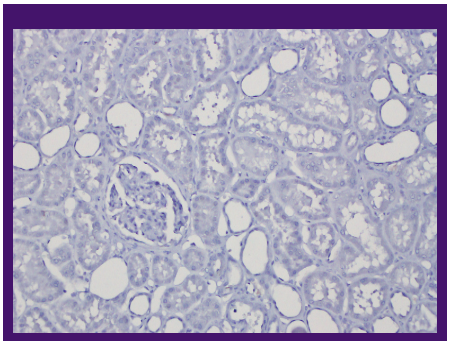

Figure 3: CA IX expression in normal kidney

References:

1. Al-Ahmadie H, et al. *Am J Surg Pathol.* 2008; 32(3):377-382.
2. Shen SS, et al. *Arch Pathol Lab Med.* 2012;136:410-417.
3. Donato D, et al. *Histopathology.* 2011;59(6):1229-1239.
4. Luong-Player A, et al. *Am J Clin Pathol.* 2014; 141(2):219-225.

(continued on page 2)

Geisinger IHC Antibody Updates *(continued from page 1)*

Cadherin-17

Cadherin-17 (CDH17) belongs to a member of the cadherin superfamily and is a calcium-dependent transmembrane glycoprotein.[1-4] The main function of CDH17 is to mediate cell-cell adhesion and to act as an intestinal peptide transporter.[1-4] A limited number of reports demonstrated that CDH17 was a highly sensitive marker for gastrointestinal adenocarcinomas and neuroendocrine neoplasms.[3,4] Panarelli et al. also reported that CDH17 was a more sensitive marker than CDX2 in identification of gastrointestinal adenocarcinomas and was observed only in a small percentage of adenocarcinomas of the lung, breast, ovary and endometrium.[4] Recently, we evaluated CDH17 expression in 18 medullary carcinomas of the colon and 1941 tumors and 358 normal tissues from various organs. Other immunomarkers, including mismatch repair proteins, CDX2, CK7, CK20, TFF3, MUC4, calretinin, p504S, villin, and synaptophysin, were also tested on the 18 medullary carcinoma cases. The results demonstrated 1) loss of MLH1 and PMS2 in over 80% of medullary carcinomas; 2) expression of CDH17 in 89% of medullary carcinomas; 3) focal expression of TFF3, MUC4, calretinin, CDX2, CK20 and synaptophysin in 72%, 72%, 67%, 67%, 28%, and 17% of 18 medullary carcinoma cases, respectively; and 4) CDH17 was expressed in 98% of the colorectal adenocarcinomas; in contrast, its expression was seen in 3.3% of non-gastrointestinal tumors.[5] CDH17 expression in medullary carcinoma of the colon is shown in Figure 4.

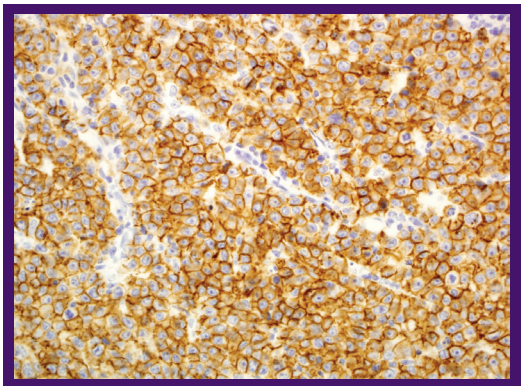

Figure 4: CDH17 expression in medullary carcinoma of the colon

References:

1. Angres B, et al. *Dev Dyn*. 2001;221(2):182-193.
2. Berndorff D, et al. *J Cell Biol*. 1994;125(6):1353-1369.
3. Su MC, et al. *Mod Pathol*. 2008;21(11):1379-1386.
4. Panarelli NC, et al. *Am J Clin Pathol*. 2012;138(2):211-222.
5. Lin F, et al. *Arch Pathol Lab Med*. Published online January 17, 2014.

SATB-2

Special AT-rich sequence binding protein 2 (SATB-2), is a recently described biomarker which functions as a nuclear matrix-associated transcription factor and an epigenetic regulator.[1,2] Magnusson et al. reported that SATB-2 in combination with CK20 can identify over 95% of all colorectal carcinomas.[2] Upper GI carcinomas and pancreatic adenocarcinomas were usually negative for SATB-2, and ovarian carcinomas and lung adenocarcinomas were positive for SATB-2 with low frequency.[2] Additionally, SATB-2 expression was reported as a novel marker of osteoblastic differentiation of bone and soft tissues tumors.[3] Recently, we studied SATB-2 expression in 18 medullary carcinoma cases and 1941 tumors and 358 normal tissues from various organs. The results demonstrated expression of SATB-2 in 89% of medullary carcinomas, 97% of colorectal adenocarcinomas, and only 3.6% of non-gastrointestinal tumors.[4] SATB-2 expression in medullary carcinoma of the colon is shown in Figure 5.

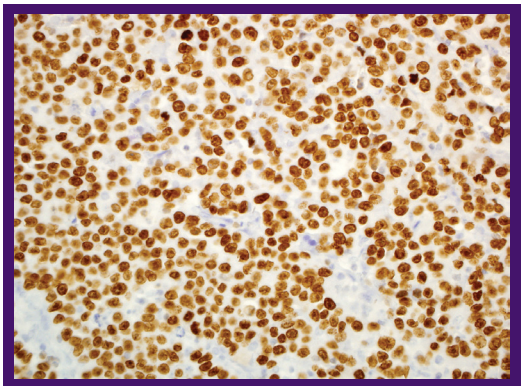

Figure 5: SATB-2 expression in medullary carcinoma of the colon

References:

1. Wang S, et al. *J Pathol*. 2009;219(1):114-122.
2. Magnusson K, et al. *Am J Surg Pathol*. 2011;35(7):937-948.
3. Conner JR, et al. *Histopathology*. 2013;63(1):36-49.
4. Lin F, et al. *Arch Pathol Lab Med*. Published online January 17, 2014.

NKX3.1

NK3 homeobox 1 (NKX3.1) is a highly sensitive and specific nuclear staining marker for both primary and metastatic prostatic adenocarcinomas (ADCs) and has been reported in virtually 100% of prostatic ADCs.[1,2] Our preliminary study demonstrated 100% of prostatic acinar ADCs (Gleason score 6, N=100) were positive for NKX3.1. An example of NKX3.1 expression in a metastatic prostatic ADC is shown in Figure 6.

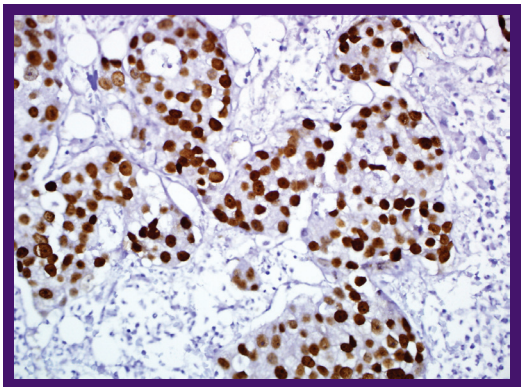

Figure 6: NKX3.1 expression in metastatic prostatic ADC

References:

1. Gurel B, et al. *Am J Surg Pathol*. 2010;34(8):1097-1105.
2. Gelmann EP, et al. *Prostate*. 2003;55(2):111-117.

Geisinger IHC Antibody Updates *(continued from page 2)*

NKX2.2

NK2 homeobox 2 (NKX2.2) is a transcription factor with a crucial role in differentiation of the central nervous system and pancreatic islets, which has been demonstrated to be expressed in 93% of Ewing sarcomas/primitive neuroectodermal tumors (PNETs) and was not expressed in the vast majority of other small round cell tumors, with the exception of olfactory neuroblastomas and a minor subset of small cell carcinomas, synovial sarcomas, mesenchymal chondrosarcomas, and malignant melanomas. NKX2.2 appears to be a more sensitive and specific marker than CD99 and friend leukemia virus integration 1 (Fli-1) for Ewing sarcoma/PNET based on limited literature. Additional studies would be needed to validate the diagnostic sensitivity and specificity of this marker. An example of NKX2.2 expression in Ewing sarcoma/PNET is shown in Figure 7.

Reference:
Yoshida A, et al. *Am J Surg Pathol*. 2012;36(7):993-999.

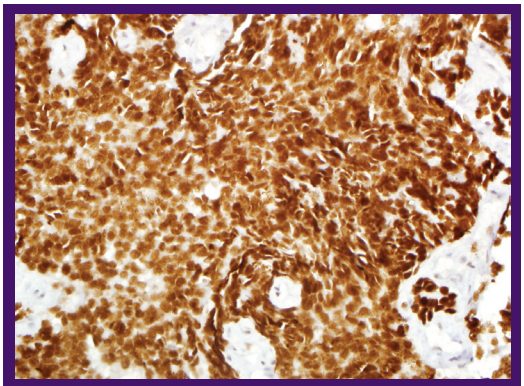

Figure 7: NKX2.2 expression in Ewing sarcoma/PNET

Immunohistochemical Panel Update

Pancreatic ductal adenocarcinoma vs. chronic pancreatitis

Antibodies	Pancreatic DADC	Pancreatitis
pVHL	–	+
Maspin	+	–
S100P	+	– or C + only
IMP3	+	–
CK17	+ or –	Usually –
MUC5AC	+ or –	–
p53	+ or –	– or very weakly +
mCEA	+	Usually – or focally +
DPC4/SMAD4	Loss (60%)	+
Mesothelin	+	- or weakly +

Note: "+"— usually greater than 75% of cases are positive; "–"— less than 5% of cases are positive; "+ or –"— usually more than 50% of cases are positive; "– or +"— less than 50% of cases are positive

Reference:
Liu H, et al. *Arch Pathol Lab Med*. 2012;136(6):601-609.

GEISINGER

Geisinger Medical Laboratories
100 North Academy Avenue
Danville, PA 17822-0131

GEISINGER IHC

NEWS

Look Inside for:

- Antibody Updates
- Immunohistochemical Panel Update

Geisinger Medical Laboratories
100 North Academy Avenue
Danville, PA 17822-0131
1.800.695.6491

www.geisingerihc.com

77744-1-2/14-MB/DS-D