PhenoPath is proud of our outstanding FISH laboratory, offering the highest quality solid tumor and hematopathology diagnostic services. With almost two decades of experience and a highly trained and knowledgeable staff, under the direction of Dr. Harry Hwang, our laboratory provides reliable, reproducible, and rapid results to our pathology and oncology colleagues and clients nationwide.

PhenoPath offers a technical FISH service (vFISH®) that enables our customers to expand their local professional services to include advanced molecular FISH test interpretation without the expense and difficulty associated with the technical process. The service includes user-friendly analytic software that facilitates the evaluation, counting, interpretation and quality control of the FISH images. vFISH® is best described as a four-step workflow process that integrates the customers’ professional review activity with PhenoPath’s technical preparation process:

**Step 1: SELECTION** The client selects the area of cancer to be analyzed on an H&E slide (slide dotting) and submits the slide and FFPE block; for fresh tissue, no selection is needed.

**Step 2: TESTING** PhenoPath processes the case and and applies fluorescently labeled DNA probes.

**Step 3: IMAGING** PhenoPath technologists and scientists scan the probed slides, adjust the images to ensure optimal image quality, and perform counts, using a Metasystems image analysis platform.

**Step 4: ANALYSIS** The client utilizes web-delivered software and images to perform analysis and generate a final report. Manual and software-generated counts are provided for comparison to client analysis, ensuring optimal correlation.

The service is designed with regulatory compliance in mind and enables the evaluating pathologist to conduct a complete professional review and interpretation of the case. Specifically, unlike other tech-only FISH services where image data review may be limited to static images, the PhenoPath vFISH® service allows the client pathologist to perform multi-channel color image analysis on their computer (i.e., their professional component).

PhenoPath provides peer-to-peer training, reference materials and a set of training cases to support our clients’ professional service launch preparation. If you would like more information about our vFISH® service, including tests available in FFPE vs. fresh tissue, please contact your sales executive or inquire with any of our pathologists (888.927.4366).

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**vFISH® – Meet your technical and scientific team**

**Shawna Pyott, PhD, FACMG**
Clinical vFISH® Supervisor
Associate Director of Clinical Cytogenetics

Dr. Pyott has extensive experience in clinical FISH from her pre- and post-doctoral career, particularly during her fellowship training in both molecular and clinical genetics. As PhenoPath’s Clinical vFISH® Technical Supervisor, she reviews PhenoPath’s data and images for quality assurance, and assists the team when questions arise.

**April Carr, BA, BS**
Clinical Laboratory Technician, FISH

April has over a decade of clinical FISH laboratory experience and works behind the scenes, setting up the FISH run, probing and DAPI staining the FISH slides, and preparing the vFISH® cases for analysis.

**Stephanie Rodriguez, MB (ASCP), HTL (ASCP), QIHC**
Molecular Supervisor, FISH

Stephanie and Ashlie scan and analyze all vFISH® cases. They review the client H&E, noting the area of tumor the client has circled, and take images of that area on the fluorescent microscope. They perform both manual and automated analyses and data acquisition, prepare the case for remote review by the client, and, following QA review, release the data in our signed documentation.

**Ashlie Cindric, MT (ASCP)**
Molecular Technologist, FISH & Cytogenetics

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PhenoPath's highly trained and knowledgeable team is key to PhenoPath’s quality FISH services. Our team continually evaluates PhenoPath's assay performance and meets regularly with PhenoPath pathologists to ensure the highest quality FISH service. The vFISH® team is actively involved in updating our FISH probe menu, to provide new FISH tests and to improve our current offerings (e.g., P53, IGH, etc.). We are also adding new probes to our test menu (next on the horizon is a panel of probes for use in melanoma).

NEW PUBLICATIONS BY PHENOPATH PATHOLOGISTS

Evaluation of contemporary prostate and urothelial lineage biomarkers in a consecutive cohort of poorly differentiated bladder neck carcinomas.


In a study performed in conjunction with Dr. Mahul Amin and colleagues at Cedars-Sinai Medical Center in Los Angeles, a number of new markers for both prostate and urothelial carcinomas were tested in the setting of poorly differentiated carcinomas presenting in the bladder neck. New bladder carcinoma markers such as GATA-3 and S100P were compared with older markers such as keratins 7 and 20 and p63; new prostate adenocarcinoma markers including NKK3.1, PS01S, and prostate-specific membrane antigen (PSMA) were compared with older markers such as PSA. In this study we found that the novel IHC markers (e.g., GATA-3 for poorly differentiated bladder carcinoma and NKK3.1 for poorly differentiated prostatic adenocarcinoma) outperformed the older markers. GATA-3 and NKK3.1 demonstrated respective sensitivities and specificities approaching 100% in this cohort of 36 cases, making it possible to be even more parsimonious in selecting IHC markers in this clinicopathologic setting.

The lung-restricted marker napsin A is highly expressed in clear cell carcinomas of the ovary.

Kandalaft PL, Gown AM, Isacson C. AJCP 142(6):830-6, 2014

The accurate diagnosis of clear cell ovarian cancer is critical, given the relative resistance of these tumors to conventional chemotherapy regimens as well as their association with Lynch syndrome. However, the morphologic spectrum of clear cell carcinomas can overlap with other ovarian carcinomas, including endometrioid and serous carcinomas. Napsin A, a member of the aspartic proteinase family, has been previously demonstrated to be an important lung adenocarcinoma marker, complementing TTF-1 in this regard. In a study performed at PhenoPath (in conjunction with Dr. Christina Isacson at CellNetix Laboratories), we demonstrated an additional application of this IHC marker: the identification of clear cell carcinomas of the ovary. Looking at a series of 123 ovarian carcinomas, we found that 100% of the 36 clear cell carcinomas were napsin A-positive; all of the serous carcinomas proved negative. However, 10% of endometrioid carcinomas did show focal napsin A expression. Napsin A thus joins PAX-8, WT-1, and estrogen receptor (ER) as markers that can help identify and subclassify ovarian carcinomas. Interestingly, these results also demonstrate immunophenotypic overlap between ovarian and renal clear cell carcinomas, as both are napsin A as well as PAX-8 positive, but negative for expression of ER and WT-1.
**ROS1**

The ROS1 oncogene encodes an orphan receptor tyrosine kinase related to anaplastic lymphoma kinase (ALK). Chromosomal rearrangements of the ROS1 gene, that include the tyrosine kinase domain with any one of 12 different partner genes, have been documented in a number of tumors, including non-small cell lung cancer (NSCLC). These translocations result in constitutive activation of ROS1 and can drive the malignant phenotype. ROS1 gene translocations occur in approximately 1% of NSCLC, more commonly in the setting of patients who have never smoked, and whose tumors are adenocarcinomas. ROS1 translocations almost always occur in the setting of tumors negative for EGFR mutations or ALK translocations. While fluorescence in situ hybridization (FISH) has been the standard method of assessment of alternations in the ROS1 gene, more recently immunohistochemistry (IHC) using antibodies to the ROS1 gene product has demonstrated comparable sensitivity and specificity. As demonstrated in a paper published in NEJM, patients with ROS1-rearranged advanced NSCLC showed a 72% response rate to crizotinib (the same tyrosine kinase inhibitor that has successfully been employed in patients with lung cancers harboring a translocation involving ALK).


**SOX10**

SOX10 is a nuclear transcription factor crucial in the differentiation of normal neural crest cells, and in the maintenance of Schwann cells and melanocytes. In normal tissues, SOX10 expression is almost completely restricted to Schwann cells, melanocytes, oligodendrocytes, mast cells, myoepithelial cells of the bronchial glands and breast, and acinar and intercalated duct cells of salivary glands. In the malignant setting, SOX10 has been demonstrated to be a highly sensitive and relatively specific marker of Schwann cell tumors and melanomas. In the identification of melanoma, it has the advantage over more traditional markers such as MART1 and HMB45 in also identifying spindle cell or desmoplastic melanomas with high sensitivity. However, SOX10 expression will not distinguish between spindle cell melanoma and peripheral nerve sheath tumors, as it is uniformly expressed in the latter. Other SOX10 positive tumors include granular cell tumors and a subset of salivary gland tumors; amongst the latter, SOX10 expression is characteristic of pleomorphic adenoma and acinic cell, adenoid cystic, and myoepithelial carcinomas, but not salivary duct, mucoepidermoid, or oncocytic carcinomas. In the skin, SOX10 is useful in identifying desmoplastic melanoma, distinguishing it from other dermal spindle cell tumors such as atypical fibroxanthoma, spindle cell carcinoma, and most sarcomas.


**CDH17**

CDH17, also known as LI-cadherin, is a calcium dependent, cell adhesion molecule that plays a role in homotypic and heterotypic cell adhesion. CDH17 is expressed, in normal tissues, almost exclusively in the small and large intestinal epithelium. Recent studies have suggested a role for antibodies to CDH17 as a useful tool for the identification of the primary site of carcinomas presenting at a metastatic site. In the malignant setting, CDH17 is expressed almost exclusively by adenocarcinomas primary to the upper as well as lower GI tract, including esophagus, colon, pancreas, and bile duct. It would appear to complement older GI tract-restricted markers such as CDX-2 and villin. However, in the large study by Panarelli and colleagues, CDH17 proved to be more sensitive than CDX-2 in the identification of adenocarcinomas of the esophagus, stomach, pancreas, and bile duct. CDH17, like CDX-2, is expressed in a very small subset of adenocarcinomas arising outside the GI tract, such as lung and endometrial adenocarcinomas. Unlike CDX-2, however, CDH17 does not appear to be expressed by mucinous ovarian carcinomas.

FEATURED
At the Next PhenoPath Conference
Steven H. Swerdlow, MD
University of Pittsburgh Medical Center

PhenoPath, Thursday, February 5, 2015, 7:00 PM

Steven H. Swerdlow, MD will present “Great expectations? Updating the WHO lymphoma classification” at the PhenoPath Conference at 7:00 pm on Thursday, February 5, 2015. Dr. Swerdlow will also give a daytime lecture, “Extra-aggressive B-cell lymphomas and the double edge sword” at noon the same day.

Dr. Swerdlow is an internationally recognized hematopathologist. A graduate of Brandeis University and Harvard Medical School, he is currently a Professor of Pathology and Director of the Division of Hematopathology at the University of Pittsburgh School of Medicine. He is a sought-after speaker having provided lectures/courses for all of the major American pathology organizations as well as for many other societies and institutions around the world.

Dr. Swerdlow is a past President of the Society for Hematopathology, former member of the Executive Committee for the European Association for Haematopathology, former Council member of the US Canadian Academy of Pathology, and currently a trustee of the American Board of Pathology. He is an invited member of the International Lymphoma Study Group, Lymphoma Research Foundation Mantle Cell Lymphoma Consortium, and a splenic lymphoma study group.

The author of more than 180 publications, 51 book chapters and author/editor of two books as well as lead editor of the 2008 edition of the WHO Bluebook on Tumours of Haematopoietic and Lymphoid Tissues, Dr. Swerdlow has concentrated on multiparameter investigations of non-Hodgkin lymphomas and the post-transplant lymphoproliferative disorders and was an active participant in the creation of the 2005 WHO-EORTC consensus classification for cutaneous lymphomas.