The Starr Cancer Consortium was established in 2006 through a generous gift from The Starr Foundation to advance research in novel ways that will have a profound impact on the understanding, diagnosis, prevention and treatment of cancer. The Starr Cancer Consortium is a collaborative effort involving five institutions: The Broad Institute of MIT and Harvard, Cold Spring Harbor Laboratory, Memorial Sloan-Kettering Cancer Center, Rockefeller University and Weill Cornell Medical College. The Starr Cancer Consortium is primarily intended to support critical mass, collaborative projects which have the potential for a transformative impact on the understanding and treatment of cancer, through the development and systematic application of molecular technologies, by investigating cancer biology or addressing important clinical problems. It is aimed at encouraging meaningful and ambitious collaborations between and among the five participating institutions to develop and apply innovative approaches to transform cancer research and ultimately diagnostic and therapeutic strategies. The Executive Committee is comprised of two scientific leaders from each of the five institutions. These are: Drs. Eric Lander, Todd Golul, Bruce Stillman, Scott Lowe, Harold Varmus, Thomas Kelly, Paul Nurse, Titia de Lange, Antonio Gotto and David Hajjar.

The goals of the Starr Cancer Consortium are: 1) to drive the development of technology from molecular characterization of cancer by forging productive alliances among scientists at the five participating institutions; 2) to apply these new technologies in joint projects directed at diverse cancers, in the process gaining a deeper understanding of the molecular basis of these cancers and defining new paradigms for cancer research, diagnosis and treatment; and 3) to accelerate research concerning the basic biological mechanisms underlying the development of various cancers. A large number of investigators working at these institutions have applied for funding through the Starr Cancer Consortium. However, as in the case of NIH and other extramural funding agencies, only the very best proposals, which offer the possibility of a transformative impact on our understanding, or an improvement in the diagnosis and treatment of cancer are funded. The Weill Cornell Department of Pathology and Laboratory Medicine has been extraordinarily successful in acquiring funding through the Starr Cancer Consortium. Four scientists have received a total of five $1M grant awards. These are: Drs. Ethel Cesarman, Selina Chen-Kiang, Mark A. Rubin and Pengbo Zhou. A brief summary of each scientific program that received funding, and a short biography of each principal investigator follows.

Tumor Development and Treatment of EBV-associated Lymphomas in Immune Competent Humanized Mice

Principal Investigator: Ethel Cesarman, MD, PhD, Weill Cornell Medical College
Co-Principal Investigators: Derek S. Tan, PhD, Memorial Sloan-Kettering Cancer Center
Total Direct Costs for Two Years $1,000,000.

There are currently no pharmacological treatments that are specific for the transforming EBV latency program. Dr. Cesarman’s laboratory has identified EBV LMP1 as a promising viral therapeutic target, wherein disruption of the LMP1-TRAF2 interaction leads to inhibition of LMP1 signaling to NF-κB, resulting in apoptosis of EBV-infected (type II/III) lymphoma cells, which are those expressing continued on page 2.
LMP1. Some unique challenges intrinsic to this project include the identification of inhibitors of protein-protein interactions, the development of high throughput screening (HTS) assays for low-affinity interactions, and the lack of good mouse models to test agents when promising inhibitors are discovered.

Tumorigenesis and treatment of EBV-associated lymphomas in immune competent humanized mice will be studied through four aims: 1) Analyze the viral gene expression pattern and differentiation stages of in vivo EBV-infected B cells. Expression of the transformation-associated EBV latent antigens is tightly connected to the differentiation stage of the infected B cells in humans. They are interested in knowing if these infection programs also exist in their infected humanized mice, and if they can give rise to different types of EBV-associated lymphomas; 2) Characterize the components and development of the in vivo primed EBV specific immune control. Dendritic cells, natural killer cells and T cells have been implicated in EBV specific immune control, and will be analyzed during primary EBV infection in vivo; 3) Investigate the influence of co-infection with the oncogenic Kaposi’s sarcoma-associated herpes virus on B cell transformation by EBV and on EBV specific immune control in vivo. Primary effusion lymphoma is always associated with KSHV infection and often with co-infection by EBV. Therefore, changes in B cell transformation and immune control of EBV after co-infection with KSHV will be analyzed; and 4) Identify inhibitors of the main EBV oncogene product, latent membrane protein 1 (LMP1). LMP1 inhibitors. If promising compounds are identified, Drs. Cesarman and Tan will test them for efficacy against EBV-associated lymphomas in vivo. Beyond oncogenic herpesvirus infections, this model should prove useful in studying pharmacological and immunological treatments of human tumors in vivo.

Pathogen Discovery in AIDS-Related Lymphoma by Next Generation Sequencing

Principal Investigator: Matthew Meyerson, MD, Broad Institute
Co-Principal Investigator: Ethel Cesarman, MD, PhD, Weill Cornell Medical College
Total Direct Costs for Two Years $1,000,000

A variety of oncogenic viruses have been found in human cancers, including Epstein-Barr virus (EBV), Kaposi’s sarcoma herpesvirus (KSHV) and human papillomavirus (HPV). The incidence of malignancies caused by these viruses is greatly increased in AIDS patients, where the most common cancer is Kaposi’s sarcoma (caused by KSHV), followed by malignant lymphoma and cervical carcinoma (caused by HPV). Among the AIDS-related lymphomas, approximately 30% contain EBV, and 4% contain KSHV. This leaves a large fraction of AIDS-related lymphomas that are potentially associated with an unknown infectious agent. The goal of this project is to discover novel viruses associated with HIV-related lymphomas of unknown origin, using next-generation sequencing approaches. Drs. Cesarman and Meyerson will apply the approach of sequence-based computational subtraction to evaluate the presence of novel sequences in AIDS-related lymphomas. They will generate cDNA libraries from mRNA from frozen AIDS-related lymphoma tissue and perform next-generation sequencing using the Illumina platform. They will subtract sequences that match the human genome and transcriptome, and test non-human sequences for their presence in larger AIDS-related lymphoma and control sample sets. They will then use any recurrent sequences to attempt to isolate whole genomes of candidate infectious agents. Even if no novel organisms are identified, the findings would be significant as this approach would suggest that a large proportion of AIDS-related lymphomas are not caused by conventional viruses. In contrast, identification of a novel infectious agent associated with cancer would have immediate pathogenetic, preventive, diagnostic and therapeutic significance.

Dr. Ethel Cesarman is collaborating with Dr. Meyerson at the Broad Institute on a project funded by the Starr Cancer Consortium to discover new pathogens in AIDS-related lymphomas using next-generation sequencing and computational subtraction, as shown on this schematic diagram.

In a project entitled “Tumor Development and Treatment of EBV-Associated Lymphomas in Immune Competent Humanized Mice” funded by the Starr Cancer Consortium, Dr. Cesarman is following up on her identification of the LMP-1 protein encoded by the Epstein Barr virus (EBV) as a therapeutic target for the treatment of EBV-associated malignancies. To develop and test new inhibitors, she is working together with her collaborators Dr. Hao Wu who has determined the structure of the interaction of EBV LMP1 with TRAF2 (shown in figure), Dr. Christian Münz (previously at Rockefeller University) who has developed a mouse model of EBV infection, and Dr. Derek Tan (at MSKCC), who has developed synthetic chemistry to make biased compound libraries with increased potential to disrupt protein-protein interactions.
Dysregulation of the cell cycle is central to tumorigenesis. Therefore, targeting the cell cycle in combination with cytotoxic killing would appear to be a rational approach to cancer therapy. Emerging evidence in human cancers further reinforces the critical importance of controlling cyclin-dependent kinase (CDK)4 and CDK6 in cancer treatment, but success with broad-spectrum CDK inhibitors has been modest because of lack of selectivity and high toxicity.

By inhibiting CDK4/CDK6 with the only known selective inhibitor, PD 0332991 (PD), Dr. Selina Chen-Kiang has developed a novel strategy to inhibit proliferation of tumor cells and prime them for cytotoxic killing in multiple myeloma, lymphoma and leukemia. Induction of G1 arrest by inhibition of CDK4/CDK6 leads to time-dependent uncoupling of gene expression from the cell cycle, and release of the G1 block allows for cytotoxic killing in multiple myeloma, lymphoma and leukemia. This demonstrated that cell cycle control of physiologic response and development is distinct, and helped to demonstrate that p18Ink4c also controls cell cycle re-entry during B cell activation and couples the cell cycle to apoptotic control in rapidly dividing and plastic plasma cell precursors.

Understanding cell cycle control of B cell immunity provided a unique intellectual framework for Dr. Chen-Kiang to investigate cell cycle dysregulation in multiple myeloma, for which she was awarded a Specialized Center of Research (SCOR) award from the Leukemia and Lymphoma Society in 2000. She assembled an interactive team of basic and clinical scientists within Weill Cornell to investigate cell cycle dysregulation in multiple myeloma in humans and animal models and to develop a mechanism-based strategy for therapeutic targeting of the cell cycle in multiple myeloma. Among their many exciting discoveries, Dr. Chen-Kiang’s team demonstrated that 1) one and only one cyclin D is expressed in each case of multiple myeloma; and 2) dysregulation of CDK4/CDK6, but any D cyclin alone, precedes loss of cell cycle control in multiple myeloma in humans. Using the only known CDK4/CDK6-specific inhibitor (PD 0332991), a small molecule that is also orally bioavailable, Dr. Chen-Kiang developed the first therapy to selectively target CDK4/CDK6 in combination with clinically relevant drugs. This strategy has been implemented in a Phase I/II clinical trial for multiple myeloma, which has shown promise, and in breast cancer as a front line treatment. This strategy will be applied to mantle cell lymphoma and acute myeloid leukemia as well.

The early detection of clinically significant prostate cancer is based largely on the blood test for prostate specific antigen (PSA). This screening test identifies cancer but also has many false positive results due to a myriad of benign conditions such as inflammation of the prostate gland. Prostate specific antigen screening currently requires performing biopsies on 100 men to detect 30 cancers. In addition to unnecessary clinical procedures, many of these cancers are not clinically significant. Therefore, the goal of Dr. Mark Rubin’s research proposal is to detect clinically significant prostate cancer by exploiting our new understanding of the human genome. Recently, variations in the number of segments of DNA, called copy number variations (CNVs) polymorphisms, have been reported as associated with common diseases such as Alzheimer’s disease and susceptibility to HIV infection. The current study will look for CNVs associated with prostate cancer risk with the hope of developing tests that can be used clinically to improve on specificity in diagnosing clinically significant prostate cancer. Dr. Rubin will use DNA from a well-defined PSA screening population. Dr. Rubin will interrogate these samples using the latest high-throughput genome scanning technology that will allow him to query all the appropriate known CNVs for associations with prostate cancer risk. Dr. Rubin expects to credential the findings in a confirmation stage on independent samples using a custom designed CNV array (BioTrove technology) that will allow for more efficient future validation. Successful completion of this project will impact the early detection of prostate cancer and our insight into why some individuals are at higher risk for developing aggressive disease.
Dr. Mark A. Rubin, Professor of Pathology and Laboratory Medicine with tenure at Weill Cornell Medical College joined the department in 2007.

The focus of Dr. Rubin’s research during the past decade has been the development of molecular biomarkers capable of distinguishing indolent from aggressive prostate cancer. He has contributed more than 180 peer-reviewed publications, predominantly in the area of prostate cancer, to the scientific literature. He holds multiple United States and international patents for molecular biomarkers. Some of his more significant work published in Nature and JAMA identified novel biomarkers including hepin, pim-1 kinase, ERG, MTA1 Jagged 1, EZH2 and alpha-methylacyl-CoA racemase.

His ability to develop a translational research team led to the landmark discovery identifying fusion of the TMPRSS2 and ETS families of transcription factors in prostate cancer. These translocations were discovered by applying a novel bioinformatics approach. These translocations are believed to be the most common translocations yet described in any solid tumor. The TMPRSS2-ETS gene fusion appears to be one of the earliest events involving prostate cancer invasion, leading to the over expression of the fused ETS gene in an androgen-regulated manner. Genprobe has licensed the rights to commercially develop urine and tissue based tests. Dr. Rubin’s Laboratory, working in close collaboration with investigators from Sweden and Dr. Todd Golub at the Broad Institute, have also recently developed a potential drug target for TMPRSS2-ETS fusion prostate cancer. These ongoing studies have the potential to influence the clinical care of the approximately 300,000 men diagnosed with prostate cancer each year in the United States.

Small Molecule Inhibitors of the Ubiquitin Pathway in Antagonizing Skin Carcinogenesis

The CUL4A ubiquitin ligase gene is frequently found amplified or overexpressed in a wide variety of tumor types, including breast and skin cancers. While recent studies have identified the components of the multi-meric CUL4A E3 ligase complex and several cellular targets, the role of CUL4A in tumorigenesis has remained largely elusive. Biochemical studies from Dr. Pengbo Zhou’s and other laboratories provided the initial insight into an inhibitory role for CUL4A in nucleotide excision repair. Dr. Zhou’s laboratory recently delineated the molecular mechanisms by which CUL4A antagonizes cellular response to UV-induced DNA damage through coordinated suppression of two major pathways: (1) CUL4A restricts the DNA repair capacity of normal cells through targeted degradation of DNA damage sensors DBD2 and XPC of the nucleotide excision repair apparatus; and (2) CUL4A limits the duration of G1/S DNA damage checkpoint through ubiquitin-mediated destruction of the p21 cyclin-dependent kinase inhibitor. Consistent with a negative role for CUL4A in the cellular response to DNA damage, Dr. Zhou’s laboratory generated a skin-specific CUL4A knockout mouse model and demonstrated that animals without CUL4A are hyper-resistant to UV-induced skin carcinogenesis. These studies led to the surprising conclusion that normal cells are not the most efficient in dealing with DNA lesions, as people had previously assumed. Instead, attenuation of CUL4A function allows further elevation of the threshold response to DNA damage and our ability to fight against malignancy.

Importantly, mice with germline deletion of CUL4A are healthy and display no developmental abnormalities, suggesting that CUL4A is an attractive target for cancer prevention. The primary objective of Dr. Zhou’s studies is to identify synthetic inhibitors of the CUL4A ubiquitin ligase through high-throughput screening of chemical libraries or phage display peptide libraries. The proposed studies integrate the biochemical, cell biological, and genetic approaches in the Zhou laboratory, the high-throughput screening expertise of the Li laboratory, and the availability of the state-of-the-art chemical and phage display libraries and HTS core facility at MSKCC and Rockefeller University to pursue the following two specific aims: (1) To develop and optimize an HTS assay for CUL4A-DDB1 interaction, with specific emphasis on interrogating their direct binding interface; and (2) To develop quantitative HTS assays to identify small molecules that disrupt DDB1-CUL4A interaction and ubiquitin ligase activity. Successful completion of the proposed studies would represent the first step towards evaluating the efficacy of pharmacological CUL4A inhibition as an effective approach for cancer prevention and intervention.

Dr. Pengbo Zhou is currently an Associate Professor of Pathology and Laboratory Medicine with tenure. He joined the faculty at Weill Cornell Medical College in November 1999.

During the past 10 years, Dr. Zhou’s laboratory has focused on deciphering the structure and functions of the Cullin 4A (CUL4A) ubiquitin ligase. Work from Dr. Zhou’s laboratory led to the initial identification of damaged DNA binding proteins and HOXA9 homeodomain protein as critical substrates of the CUL4A machinery. Using a combination of biochemical, cell, molecular and genetic approaches, Dr. Zhou’s laboratory revealed a critical role for CUL4A in suppressing DNA repair and DNA damage response, as well as controlling normal and malignant hematopoiesis, resulting in multiple publications in Molecular Cell, Cell, PNAS, EMBO Journal, and Cancer Research. Dr. Zhou has received many prestigious awards during the past decade, including the Kimmel Scholar from the Sidney Kimmel Foundation for Cancer Research, the Leukemia and Lymphoma Society Scholar, and the Irma T. Hirschl Career Scientist Award. He is a charter member of the NIH Study Section on Molecular Oncogenesis. His research programs have been funded by the NCI, the Starr Foundation, the Tri-institutional Stem Cell Initiative, the New York State Stem Cell Board (NYSTEM), the Leukemia and Lymphoma Society, the Irma T Hirschl Trust, the Sidney Kimmel Foundation for Cancer Research, the Mary Kay Ash Charitable Foundation, the AMDeC Foundation, the Dorothy Rodbell Cohen Foundation for Sarcoma Research, the Susan G. Komen Breast Cancer Foundation, and now the Starr Cancer Consortium.
Keynotes
by Domenick J. Falcone, PhD

Dr. Rebecca Baergen served on the Publications Committee of the Society for Pediatric Pathology at the Interim Meeting in the fall and at the USCAP in Boston. She was invited to become a member of the Editorial Board of Pediatric and Developmental Pathology. Dr. Baergen won an award at the Society for Pediatric Pathology meeting in Louisville, KY for her abstract on “Villitis and Clotting.” Dr. Baergen was appointed an Ambassador to the United States and Canadian Academy of Pathology. She presented three abstracts as posters at the Society for Maternal-Fetal Medicine in San Diego, CA and one abstract at the USCAP meeting in Boston. Dr. Baergen was recently interviewed by Roseanne Colletti from NBC news on the importance of placental examination.

Dr. Ethel Cesarman is serving on the Weill Cornell Medical College Committee of Review, the Cancer Center Internal Advisory Board and as the Pathology Representative and Vice Chair of the General Faculty Council. She is the Director of the Immunology Program Training Grant. Dr. Cesarman was an invited speaker for a seminar series in the Department of Microbiology and Immunology at the Uniformed Services University of the Health Sciences, F. Edward Hebert School of Medicine (Jan. 2009) and the Department of Molecular Genetics and Microbiology, Stony Brook University, NY (May 2009). She was an invited speaker at a symposium entitled “25 Years After Discovering HIV as the Cause of AIDS” which was held to honor Dr. Robert Gallo in Baltimore, MD (May 2009). In these presentations, Dr. Cesarman spoke about her work on the molecular mechanisms of lymphomagenesis caused by the Kaposi’s sarcoma herpesvirus KSHV and Epstein-Barr virus, and recent progress by her laboratory in this field, which includes development of animal models and approaches for therapeutic targeting. Internationally, she participated in a meeting organized by the Tata Memorial Hospital in Mumbai, India entitled “An update on Lymphoma Pathology” (Nov. 2008). She also served as a working group member for the International Agency for Research on Cancer (IARC) Monograph Working Vol. 100 on Biological Carcinogens, Lyon, France. She wrote chapters on HIV and KSHV, and participated in the discussion meeting held at the IARC on Feb. 2009. Three abstracts from Dr. Cesarman’s laboratory were presented orally at the 12th International Workshop on KSHV and Related Agents. Birmingham, UK, July 2008: Uththara Nayar gave a presentation entitled “Heightened redox status of primary effusion lymphoma cells can be exploited therapeutically by decreasing resistance to oxidative stress;” Gianna Ballon gave a presentation entitled “Generation of vFLIP transgenic mice: A model to study KSHV-associated lymphomagenesis;” and Dr. Cesarman presented on behalf of Daniel DiBartolo an abstract entitled “Heightened redox status of primary effusion lymphoma cells can be exploited therapeutically by decreasing resistance to oxidative stress. Dr. DiBartolo presented two posters at the International Herpesvirus Workshop in Estoril Portugal in July 2008. Gianna Ballon gave oral presentations at the American Society for Hematology as well as at the 11th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies meetings, entitled: “Generation of vFLIP transgenic mice: A model to study KSHV-associated lymphomagenesis.” Dr. Cesarman presented two additional abstracts at the Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies, entitled: “Early events of B-cell receptor signaling are not essential for the proliferation and viability of AIDS-related lymphoma” (first author is Pin Lu and co-last author is Lynn Wang) and “Immunophenotypic analysis of AIDS-related diffuse large B-cell lymphoma and clinical implications in patients from AIDS Malignancy Consortium clinical trials 010 and 034.”

Dr. Ruba Deeb presented a poster at the 2009 11th International Winter Eicosanoid Conference. The title of her presentation that won a meritorious scientific award was “Structural Evidence for the Selectivity of Tyrosine Nitration in Cyclooxygenase.”

Dr. Domenick J. Falcone was an invited speaker for a seminar series at the Department of Biochemistry and Molecular Biology, New York Medical College (December 2008). The title of his talk was “EP4 Prostanoid Receptor: A Therapeutic Target for the Treatment of Vascular Disease.” Dr. Falcone served as co-chair of the Vascular Biology and Angiogenesis session of the 2009 Workshop on Molecular and Cellular Biology of Plasminogen Activation, Cold Spring Harbor, NY (March 31-April 4). In addition, he served on the abstract selection committee for the annual meeting of the American Heart Association, Orlando, FL (November). Dr. Falcone has received an award from the Alice Bohmfalk Charitable Trust ($26,250) and will be awarded a new R01 grant from the NIH/NHLBI: “PG2E2 receptors as therapeutic targets in occlusive and aneurysmal vascular diseases” ($1,000,000). During the convocation in June, Dr. Falcone received the First Year Teaching Award from the Class of 2012 and was named to the Senior List by the Class of 2009 for excellence in teaching.

Dr. Syed Hoda lectured on various breast pathology and surgical pathology related topics at multiple national and international venues including the ASCP Annual Meeting in Baltimore, MD where he presented the 2008 Arthur Purdy Stout Anatomic Pathology Slide Seminar entitled “Evolving Entities in Breast Pathology” with Dr Edi Brogi (October 2008). Dr Hoda delivered multiple presentations at the International Surgical Pathology Symposium in King Faisal Specialist Hospital in Riyadh, Saudi Arabia; School of Breast Oncology in Atlanta, GA (November 2008); ASCP Weekend of Pathology in Montreal, Quebec, (June 2009); and Turkish Pathology Society in Istanbul (June 2009). Together with Dr. Gloria Young and Dr. Suzanne Brandt, Dr. Hoda presented “Diagnostic Difficulties in Low-Grade Adenosquamous Carcinoma of Breast” at the USCAP Annual Meeting in Boston, MA (March 2009). In June 2009, Dr. Hoda was appointed as the Book Review Editor for American Journal of Clinical Pathology, the official journal of the American Society of Clinical Pathology.

Dr. Stephen G. Jenkins was an invited speaker at several symposia and chaired a workshop on Antimicrobial Resistance at the joint meeting of the Infectious Disease Society of America and the Interscience Conference on Antimicrobial Agents and Chemotherapy in Washington, DC in October, 2008. Dr. Jenkins coordinated the U.S. faculty and lectured on “Gram-positive antimicrobial resistance” at a Latin American workshop jointly sponsored by the American Society for Clinical Microbiology and the European Society for Clinical Microbiology and Infectious Diseases, in Mexico City last May. He will be coordinating and lecturing this October at a similar workshop sponsored by the same two organizations, which will be held in Cairo, Egypt.

Dr. Joan G. Jones served a second term as President of the New York Pathological Society. The theme for the President’s Symposium, held on May 2, 2009 was “Update on Selected Topics in Genitourinary Pathology,” and included Drs. Mark Rubin, Larry True, Peter Humphrey, Jonathan Epstein, Victor Reuter, and Mahul Amin as faculty. Nearly 90 members and non-members attended, and all the presentations were very well received. An article entitled “Tumor Microenvironment of Metastasis (TMEM) in Human Breast Carcinoma: A Potential Prognostic Marker Linked to Hematogenous Dissemination” by Robinson, Sica, Liu, Rohan, Gertler, Condeelis, and Jones appeared in the March 24, 2009 online version of the journal Clinical Cancer Research. A press release from Cornell was subsequently picked up by the LA Times, Medscape, PA news, the UK press, and others. continued on page 9
Welcome to Our New Residents

We are very pleased to welcome our seven new first year residents who joined the Pathology Residency Training Program in July 2009, as well as Dr. Kathy Kawaguchi who joined the program in October 2009.

- **Dr. Kathy Kawaguchi** completed her medical training at the Pritzker School of Medicine of the University of Chicago in 2006, including a summer of research at the National Institutes of Health. She then entered the General Surgery Residency Program at the University of Illinois, and completed two years of surgery training.

- **Dr. Rachel Kaplan** received her MD in May 2009 from the Medical College of Wisconsin.

- **Dr. Florence Loo** received her MD in May 2009 from Case Western Reserve University School of Medicine. She was the recipient of the Taketa Scholarship, Case Western Reserve University Scholarship (2006-2007) and the Strong Children’s Research Center (SCRC) Research Fellowship (2006). In addition she was the recipient of an abstract award for “Lepow Science Research Day” (2007).

- **Dr. Kathryn Piotti** received her MD in May 2009 from the University of Medicine & Dentistry of New Jersey/R.W. Johnson Medical School. She graduated in 2005 from Syracuse University where she was Magna Cum Laude and Phi Beta Kappa.

- **Dr. David Pisapia** received his MD in June 2009 from Weill Cornell Medical College.

- **Dr. Sruthi Reddy** received her MD in May 2009 from New York University School of Medicine.

- **Dr. Alexis Scherl** received her MD/PhD in June 2009 from the Albert Einstein College of Medicine/ Yeshiva University.

- **Dr. Xuan Wang** received her MD in 1997 from the Medical Center of Fudan University (formerly Shanghai Medical University). In 2004, she received her PhD, in Molecular and Cell Biology from Brandeis University. From 2004 to June 2009, she was a post-doctoral fellow with Dr. Elaine Fuchs at The Rockefeller University.

Welcome to Our New Fellows

- **Dr. Melissa Arabadjief** is a Hematopathology Fellow. She received her MD in 2005 from the St. Louis University School of Medicine and did her pathology training at Baystate Medical Center.

- **Dr. Garrett Desman** is a Dermatopathology Fellow in the joint MSKCC-NYPH training program. He received his MD in 2004, from the University of Cincinnati College of Medicine. He did his pathology training at Mt. Sinai and in 2008 became the Oncology Fellow at MSKCC.

- **Dr. Jeffery Henderson** is a Gastrointestinal Pathology Fellow in our joint NYPH-MSKCC training program. He received his MD in 2005 from the University of Arizona College of Medicine. He also did his pathology training at the University of Arizona.
Recent House Staff Events

Scuba diving in the Bahamas.

(Left to right) Dr. Joan Jones, Dr. Yao-Tseng Chen & Dr. Kunal Karia at the Annual House Staff Dinner.

Residents at the annual karaoke party at Dr. Chen’s.

Trivia night.

Selected by the house staff, Dr. Paul Rosen receives the M. Desmond Burke Teaching Award.

2008 Holiday Party.

Congratulations to Our Graduating Residents

Nine of our residents moved on to fellowship training in July 2009. We wish them all the best!

- Dr. Suzanne Arinsburg, completed Clinical Pathology training and now is a Transfusion Medicine Fellow at the New York Blood Center.

- Dr. Yingbei Chen, who was our Chief Resident in 2008-2009 and received the Distinguished House Staff Award in 2009, is a Gynecologic Pathology Fellow at the Johns Hopkins University Medical Center.

- Dr. Claudia Cohn is a Transfusion Medicine Fellow at the University of California, San Francisco.

- Dr. Jeannelyn Estrella is a Surgical Pathology Fellow at MD Anderson Cancer Center and next year will continue as a Gastrointestinal Pathology Fellow at MD Anderson.

- Dr. Kristina Loukeris is continuing with us as a Cytopathology Fellow at New York-Presbyterian Hospital/Weill Cornell Medical Center.

- Dr. Brian Robinson is a Genitourinary Pathology Fellow at Johns Hopkins University Medical Center.

- Dr. Raanan Sela is a Gastrointestinal Pathology Fellow at New York-Presbyterian Hospital-Columbia University Medical Center.

- Dr. Gloria Young is an Oncologic Pathology Fellow at Memorial Sloan-Kettering Cancer Center and will continue next year as a Gastrointestinal Pathology Fellow in the joint NYPH-MSKCC program.

Faculty Promotions

Pengbo Zhou, PhD to Associate Professor with Tenure
Andrea Cerutti, MD to Associate Professor with Tenure
Ethel Cesarmian, MD, PhD to Professor with Tenure
Sandra Shin, MD to Associate Professor
Rhonda Yantiss, MD to Associate Professor
Y. Lynn Wang, MD, PhD to Associate Professor
Wayne Tam, MD, PhD to Associate Professor
Francesca Dimichelis, PhD to Assistant Professor
Brian Lamon, PhD to Assistant Professor
Carrie Besanceney, MD to Assistant Professor

CME Conference Update

The Tutorial on Pathology of the GI Tract, Pancreas and Liver
November 9-13, 2009
Boca Raton Marriott, Boca Raton, Florida
Course Director: Rhonda K. Yantiss, MD
Accreditation: 34.0 AMA PRA Category 1 Credit(s)™

Tutorial on Neoplastic Hematopathology
January 25-29, 2010
Marco Island Marriott Resort, Golf Club & Spa
Marco Island, Florida
Course Director: David M. Knowles, MD
Accreditation: 34.0 AMA PRA Category 1 Credit(s)™

Reserve early! Space is limited.
For more information or to register for all courses, please contact: Ms. Jessica Pfeifer (212) 746-6464 • jep2018@med.cornell.edu
www.cornellpathology.org
Focus
by Audrey N. Schuetz, MD, MPH

Laboratory Development in Borneo, Spring 2009

This past spring, I traveled to a village in rural Borneo (West Kalimantan, Indonesia) to assist in developing a small clinic laboratory. During my 6-week stay, I introduced new tests and improved upon existing ones. I also ran a quality assurance review and assessed for future lab capabilities.

In preparation for this project, other than brushing up on several tests which I hadn’t seen since the beginning of residency (i.e., the manual platelet count in peripheral blood), I researched the necessary instruments and equipment which I purchased through a grant and carried the 10,600+ miles from New York City to the village. The airline charged a large excess baggage fee for the 6 boxes I brought, filled with equipment for the lab, including a rotator, a microscope, hordes of TB masks and gloves, reagents for making stains, rapid HIV test kits, and hundreds of centrifuge tubes and sputum collection containers. All the equipment and chemicals with their Material Safety Data Sheets (MSDS), of course, had to clear customs when I arrived. The journey itself consisted of three long airplane flights to the region’s capital in Pontianak. After that, there was a 7-hour boat ride, during which twenty-four Indonesians and I were squeezed into a small boat made for at most 8 people, with our luggage piled on the roof above our heads. The ride took us through Borneo’s beautiful mangrove swamp jungles and a final, choppy stretch over the South China Sea to the village.

The ASRI healthcare clinic (acronym stands for “Harmoniously Balanced” in Bahasa Indonesian) where I spent my time was founded in 2007 by an American doctor who, before medical school, was researching orangutans in the forests of Borneo and realized the need for medical care in that region. Having gone to medical school expressly to eventually set up this clinic, she continues to oversee the clinic and consults on difficult cases, but the clinic itself is staffed by Indonesians: 3 physicians, several nurses, and one dentist. It is located in a village of 12,000 and lies at foothills of a national park in southwestern Borneo.

As the newest clinic in this area of Borneo, ASRI provides greatly needed medical care in Indonesia, which has 16 physicians per 100,000 people, 12 times lower than the ratio in the United States. About the size of a volleyball court, the clinic houses three exam rooms, a laboratory, and a kitchen in the rear. The cooks provide the staff with hot tea breaks and daily lunches from the clinic’s garden, as there is no reliable refrigeration, and the staff bikes to work from far away. Although there is a small refrigerator, the electricity blacks out as often as five times a day. When that happens, the staff must make light candles, or, if an emergency requires electricity, they turn on a generator. Interestingly, the payment system for patients is based on bartering. Patients can pay for health care in money, in labor (i.e., by washing bed sheets or planting in the garden), or by trading their own food or handmade woven grass floor mats.

The nearest hospital is two hours away, and if a patient requires anything more than a minor surgery, s/he must travel the seven-hour journey to Pontianak, the regional capital. Patients with cancer, diabetes, high blood pressure, severe diarrhea and a variety of other illnesses are seen at ASRI, but the area’s largest health problem is tuberculosis. It is estimated that more than 20 percent of the local population has TB. I consulted on several cases of fungal diseases (chromoblastomycosis), disseminated cryptococcosis, cancers metastatic to skin and lymph nodes, and even an advanced case of Grave’s disease with the classic findings of pretibial and periorbital myxedema and acropathy.

The dedicated lab person with whom I worked was Wilfrimus, a nurse, who, though not formally lab-trained, has taken some interest in the clinic’s laboratory. Before my arrival, Will was performing malaria and tuberculosis smears, Gram stains, and urine dipsticks, and he was preparing the lab’s stains and reagents (instead of buying them premade, which saves on cost and is more sustainable). He had been trained the year previously in stain preparation by another visiting microbiologist from the U.S.

I trained Will in several new procedures, including HIV and syphilis testing, manual white blood cell and platelet counts from blood and body fluids, urine sediment exams for crystals and casts, skin scrapings for fungus, and stool parasite examinations. We also focused much of our time on improving malaria and tuberculosis smears, and I performed quality assurance on the previous year’s smears. One of the persistent problems I encountered was false positive Plasmodium vivax readings, due to the presence of macrocytes, basophilic stippling, and Cabot rings. Since the clinic doctors and nurses were also interested in the lab, Will and I shared our findings with them, pulling them over to the microscope to show them an interesting fungus from a patient’s foot, or a metastatic cancer. At the end of my visit, I gave a formal presentation on Plasmodium knowlesi, which has been seen in that area of the country, while Will translated into Indonesian.
We also instituted some changes in lab-related clinic practices. One problem was improper collection of sputum for TB. Patients had been carrying their samples to the lab located at the back of building, through the waiting room and nearby examination rooms. In order to avoid exposing other patients to TB, the sputum was collected in expensive screw-top plastic containers, which were then soaked, washed and reused. However, if a TB collection container is reused, TB from a previous patient may adhere to the plastic despite the washing process and carry over to stain positive in the next patient’s sputum. We suggested, instead, that patients cough up their samples outside the lab into cheap open plastic weigh boats and then hand their sample to us through the barred lab window which opens to the outside. In those cases, we were waiting in the lab with our TB masks already on. The open “boat” container was then thrown away, thus avoiding false-positive smears when reusing containers. There were sometimes creative solutions such as these which we were required to come up with, given the lab’s cost and sustainability issues.

A large portion of the clinic work is the outreach, or mobile clinic visits. Over the course of two days, we visited two remote villages, accessible by a several-hour truck ride, followed by a 5-hour boat trip down the rivers.

At those villages, we treated and saw about 35 patients per day, handing out parasite medications to families, performing consultations, and offering basic laboratory tests. Having brought over a battery-powered microscope with LED-light source for mobile clinic visits, I had the opportunity to use this in the field. This replaced the prior field microscope, which was a half-pint-sized, reverse optics scope, with one eyepiece-incredibly cumbersome to use.

Near the end of my visit, the local government health clinic sent over 8 of their lab analysts and nurses for lab training. Part of my time was spent teaching the newer analysts how to properly use and care for a microscope and how to wear TB masks, while I trained the more experienced analysts on TB smear preparation and malaria smear reviews.

The experience was very different from work in New York City. While stains on the slides were drying, we’d watch the ducks and chickens running around in the neighbor’s yard through the open window. Instead of dodging rushed New Yorkers on the commute to work, I walked past ducks and goats in the road and listened to the owl-like hooting of the gibbon monkeys in the hills. I really enjoyed my time and was very happy to have the chance to help this laboratory. Currently, we are working on a laboratory design for the new laboratory, which the clinic hopes to open in a year. □
directed by Dr. Daniel Knowles which was held in Marco Island, Florida. He was invited by Montefiore-Albert Einstein Medical School, New York, NY as a visiting professor and lecturer at the Pathology Grand Rounds on February 12, 2009. In March 2009, Dr. Orazi participated in the Annual Meeting of the United States and Canadian Academy of Pathology held in Boston, MA. At the USCAP, Dr. Orazi attended the annual meeting of the Executive Committee of the Society for Hematopathology where he serves as member-at-large. He also gave a talk on myelodysplastic syndromes and related disorders at the Companion Meeting organized by the Society of Hematopathology. In addition to attending the annual meetings of the editorial boards upon which he serves, Dr. Orazi co-authored with Dr. April Chiu a poster on Splenic Hamartomas. Dr. Orazi continues to be the Pathology Chair for the Myeloproliferative Disorders Research Consortium (MPD-RC) and he attended the annual Investigators Meeting held on Wednesday April 1st and Thursday April 2nd, 2009 at Mount Sinai School of Medicine, New York, NY. Dr. Orazi was an invited speaker at the Fourth Annual International Symposium on New Approaches to the Biology and Treatment of MDS and MPN which was held at MD Anderson Cancer Center on April 24-26, 2009 in Houston, TX. Dr. Orazi delivered two lectures: one on myelodysplastic syndromes and a second one on overlapping myeloproliferative disorders, and chaired one session of the meeting. He participated as invited faculty in the 9th International Course on Bone Marrow Biopsy Pathology which was held in Geneva, Switzerland May 7-9th 2009. Dr. Orazi gave two oral presentations and was a panelist and chairperson for the Bone Marrow Workshop which followed the meeting. Dr. Orazi continues to serve as a member and grant reviewer for the American Institute of Biological Sciences. In 2008, he reviewed grant proposals submitted to the Department of Defense-Congressionally Directed Medical Research Programs (CDMRP). In May 2009, Dr. Orazi was elected Vice-President of the New York Pathological Society.

Dr. Edyta Pirog presented a poster at the 25th International Papillomavirus Conference in Malmo, Sweden, entitled: “Comprehensive analysis of HPV and Chlamydia trachomatis in cervical adenocarcinomas.” Dr. Pirog lectured on “Current trends in HPV screening” at the Maria Sklodowska-Curie Institute of Oncology in Warsaw, Poland.

Dr. Audrey N. Schuetz was a 2008-2009 Grant Recipient of the Yale/Johnson & Johnson Physicians Scholars in International Health $4000 stipend in support of a six-week trip to Borneo, Indonesia for development of a clinic laboratory. Dr. Schuetz was a faculty speaker at the Antibiotic Resistance Workshop, Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAC/Infectious Disease Society of America (IDSA) annual conference on 10/2008, lecturing on “Antibiotic Resistance among Staphylococci and Enterococci.”

Dr. Maria Shevchuk was an invited lecturer at the Annual Scientific Symposium of the the Hellenic Medical Society of New York on December 5, 2008. The program, chaired by Dr. Alexander Sotropouloes, also included Dr. Nicholas Romas, Chairman of Urology at Lukes-Roosevelt Medical Center, and Dr. Christopher Logothetis, Chairman of Genitourinary Medical Oncology at MD Anderson Medical Center. In her lecture, entitled “The Art of a Pathologic Diagnosis,” Dr. Shevchuk spoke about the pathologic diagnosis of prostate carcinoma, specifically describing the architecture or tissue patterns as the main criteria for separating benign from malignant prostate. These patterns bear some similarity to the patterns seen in great works of art. There is, therefore, an aesthetic component to practicing surgical pathology. Dr. Shevchuk’s talk was positively reviewed in the National Herald newspaper of December 8, 2008.

Dr. Wayne Tam was an invited plenary speaker at the Association for Molecular Pathology Annual Meeting on October 31, 2008. The title of his lecture was “MicroRNAs in tumorigenesis: a primer.” He also gave a platform presentation at the 2009 USCAP meeting on “MicroRNA-155 targets the transcription repressor ZNF652 in chronic lymphocytic leukemia.”

Dr. Rita K. Upmacus attended the 237th American Chemical Society National Meeting in Salt Lake City, March 2009 where she gave a presentation entitled “Beneficial role of inducible nitric oxide synthase in thrombosis” (R.K. Upmacus, H. Shen, L.E.S. Benguigui, D.P. Hajjar and K.A. Hajjar). Dr. Upmacus was also a coauthor on abstracts presented at the Winter Eicosanoid Meeting in Baltimore (March 2009) and at The FASEB meeting in New Orleans (April 2009) (BD Lamon, R.K. Upmacus, R.S. Deeb and D.P. Hajjar). These presentations were entitled “Nitric oxide inhibition enhances cyclooxygenase-2 induction in smooth muscle cells through modulation of phosphorylation signaling events” and “Inducible nitric oxide synthase contributes to MAPK-phosphatase induction and abundance of COX-2 expression in an inflammatory setting,” respectively. Dr. Upmacus chaired an American Chemical Society Award selection committee (May 2009) and was an invited speaker at the Gordon Conference on Atherosclerosis; the title of her talk was “Nitrate and oxidative stress: thinking outside the plaque” (June 2009).

Dr. Rhonda K. Yantiss was selected to serve as the Chairperson of the Rodger C. Haggitt Gastrointestinal Pathology Society Education Committee, as well as on the abstract review committee of the gastrointestinal pathology section of the United States and Canadian Academy of Pathology. She was invited to lecture on the topic of hamartomatous polyps at the 2008 Collaborative Group of the Americas on Inherited Colorectal Cancer Summit Meeting in Cleveland, Ohio. She also presented at the Rodger C. Haggitt Gastrointestinal Pathology Society evening session, moderated a preferred paper session at the 2009 United States and Canadian Academy of Pathology National Meeting in Boston, Massachusetts, and co-authored three abstracts at that meeting, which were presented by Drs. Emily Loyd and Nicole Panarelli. Dr. Yantiss was also invited to speak at several post-graduate courses, including the Weill Cornell Medical College Update of Pediatric Gastroenterology, The Big Apple Review and Update: The Art and Science of Surgical Pathology, and the Memorial Sloan-Kettering Cancer Center Post-Graduate Course: The Surgical Pathology of Neoplastic Disease. She serves as an ad hoc reviewer for thirteen journals and was recently appointed to the editorial boards of the Archives of Pathology and Laboratory Medicine and Modern Pathology. Her collaborative efforts with Dr. Andrew Dannenberg resulted in continued research support from the New York Crohn’s foundation. Dr. Yantiss has also been active in the Weill Medical College. She serves on the Continuing Medical Education Committee and co-directs the gastrointestinal pathophysiology section of the second year medical student course.

Faculty Publications in 2009


Faculty Publications

continued


Tharrl M, Russell D, Hoda RS: Use of the ThinPrep Imaging System does not result in higher ASC-US rates or subsequent referrals to coloscopy. Cytopsial 5:10, 2008.


Cellini C, Hoda SA, Spigelnd N: Lupus-associated vasculitis

**More Newly Awarded Grants in Pathology**

**National Institutes of Health**

**National Cancer Institute**

Title: Regulation of Nucleotide Excision Repair by Proteolysis
Principal Investigator: Pengbo Zhou, PhD
Period of Support: 06/01/09-09/30/14
Total Direct Costs: $854,430

**National Institutes of Health**

**National Cancer Institute**

Title: Mouse Model of Endometrial Tumorigenesis
Principal Investigator: Lora Hedrick Ellenson, MD
Period of Support: 07/01/09-05/31/13
Total Direct Costs: $782,280

**Department of Defense PCRP**

**New Investigator Award**

Title: Towards understanding the role of TMPRSS2-ERG Variants in prostate cancer progression
Principal Investigator: David S. Rickman, PhD
Period of Support: 05/06/09-05/05/11
Total Direct Costs: $225,000

**Clinical and Translational Science Center**

**Pilot Award**

Title: Restoration of Fas-mediated Apoptosis in Acute Leukemia: Molecular Basis and therapeutic strategies
Principal Investigator: Y. Lynn Wang, MD, PhD
Period of Support: 08/01/09-05/31/10
Total Direct Costs: $50,000

**Cancer Research and Treatment Fund**

Title: Molecular basis for discordance between mutant JAK2 allele-burden and disease severity in polycythemia vera
Principal Investigator: Y. Lynn Wang, MD, PhD
Period of Support: 07/01/09-06/30/10
Total Direct Costs: $50,000