Introducing the Geisinger IHC Laboratory and Newsletter

Geisinger Medical Laboratories announced the launch of its IHC Laboratory, Geisinger IHC, at the 102nd USCAP Annual Meeting in Baltimore in March. Geisinger IHC provides an extensive and growing antibody library and delivers fast, accurate, reliable and reproducible results. We offer flexible service, including technical only, technical and professional, and case consultation with diagnosis by 20 AP or AP/CP board-certified subspecialized pathologists. There is strong science and support behind Geisinger IHC:


• The companion website (www.ihcfaq.com): Our way of keeping IHC information up-to-date. The site features newly introduced antibodies and evidence-based differential diagnostic panels that we have found useful in our practice, including our optimized staining protocols, clinical applications and pitfalls, microscopic and tissue microarray images and related references.

• Focus on research in IHC related-projects: As the result, the group has contributed over 200 articles to peer-reviewed pathology journals and poster/platform presentations to pathology societies in the past 7-8 years.

In conjunction with our new IHC Laboratory, we’ve developed the Geisinger IHC Newsletter. It will be published on a quarterly basis in order to provide the most useful, practical and updated information. It will focus on new antibodies, antibody protocol updates, diagnostic antibody panel updates, useful literature updates, Geisinger IHC news, and issues of IHC quality control, regulation, standardization, utilization, and billing.

For additional information about our IHC lab, please visit our website at www.GeisingerIHC.com.

Geisinger IHC Antibody and Panel Updates

Geisinger IHC continually tests new antibodies, new clones, new panels and protocols to determine the best possible marker or panel of markers to use in our practice.

Maspin/pVHL double stain for diagnosis of pancreatic adenocarcinoma

Differentiation of ductal adenocarcinoma of the pancreas from non-neoplastic pancreatic tissues can be challenging, especially in small biopsies and fine needle aspiration specimens.

(continued on page 2)
### Tissue Microarray (TMA)

**External positive control (EPC)** is an important method of quality control for IHC staining and is required by the College of American Pathologists (CAP) and many IHC vendors.

In the past, we relied on a single-tissue block or multi-tissue sausage block for this purpose. In order to cover a large and expanding antibody inventory, which currently contains more than 200 antibodies, the lab had to keep a list of tissue blocks for EPC. Sometimes, it became too challenging for technologists to identify the correct EPC for an antibody. Another challenge was too much tissue consumption, particularly for tumor tissues. From a quality control point, the lack of staining consistency and reproducibility was also problematic because different tissue blocks were used for different antibody runs.

To overcome these shortcomings, the lab started to invest time and effort into building a set of TMA blocks for EPC use. These blocks each contain multiple 2-mm cores of normal and/or tumor tissue. They are specifically designed to either maximize tissue representation for broad antibody coverage and target unique pathological conditions. Tissues are taken exclusively from selected blocks with demonstrable positive immunoreactivity for desired antibodies.

The new TMA EPCs appear on IHC stained slides as neatly arranged rows of circular tissue which only occupy a small space and leave ample space for testing samples. Not only do they have a superior visual appearance, they are also extremely easy to read under the microscope. Their multi-tissue composition empowers users to simultaneously compare immunoreactivity in not only one but many normal tissues or tumor types, which usually provides both positive and negative controls on the same TMA section. TMA EPCs have also demonstrated superior performance in staining consistency and reproducibility as compared to the old-fashioned EPCs. Since TMA EPCs use small tissue cores, they will also save precious tumor tissue.

Using TMAs as EPCs is above and beyond current standard laboratory practice. It sets a new milestone in our lab’s continuous effort to improve the quality and technology of IHC.

### Geisinger IHC Panel Updates

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**Legend:** + greater than 75% of cases positive; − less than 5% of cases positive

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### Select Abstracts from the 2013 USCAP Meeting

**Part 1 of 2**

#### GATA3:
- Usually positive in collecting duct carcinoma and negative in renal pelvis urothelial carcinoma (Abstract #881).
- GATA3 positivity was noted in 89% of renal, 100% of microspapillary, and 57% of papillary urothelial carcinoma (Abstract #1066).
- GATA3 immunostaining is relatively common in salivary gland neoplasms, especially in salivary duct carcinoma or mammary analogue secretory carcinoma (Abstract #1307).
- GATA3 was positive in 83% of urinary bladder paragangliomas and 75% of paragangliomas outside of the bladder (Abstract #1041).
- GATA3 expression was seen in 31/35 (89%) paragangliomas, 20/21 (95%) pheochromocytomas, and all neuroblastomas, ganglioneuroblastomas, and ganglioneuromas (Abstract #566).
- GATA3 expression in 96 cases of ER-negative ductal carcinoma; overall, 59% of TMA and 79% of CNB cases showed nuclear staining for GATA3, with the majority (73%) being strong and diffuse (Abstract #216).

#### PAX8:
- In addition to renal cell carcinomas, GYN tumors, thyroid follicular cell origin, thymic tumors, and pancreatic neuroendocrine tumors, other tumors can be positive for PAX8:
  - PAX8 may be detected in a subset of high-grade metastatic breast carcinomas but is generally expressed in a minority of cells (Abstract #2036).
  - PAX8 is usually expressed in collecting duct carcinoma and negative in urothelial carcinoma of the renal pelvis (Abstract #982).
  - PAX8 can be positive in low-grade and high-grade noninvasive urothelial carcinomas (Abstract #1023).

More abstracts will be reviewed in our next issue.

For additional information about these and other USCAP abstracts, refer to Mod Pathol. 2013;26(S2) or visit http://www.nature.com/modpathol/journal/v26/s2/index.html.

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

At Geisinger IHC, we investigated the utility of 26 immunohistochemical markers (CAM 5.2, CK7, CK20, CK17, CK19, MUC1, MUC2, MUC4, MUC5AC, MUC6, p53, DPC4/SMAD4, CDX2, pVHL, S100P, IMP-3, maspin, mesothelin, claudin 4, claudin 18, annexin A8, fasin, PSCA, MOC31, CEA, and CA19-9) in the diagnosis of ductal adenocarcinoma of the pancreas. Our data demonstrate that pVHL, maspin, S100P and IMP-3 are the best diagnostic panel of immunomarkers for confirming the presence of ductal adenocarcinoma in both surgical and fine needle aspiration specimens.

#### GATA3 for carcinoma of breast or urothelial primary

**GATA3 expression has been reported in urothelial and breast carcinomas.** At Geisinger, we performed immunohistochemical evaluation of GATA3 expression in 1,110 carcinomas and 310 cases of normal tissue using tissue microarray sections, 48 breast and bladder biopsy specimens, and 53 breast fine-needle aspiration biopsy samples. Sixty-two of 72 urothelial carcinomas (86%) and 138 of 147 breast carcinomas (94%) tested positive for GATA3. All other cases, except 2 of 96 endometrial carcinomas, tested negative for GATA3. On fine-needle aspiration biopsy samples, 88% of primary breast carcinomas and 82% of metastatic breast carcinomas tested positive for GATA3. Our study revealed that GATA3 is a sensitive and specific marker for the diagnosis of breast and urothelial carcinomas. When working on a tumor of unknown origin, GATA3 should be routinely included in the initial screening panel if either a breast or urothelial primary tumor is suspected. A more recent study at Geisinger IHC demonstrated approximately 70% of ER-negative breast carcinomas were also positive for GATA3.

#### References:
GATA3 expression for the diagnosis of breast and urothelial carcinomas.

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Geisinger IHC Panel Updates

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- Geisinger IHC Antibody & Panel Updates
- Summary of Select Abstracts from 2013 USCAP Meeting
- TMAs as External Positive Controls