The most common pediatric malignancy in sub-Saharan Africa is endemic Burkitt lymphoma (eBL), a form of non-Hodgkin lymphoma that is the fastest growing of all human tumors. In African children, the risk of eBL is associated with early exposure to the Epstein-Barr virus, the same virus that causes mononucleosis. eBL risk is also correlated with the incidence of malaria, leading some experts to believe that chronic malarial infection may predispose children to develop eBL. Although rapidly fatal if untreated, eBL is often curable with relatively short-term, inexpensive chemotherapy if diagnosed before the disease overwhelms the patient.

The Seattle-based Burkitt’s Lymphoma Fund for Africa or BLFA (originally Burkitt’s Lymphoma Kenya Fund), founded by Miriam Sevy in April 2010, is an all-volunteer nonprofit organization that has raised hundreds of thousands of dollars to help treat African eBL patients, often for less than $500 per patient. The BLFA’s effectiveness has been enhanced by partnerships with several nonprofit organizations, both within the United States and in the African locations of Kisumu, Kenya, Kampala, Uganda, and Shirati, Tanzania. Hundreds of young lives have been saved by the BLFA’s efforts, but because of delays in establishing the diagnosis in many parts of Africa, children continue to succumb to the disease before therapy can be initiated. Therefore, improving the accuracy and speed of eBL diagnosis is a key near-term BLFA priority.

PhenoPath’s Associate Medical Director and Director of Hematopathology, Dr. Steve Kussick, has been involved with the BLFA for about four years. Over the last year, he helped launch the BLFA Medical Advisory Committee composed of both African and American medical and public health professionals, with the major goals of expediting eBL diagnosis in Africa and optimizing treatment regimens for BLFA patients. In September 2013, Dr. Kussick travelled to Uganda and Kenya to observe BLFA’s operations, and to lay the groundwork for expediting the pathologic diagnosis of eBL.

After this enlightening trip, Dr. Kussick and Miriam Sevy created the BLFA Pathology Project to implement their plan to improve eBL diagnosis in Africa by taking advantage of the speed and accuracy of flow cytometry. Dr. Kussick’s vision is to set up flow cytometry laboratories in Kisuma and Kampala, in cooperation with our local partner organizations at these two sites. Because flow cytometry uses freshly obtained tissue and can be accomplished within hours of a biopsy, and because the flow findings can be reviewed remotely in real time over the internet along with microscopic images of the cells being evaluated, this testing method will allow Dr. Kussick and other hematopathologist volunteers to render diagnoses within hours, rather than days or weeks, of an eBL patient coming to medical attention. Of course, the ultimate goal is to train African physicians at these sites to interpret the flow data and render their own diagnoses. As Dr. Kussick notes “Because of how curable eBL is if the appropriate diagnosis is made in a timely manner, the BLFA Pathology Project represents a wonderful opportunity for our hematopathology community to help save lives among the unfortunate children stricken with this aggressive cancer.”

PhenoPath has been a proud supporter of BLFA and encourages you to learn more at the BLFA website: blfundafrika.org. Note that a major fundraiser for the BLFA Pathology Project is planned for June 8, 2014; please see the BLFA website for details.
Hereditary non-polyposis colorectal carcinoma (HNPCC), also known as Lynch Syndrome, is an autosomal dominant hereditary cancer syndrome associated with germline mutations in one of the mismatch repair (MMR) genes (MLH1, MSH2, MSH6, and PMS2). As a consequence of these mutations, tumors from individuals with HNPCC/Lynch syndrome exhibit a phenomenon known as microsatellite instability (MSI). In addition, between 10 and 15 percent of sporadic colonic adenocarcinomas appear to display MSI, albeit via a different mechanism (e.g., CpG island methylation).

Microsatellites are repetitive sequences distributed throughout the genome that consist of single/multiple nucleotide repeats that are often copied incorrectly by DNA polymerase. In tumors with mismatch repair defects, these expansions or contractions in the number of nucleotide repeats are not repaired, leading to the phenomenon of MSI. PCR is used to amplify specific microsatellite repeats within the genome, and the number/length of the nucleotide repeats is compared in tumor cells versus normal cells. If the length of the repeat sequences from tumor versus normal differs, MSI is present.

This PCR-based testing complements the immunohistochemistry-based assay also available at PhenoPath, in which the loss of one or more of the MMR proteins can be determined. While the IHC-based method detects loss of MMR protein expression, the PCR-based assay detects the end result of MMR dysfunction – MSI. While IHC can detect approximately >90% of the tumors with a defective MMR system, IHC may miss tumors containing mutations that produce a defective protein that is still expressed (i.e., missense mutations). Our new MSI PCR assay provides an additional tool to help clinicians and pathologists evaluate for HNPCC/Lynch Syndrome and the presence of MSI-type sporadic colorectal adenocarcinomas. Evaluation for MSI may also be useful in clinical decision-making, as sporadic colon cancers with MSI have a better prognosis compared to those with intact MMR systems, and appear to respond differently to adjuvant chemotherapy.

PhenoPath now offers testing to evaluate FUS (16p11) translocations. The FUS gene (Fused in Sarcoma) is a member of the TET family of proteins that also includes Ewing sarcoma (EWS). It is a multifunctional protein involved in both transcriptional activation and RNA binding. Rearrangements involving the FUS gene have been described in low-grade fibromyxoid sarcoma (LGFM), which result in the t(11;16) or t(7;16), as well as myxoid/round cell liposarcoma (MLS), resulting in a t(12;16). The detection of such FUS gene rearrangements by FISH can aid in the diagnosis of these entities. This FISH assay uses a sensitive breakapart probe that when positive typically shows a “broken” or separated red and green signal with a fused signal in affected cells, as shown in the left image.

References:
World Health Organization Classification of tumors: Pathology and Genetics of Tumors of Soft Tissue and Bone. IARC 2002 Fletcher et al., p. 42

PhenoPath has released two new disease brochures, “Breast” and “Lung”, highlighting best practices and current recommendations for pathology testing in these settings. To receive your copy, email lab@phenopath.com.
The expression of CD14 by IHC is a useful biomarker for distinguishing neoplasms of monocytic and Langerhans cell origin from other hematolymphoid neoplasms. CD14 is a glycoprotein expressed on mature monocytes, histiocytes/macrophages, Langerhans cells, and to a lesser degree on neutrophils and is a receptor for bacterial lipopolysaccharide (LPS), thus functioning as an opsonic receptor to facilitate phagocytic uptake. Evaluation of CD14 expression, in correlation with other appropriate immunohistochemical studies, may prove useful in the diagnosis of acute myeloid leukemia (AML) with monocytic or myelomonocytic differentiation, Langerhans cell histiocytosis (LCH), Langerhans cell sarcoma (LCS), chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia (JMML), myeloid sarcoma with monocytic differentiation, and histiocytic sarcoma. CD14 exhibits a membranous and cytoplasmic subcellular localization pattern.

CD38 is a 46 kDa type II transmembrane glycoprotein with a short N-terminal cytoplasmic tail (20 amino acids) and a long extracellular domain (256 amino acids). It has enzymatic activity as a cyclic ADP ribose hydrolase, which contributes to the regulation of intracellular calcium. The ligand of CD38 is CD31. CD38 is expressed by a variety of leukocytes, including plasma cells (which show the highest levels of expression), immature and mature B and T cells, NK cells, monocytes, macrophages, and myeloid progenitors. In mature B cells, CD38 expression is induced when B cells enter the germinal center, then decreases in post-germinal center memory B cells, and reaches its maximum levels as B cells terminally differentiate to plasma cells. In HIV, increased T cell CD38 expression is associated with disease progression. CD38 expression has been described in non-hematopoietic tissues. When one needs to identify plasma cells at a mucosal site, CD38 is preferable to CD138 as a plasma cell marker, since CD138 is frequently expressed on adjacent epithelial cells.

Receptionists typically operate the front desk of a business. They answer phones, greet clients, provide directions or information, and organize files. To excel as a receptionist, you need the right combination of personal traits and professional skills. In a service business such as PhenoPath, a great receptionist is invaluable and must quickly determine the needs of individual prospects or clients and then ensure those needs are met as efficiently and courteously as possible. PhenoPath is fortunate to have not only one but TWO top-notch individuals that meet the above qualifications.

Roberta is PhenoPath’s main Receptionist; she has been with PhenoPath since July of 2012. Some of the client comments we have received about Roberta range from ‘WOW – what a wonderful voice that woman Roberta has – she should consider going into talk radio’, to ‘Roberta is always so cheerful and a delight to speak with’, and ‘Roberta is always so professional and helpful when we call in.’

Heather has been with PhenoPath since January of 2012, and divides her time between backing up Roberta at the front desk and supporting the Finance department. Some of the comments we have heard about Heather range from ‘Heather is always very helpful and friendly’, to ‘Heather is very kind and such a help when I am trying to hunt down answers for our clients’. Heather is a people pleaser and nothing makes her happier than being able to make someone else’s day.

A Receptionist is the public face of a business and often the first person a customer or client sees or the first voice they hear over the phone. PhenoPath is truly fortunate to have these two wonderful ladies representing the face of PhenoPath.
FEATURING
At Our Spring Quarterly Conference
David J. Grignon, MD
Indiana University, Indianapolis, IN
PhenoPath Laboratories, May 15, 2014, 6:30 PM (light dinner), 7:30 PM (talk)

David John Grignon, MD will present “What is New and Clinically Relevant in the Pathology of Bladder Cancer” at the PhenoPath Spring Conference at 7:30pm on Thursday, May 15, 2014. Dr. Grignon will also give a daytime lecture, “The 2012 ISUP Vancouver Classification of RCC,” at noon the same day.

Dr. David Grignon is Centennial Professor and Vice Chair for Clinical Programs in the Department of Pathology and Laboratory Medicine at Indiana University. Prior to joining the faculty at Indiana University in 2007, Dr. Grignon had served as the Director of Anatomic Pathology at Harper-University Hospital (1996-1999) and Chairman of the Department of Pathology at Wayne State University in Detroit, MI (1999-2007). He obtained his MD degree and completed training in Anatomic Pathology at the University of Western Ontario in London, Canada followed by a 2 year Fellowship in Surgical Pathology and Genitourinary Pathology at the MD Anderson Cancer Center in Houston, TX.

Dr. Grignon is recognized nationally and internationally for his expertise in the area of urologic pathology. He has published over 350 research/review articles and 27 book chapters. He is an author or editor of 5 books including the 4th Series AFIP fascicle on Tumors of the Kidney, Bladder, and Related Urinary Structures, a monograph on Gleason Grading of Prostate Cancer and the just released text, Urological Pathology. A major focus of Dr. Grignon’s career has been education and he has presented over 300 invited lectures and courses in more than 30 countries. He has directed numerous courses for all the major organizations in pathology and currently directs the annual 4-day special course in urologic pathology sponsored by the ASCP.