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## Updated B-Cell Lymphoma IHC Markers and Panel

Contributed by Dr. Xiaohong (Mary) Zhang

Over the last few decades, a panel of IHC markers such as CD3, CD5, CD10, CD20, CD23, Bcl-1, Bcl-2, and Bcl-6 has proven to be useful and effective in the majority of cases when working on a mature B-cell lymphocytic neoplasm. With advances in molecular biology and biomarker discovery, many additional markers have been reported in the literature. A group of relatively sensitive and specific biomarkers has been identified for various types of lymphomas: 1) human germinal center-associated lymphoma (HGAL)/GCET2, LIM-only transcription factor 2 (LMO2) and stathmin for follicular lymphoma; 2) lymphoid enhancer-binding factor-1 (LEF-1), CD200 and membranous CD160 were present in virtually all neoplastic cells of B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL); 3) SOX11 expression was found in almost all cases of mantle cell lymphoma (MCL), including both cyclin D1-positive and cyclin D1-negative types, as well as cyclin D1-negative blastoid MCL; and 4) immunoglobulin superfamily receptor translocation-associated 1 (IRTA1) was expressed on the surface and cytoplasm of neoplastic cells of extranodal and nodal marginal zone lymphomas (MZLs) and some CLLs/SLLs and MCLs. The utility of these new markers is summarized in the following table. A detailed review and discussion of these new markers will be published in the *Archives of Pathology and Laboratory Medicine* in an article by X. Zhang and N. Aguilera.

### New IHC Markers for Small B-Lymphocytic Neoplasms

	CLL/SLL	MCL	FL	MZL	LPL/WM
<b>LEF-1</b>	+	-	-	-	-
<b>CD160</b>	+	-*	-	-	-
<b>CD200</b>	+	-	-	-	+
<b>SOX11</b>	-	+	-	-	-
<b>HGAL</b>	-	-	+	-	-
<b>LMO2</b>	-	-	+	-	-
<b>Stathmin</b>	-	+	+	-	-
<b>GCET1</b>	-	-	+	-	-
<b>IRTA1</b>	+	+	-*	+	-

**Note:** +: positive in majority of cases; -: negative in majority of cases; \*: small percentage of cases positive. CLL/SLL – chronic lymphocytic leukemia/small lymphocytic lymphoma; FL – follicular lymphoma; LPL/WM – lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia; MCL – mantle cell lymphoma; MZL – marginal zone lymphoma

### Reference:

Zhang X, Aguilera N. New immunohistochemistry for B-cell lymphoma and Hodgkin lymphoma – review article. *Arch Pathol Lab Med.* 2014; in press.

# FISH Testing at Geisinger Medical Laboratories (GML)

Contributed by Dr. Hong Yin, Michele Zelonis and Dana Snyder

GML has recently expanded its FISH test menu with a focus on solid tumors. These tests include HER2 for breast carcinoma and esophageal/gastric adenocarcinoma, ALK for lung adenocarcinoma, MDM2 for well-differentiated liposarcoma, and UroVysion for urothelial carcinoma. FISH probes for EWSR1, SYT, and 1p19q are currently undergoing validation and will be available in the near future.

## ALK

The discovery of the biologic and therapeutic importance of ALK and EGFR has changed the way non-small cell lung carcinomas (NSCLCs) are diagnosed and treated. The FDA has approved crizotinib, an ALK inhibitor, for patients with locally advanced or metastatic NSCLC who have the ALK gene rearrangement. Response rate to the drug has been shown to be 57%, with 72% progression-free survival at 6 months. ALK FISH is recommended for patients with lung adenocarcinoma and mixed carcinoma with adenocarcinoma component.

## HER2

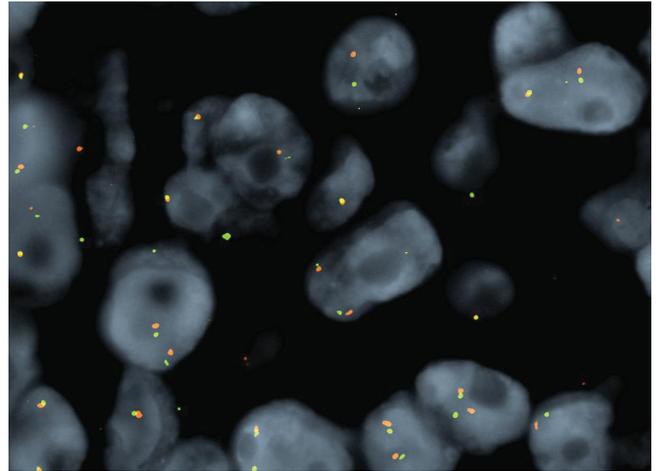
The new IQFISH from Dako, an FDA-approved test for breast and GI HER2, has reduced the overnight hybridization time to 3.5 hours. Confirmation by HER2 FISH is recommended for both breast carcinoma and adenocarcinoma from the stomach or gastroesophageal junction with 2+ HER2 by IHC. Currently, in our institution, all esophageal/gastric adenocarcinomas are tested for HER2 overexpression/amplification by both IHC and FISH.

## MDM2

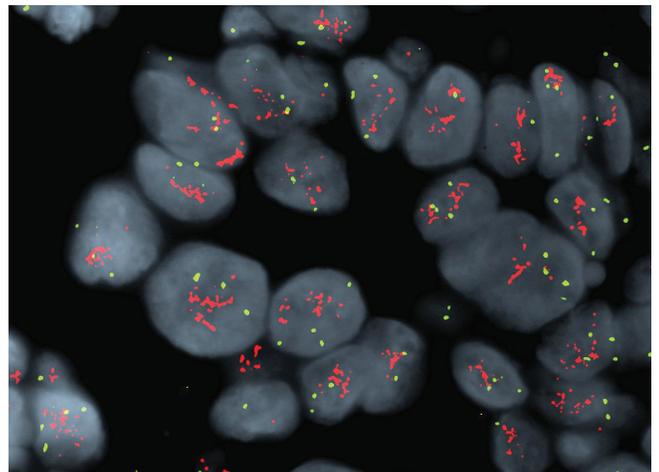
MDM2 amplification by FISH is a more sensitive and specific method than IHC for detecting well-differentiated liposarcomas/atypical lipomatous tumors.

## UroVysion

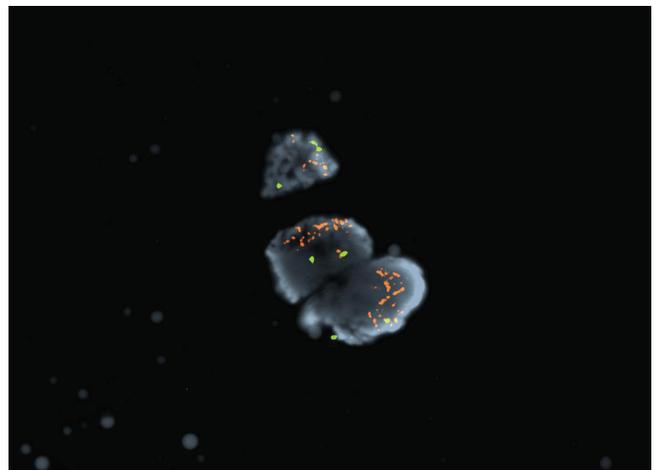
Urothelial carcinoma of the bladder is the second most common urothelial malignancy. The use of molecular markers has facilitated the development of novel and more accurate diagnostic, prognostic and therapeutic strategies. UroVysion is an FDA-approved test for monitoring the recurrence of bladder cancer.



ALK positive in lung adenocarcinoma



Amplified Gastric IQFISH HER2 FISH



Amplified MDM2 in a well-differentiated liposarcoma

## Select Abstracts from the USCAP 2014 meeting (Part II)

1. The value of **SATB2** immunostaining in the distinction between small intestinal and colorectal adenocarcinoma was studied by Kim CJ et al. at UCLA (**Abstract #749**). 54 cases of primary non-ampullary small intestinal adenocarcinoma (SIA) were compared with 35 cases of primary colorectal carcinoma (CRC). In SIA, 43% (23 of 54) of cases showed SATB2 expression; however, only 17% (4 of 54) showed a strong and diffuse staining pattern. In contrast, 94% (33 of 35;  $p < 0.001$ ) of CRCs showed SATB2 expression, with 82% (27 of 35;  $p < 0.001$ ) demonstrating a strong and diffuse staining pattern. The authors concluded that while SATB2 is not entirely CRC-specific, lack of SATB2 expression strongly suggests a small intestinal primary when the distinction from CRC is necessary.
2. Kermanshahi TR et al. at UPMC (**Abstract #811**) studied **LEF-1**, a DNA-binding protein that interacts with  $\beta$ -catenin and activates Wnt-responsive target genes in carcinogenesis, in 602 gastrointestinal tract tumors. LEF-1 nuclear staining was found in 37% (88/241) of colorectal adenocarcinomas (CRCs) while less than 10% of tumors from other parts of the GI tract showed weak focal staining. LEF-1-positive CRCs more frequently demonstrated KRAS mutation than LEF-1-negative CRCs (39% vs. 16%,  $p = 0.005$ ). They concluded that LEF-1 may be useful in distinguishing CRC from upper GI and pancreatic adenocarcinoma.
3. **GATA3** is expressed in vulvar Paget's disease (**Abstracts #1296 and #1174**). The authors studied GATA3 expression in 24 cases of vulvar Paget's disease (PD). Positive staining was seen in all cases. GATA3 stained more tumor cells than GCDFP15 in the majority of cases. GATA3 staining was generally retained in the invasive component associated with vulvar PDs. They concluded that GATA3 is a sensitive marker for vulvar PD.
4. Loss of **PAX2** nuclear expression is a useful diagnostic feature for in situ and invasive endocervical adenocarcinoma (**Abstract #1150**). The authors studied PAX2 expression in 60 endocervical adenocarcinomas, 128 endometrial adenocarcinomas and 41 ovarian serous carcinomas. A complete loss of PAX2 nuclear staining was observed in 100% of endocervical carcinomas in situ (16/16) and 95% of invasive endocervical adenocarcinomas (42/44), including 5 cases that were negative for p16, 3 minimal deviation adenocarcinomas and 3 gastric-type adenocarcinomas. The 2 cases of endocervical adenocarcinoma that retained strong PAX2 expression were high-grade carcinomas with clear cell morphology. In contrast, PAX2 loss was seen in 45% of endometrial adenocarcinomas and 42% of ovarian serous carcinomas, respectively. They concluded that loss of PAX2 expression is a very useful diagnostic feature of malignant endocervical glandular lesions. It is also potentially useful in differentiating endocervical adenocarcinoma from endometrial adenocarcinoma.
5. Zakaria Grada et al. (**Abstract #955**) reported that normal adult kidney tissues were negative for **cadherin 17** (CDH17) staining. In the metanephric adenoma (MA) group, CDH17 expression was seen in a membranous staining pattern with lateral intercellular border accentuation. CDH17 immunoreactivity was observed in all components of MA (acinar, tubular, and papillary). The majority of MAs (78%) demonstrated CDH17 immunoreactivity, while all cases of epithelial-predominant Wilms tumor (e-WT) and solid variant of papillary renal cell carcinoma (s-PRCC) were negative ( $p < 0.0001$ ). Ten of 14 (71%) positive MAs exhibited moderate to strong (2-3+) CDH17 expression. All MAs were strongly positive (3+) for CD57; however, this marker was moderately to strongly positive (2-3+) in 6 (35%) e-WTs and 2 (13%) s-PRCCs. AMACR was strongly (3+) positive in all s-PRCCs, although moderate reactivity was seen in 3 (17%) e-WTs and 1 MA (6%). WT-1 was negative in s-PRCC and was positive in all cases of e-WT and MA. CDH17 is a sensitive (78%) and highly specific (100%) marker for MA and should be considered in the IHC panel for distinguishing MA from its mimics.

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## GEISINGER IHC

### NEWS

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