Focus

Daniel M. Knowles, MD receives prestigious ASCP 2007 Philip Levine Award for Outstanding Research

The American Society of Clinical Pathology Philip Levine Award for Outstanding Research recognizes researchers who have made a significant contribution in the areas of immunohematology, immunopathology and molecular pathology. The award is named after the late Philip Levine, MD who made many distinguished contributions to clinical medicine including determining the etiology of Rh hemolytic disease of newborns. Philip Levine was born in Poland Russia. He moved with his family to New York when he was eight years old where his family took on a more English sounding surname. He received his medical degree from Cornell University in 1923. In 1925, he became an assistant to Karl Landsteiner at the Rockefeller Institute. He later became involved in bacteriophage research at the University of Wisconsin-Madison and began work as a bacteriologist and serologist at Newark Beth Israel Hospital in New Jersey in 1935. In 1939, while working at the Newark Beth Israel Hospital, Philip Levine and Rufus Stetson published their findings about a family who had a stillborn baby who had died of hemolytic disease of the newborn. This publication included the first suggestion that a mother could make blood group antibodies owing to immune sensitization to her fetus' red blood cells. In 1946 Philip Levine shared the Albert Lasker Award with Karl Landsteiner and Alexander Weriner for their work on the rhesus factor, hemolytic disease of the newborn and blood transfusion. The American Society of Clinical Pathologists initiated an award for outstanding research, naming it the Philip Levine Award, in 1969. The first recipient was Robin R.A. Coombs. Subsequent recipients included Ruth Sanger, R.R. Race, Louis Diamond, Paul Terasaki, Wendell Rosse, Elvin Kabat, Georges Kohler, Cesar Milstein, Peter Nowell, Beruj Benacerraf, Burt Vogelstein, and Janet Rowley, among many others.
Research Highlights

TMPRSS2-ETS Fusion Prostate Cancer: Biologic and Clinical Implications

Francesca Demichelis and Mark A. Rubin

TMPRSS2-ETS fusion was recently reported by Tomlins et al. as the first recurrent genomic alteration in prostate cancer and has been now confirmed by multiple independent groups. The ETS-related gene (ERG) is the most common fusion partner for the androgen regulated gene TMPRSS2. Both genes are located within 3Mb on chromosome 21 and the most common mechanism for fusion is through an interstitial deletion (Perner, 2006 #2885) (Figure 1). ETV1 and ETV4, other members of the ETS family, have been detected only in gene fusion is still unclear. PSA screened hospital based cancer, however the proportion of cases that harbor the TMPRSS2-ERG fusion is a frequent and early event in prostate cancer pathogenesis with distinct biology and a more aggressive phenotype.

TMPRSS2-ETS fusion is a frequent event in prostate cancer, however the proportion of cases that harbor the gene fusion is still unclear. PSA screened hospital based cohort studies detect a frequency of TMPRSS2-ERG fusion, ranging between 40% and 78%. Well characterized prostatectomy series show frequencies around 50% (gray bars for negative and blue bar for positive status), by qPCR and/or by FISH. One limitation of these hospital based cohorts is that they are skewed towards patients amenable to surgery, usually with elevated PSA (PSA > 4.0 ng/ml) and clinically organ confined prostate cancer (clinical stage T2). Approximately 15% of TMPRSS2-ERG fusion is detected in a Swedish population based series of men with prostate cancer identified through transurethral resections for urinary symptoms and followed expectantly (Watchful Waiting). A larger study on population based cohort from our group confirms this low proportion (unpublished data) as does a recent study from the United Kingdom. This low proportion may reflect the high percentage of low grade tumors in this cohort. Regardless of the exact proportion, the total number of estimated cases of TMPRSS2-ERG fusion prostate cancer is substantial and will increase dramatically over the next decades with the aging of the U.S. population as recently reported by the Surveillance, Epidemiology, and End Results (SEER) with anywhere from 100,000 to 250,000 cases by year 2050.

Unlike PTEN mutations, which occur late in prostate cancer disease progression, TMPRSS2-ERG fusion appears to be an early molecular event in the development of neoplasia. To date, gene fusion has not been detected in situ in benign prostate tissue including prostatic atrophy. Two reports suggest that 20% of high grade prostatic intraepithelial neoplasia (High Grade PIN) demonstrate TMPRSS2-ERG fusion. Gene fusion identified in High Grade PIN is typically in close proximity to invasive prostate cancer. Perhaps most striking is that within a discrete tumor nodule, gene fusion is observed as a clonal event involving nearly all the tumor cell population. Were this a late event, we would anticipate seeing a gradation of fusion patterns, with some cases showing only focal TMPRSS2-ERG fusion to extreme cases with homogeneous gene fusion.

Interestingly, recent data indicates a distinct morphologic phenotype associated with the TMPRSS2-ERG fusion prostate cancer. Mosquera et al. explored gene fusion status of a large set of prostate cancers and detected significant associations with common morphologic features, representing the first observation of a specific somatic alteration tied to phenotypic changes in prostate cancer. The best morphologic model to predict TMPRSS2-ERG fusion status is comprised of five morphologic features: blue-tinged mucin, cribriform growth pattern, macronucleoli, intraductal tumor spread, and signet-ring cell-like carcinoma (Figure 2). In addition to some potentially useful clinical implications for diagnosis and risk assessment, the association between phenotype and TMPRSS2-ERG fusion suggests that molecular alterations consistently occur in TMPRSS2-ERG prostate cancer downstream the initial fusion event. Indeed, Tomlins et al. describe a distinct ETS signature. We anticipate that future studies on the pathways altered by TMPRSS2-ETS fusion will provide insight into potential therapeutic targets.

Figure 1: A-C. Genomic deletions on chromosome 21 between ERG and TMPRSS2. Interrogating high density 100K SNP arrays (~110,000 loci on the genome) on a panel of 30 PCA samples, we observed a commonly deleted area on chromosome 21q22.2-22.3, spanning the region between ERG and TMPRSS2. A: Samples, including 6 cell lines, 13 xenografts and 11 metastatic PCA samples, were characterized for TMPRSS2-ERG and TMPRSS2-ETV1 status (gray bars for negative and blue bar for positive status), by qPCR and/or by FISH. B: Magnification of the green framed box in A. Signal intensity on the right side is proportional to copy number intensity of a hormone refractory metastatic PCA sample (MET6-9). Interestingly, for TMPRSS2-ERG rearrangement positive tumors, 71% (5 of 7) of hormone refractory PCA demonstrate a deletion between TMPRSS2 and the ERG loci whereas deletion was only identified in 1 of 4 hormone naïve metastatic PCA samples (ULM LN 13). C: Magnification of the black framed box in A. SNP data include 15 loci along ERG, distributed from the gene promoter to intron 5 and 1 SNP on the 3’UTR of TMPRSS2. There is significant homogeneity for the deletion borders with two sub-classes, distinguished by the start point of the deletion—either 38.765 Mb or 38.911 Mb).
Research Highlights continued

These findings about association with biochemical failure should be viewed with caution, since biochemical failure is a poor surrogate endpoint for clinically meaningful endpoints such as clinical relapse and death as demonstrated by three recent studies. Porter et al. observed 45.5% PSA biochemical failure in a radical prostatectomy series but prostate cancer specific death occurred in only 18.5% of the population with a follow up time of up to 25 years. Carver et al. reported on a population of men with T3 prostate cancer who underwent radical prostatectomy, in which only 36% of patients with PSA biochemical failure had disease progression. Ward et al. found that in a population of 3897 radical prostatectomy patients, only 8.3% of the men with PSA biochemical failure died of prostate cancer. Thus PSA failure is associated with prostate cancer death but the majority of men with PSA biochemical failure will die of other causes. When looking at prostate cancer specific death as clinical endpoint, we observe a significant association in the expectant therapy cohort (Figure 3) and the result is confirmed on a larger cohort of over 350 prostate cancers (unpublished data), indicating that the natural course of TMPRSS2-ERG fusion prostate cancer is that of an aggressive tumor. Men with TMPRSS2-ERG fusion prostate cancer might particularly benefit from curative therapy, and these findings suggest a strategy to further stratify patients for expectant therapy by assessing fusion status in addition to serum PSA levels, digital rectal examination results, and needle biopsy Gleason score.

In summary, TMPRSS2-ERG gene fusion is a frequent, early event in the genesis of prostate cancer. TMPRSS2-ERG fusion may also become an important diagnostic marker as it is highly specific for prostate cancer and detectable in urine. In addition, it has the potential to work as risk predictor of adverse clinical outcome.

References

Figure 2: H&E stains and corresponding FISH images of TMPRSS2-ERG fusion assay. A: PCA Gleason pattern 3 showing blue-tinged mucin. Note benign prostatic glands at 12 and 3 o’clock. B: FISH image of the red-boxed area in A. One yellow and one red signal are present in each nucleus, demonstrating the presence of TMPRSS2-ERG fusion through deletion. The double-framed yellow inset is a magnification of the yellow-boxed area, showing two representative nuclei of the PCA gland. C: PCA Gleason pattern 4 with cribriform appearance. D: FISH image of the red-boxed area in C. One yellow and one red signal are present in each nucleus, demonstrating the presence of TMPRSS2-ERG fusion through deletion. The double-framed yellow inset is a magnification of the yellow-boxed area showing two representative nuclei of the PCA area. Original magnification of H&E images, 20x objective. Original magnification of FISH images, 60x objective. (Mosquera et al., J Pathology, 2007)
Research Highlights


David Rickman, PhD will lead Prostate Cancer Genomics Effort

David Rickman, PhD has joined the laboratory of Dr. Mark Rubin as an Instructor to lend his expertise in genome-wide screening approaches to address clinically relevant issues of prostate cancer progression. He will lead efforts on expression profiling of prostate cancer and development of novel platforms to analyze biomarker panels. Dr. Rickman obtained a doctorate in molecular biology in 1997 from Mt. Sinai Medical School in New York and has nearly 10 years experience in the area of cancer biomarker research. His interest in cancer biology and biomarkers began during his post-doctoral fellowship with Dr. Samir Hanash at the University of Michigan Medical School where he discovered that the axonal cell adhesion molecule TAX-1 is amplified and aberrantly expressed in malignant gliomas. Using expression profiling technologies, he went on to delineate specific gene signatures that discriminate low and high grade gliomas.

Following this fellowship he moved to Paris, France and became project leader for the French Cancer Biomarker Program initiated by the French NCI (Ligue Nationale Contre le Cancer). The aim of this multi-million dollar per year program was to identify clinically relevant biomarkers for multiple cancer types across institutions in France. He was able to help develop multiple collaborative groups. Successful collaborations led to a novel classification of hepatocellular carcinomas into distinct subgroups related to clinical and genetic characteristics; the demonstration of a molecular link between angioimmunoblastic T-cell lymphoma (AITL) and follicular helper T (T(HF)) cells, and that in non-inflammatory breast cancers, TP53 status is a key predictive factor for response to the dose-dense epirubicin-cyclophosphamide regimen. The breast cancer work further suggests important clinical implications regarding treatment.

References
In December 2006, Dr. Andrea Cerutti lectured on the “Regulation of frontline Ig class switching by epithelial cells” at a Federation of Clinical Immunology Societies meeting held in New York. In March 2007, she lectured on the same topic at the Catalan Research Institute for Advanced Studies in Barcelona, Spain. In April 2007, she discussed the “Interaction between HIV and B cells” at the University of Pittsburgh. In May 2007, he gave a seminar on the same topic at an AIDS Enterprise Working Group meeting in Reston, Virginia. He then traveled to Miami to participate in the annual American Association of Immunologists (AAI) meeting, where a member of his lab, Dr. Weifeng Xu, received the prestigious AAI-Huang Foundation Trainee Achievement Award. In July 2007, he was a keynote speaker at the 13th International Congress of Mucosal Immunology in Tokyo, where he discussed “The role of innate immune signals in CLL” in a seminar organized by the Cornell CLL Research Center. In addition to lecturing, Dr. Cerutti served on various committees. In November 2006 and February 2007, he traveled to Bethesda to participate in two NIH-NIAID review committees, and in May 2007 he served as an advisor in an International AIDS Vaccine Initiative workshop held in New York. Then, he organized a Starr Consortium workshop on hematological malignancies at Weill Cornell Medical College and continued to serve as lecturer in the Host Defenses Course for medical students, director of the Pathology Research Seminar Series, and director of the Research in Progress (RIP) course of the Immunology and Microbial Pathogenesis Program. This graduate Program nominated him chair of the Admission Candidacy Exam (ACE) committee. Dr. Cerutti also served as coordinating reviewer for the American Society of Hematology on the topic “Immunodeficiency, including HIV and AIDS-related malignancies. Finally, she presented a mentor award at the Second Annual Postdoc Research Day at Weill Cornell. He was also awarded an R01 grant supplement ($100,000) by NIH-NIAID to initiate studies on neutralizing antibodies to HIV. As for Dr. Cerutti’s lab members, Dr. Ruba Deeb received a Cancer Research Institute Fellowship ($24,000) and Dr. Weifeng Xu received funding ($40,000) from the NIH Training Grant. Finally, Weill Cornell Public Affairs office issued press releases on articles published this year in Nature Immunology and Immunity by Dr. Cerutti’s lab.

Dr. Ethel Cesarman has been involved in numerous activities within Weill Cornell Medical College. She is currently serving on the Committee of Review, the Cancer Center Internal Advisory Committee and as the Pathology Representative to the General Faculty Council. She is the new Director of the Immunology Program Training Grant. In the past year she served on the Examining Committee as chairperson for the Thesis Defense of two graduate students of the Immunology and Microbial Pathogenesis Graduate Program: Fei Duan and Pavel Pugach. Dr. Darya Bubman, a graduate student in Dr. Cesarman’s lab graduated last October and went on to receive a prestigious AAAS Diplomacy Fellowship and is currently a fellow in the State Department. Dr. Cesarman organized a Workshop as Part of the Starr Cancer Consortium entitled “Global Changes in Hematologic Neoplasms” on April 24, 2007. Dr. Cesarman was invited to give a seminar at the “Instituto Nacional de Cancerologia” in Mexico City in August, where she presented an overview on viral lymphomagenesis, and work from her laboratory. Dr. Cesarman served as a coordinating reviewer for the American Society of Hematology (ASH) on the topic of Immunodeficiency, including HIV and AIDS-Related Malignancies and attended the ASH meeting in Orlando, FL in December 2006 where she served as a moderator and coauthored a presentation by Dr. Amy Chadburn entitled “Neither germinal center (GC) vs. non-germinal center (Non-GC) phenotype nor FOXP1 correlate with outcome in AIDS-associated diffuse large B cell lymphoma (DLBCL): Study of patients from AIDS Malignancies Consortium trials 010 and 034.” Work done primarily by Dr. Ilaria Guasparrin at Dr. Cesarman’s lab was presented at the International Herpesvirus Workshop in Asheville, NC, July 2007, and entitled “EBV LMP2A mediates LMP1 signaling and survival of lymphoma cells through TRAF2 regulation.” Two abstracts from the lab were presented at the 10th International Workshop on KSHV and Related Agents in Portland OR, August 2007, the first authors of which were Darya Bubman and Daniel DiBartolo. These were entitled, respectively, “KSHV vFLIP induced reactive oxygen species in primary effusion lymphoma (PEL)” and “KSHV induces resistance to TGF-beta through downregulation of TGF-beta receptor II expression.” At this same meeting, Dr. Amy Chadburn also gave a presentation coauthored by Drs. Cesarman, Tam and Knowles entitled “Immunophenotypic analysis of KSHV (HHV-8) infected B cells in multicentric Castleman’s disease (MCD) in HIV+ individuals.”

In December 2006, Dr. Amy Chadburn traveled to Orlando, Florida, where she presented “Neither Germain Center (GC) vs Non-Germinal Center (Non-GC) Phenotype nor FOXP1 Expression Correlate with Outcome in AIDS-Associated Diffuse Large B-Cell Lymphoma (DLBCL): Study of Patients from AIDS Malignancies Consortium Trials 010 and 034” at the 2006 American Society of Hematology meeting. She was also a co-author on another 8 abstracts presented at that meeting. In March, 2007, she attended the annual United States and Canadian Academy of Pathology (USCAP) meeting. She was, with other members of the department, involved in the fellowship fair, a forum where residents from the entire country can investigate the fellowship programs offered at the different institutions. At the USCAP meeting, she chaired one of the hematopathology oral presentation sessions. She co-authored 7 abstracts which were presented at this USCAP meeting, including a poster presented by the hematopathology fellow, Dr. Ila Bansal, “ZAP70 Expression Determined by Immunohistochemistry (IHC) of Cell Cytos Correlates with IgH Mutation Status and Cytoisogenics in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)” and an abstract on multicentric Castleman’s disease which she presented at a platform hematopathology session. Dr. Chadburn was also part of the Society of Hematopathology membership committee that nominated new members at this meeting. In May Dr. Chadburn was selected to become the faculty liaison for medical students, residents and fellows rotating through the department. In August, Dr. Chadburn traveled to Portland, Oregon, where she presented at the Kaposi Sarcoma Herpesvirus Annual meeting on her collaborative work “Immunophenotypic (IP) Analysis of the Kaposi Sarcoma Herpesvirus (KSHV, HHV-8) Infected B Cells in HIV+ Multicentric Castleman’s Disease (MCD).” She also lectured at the 10th Annual Association of Physician Assistants in Oncology (APAO) Conference here in New York City on the “Principles of Immunophenotypic Analysis.” She continues to chair the department’s Translational Research Committee. She is also active, with Dr. Cesarman, reviewing cases for the AIDS Malignancy Consortium (AMC) and for the ACSIR (AIDS and Cancer Specimen Resource).

Dr. Yao-Tseng Chen was the invited speaker for Pathology Grand Rounds at the Johns Hopkins Medical Center in April 2007, where he lectured on “Renal cell carcinoma and oncocyotoma: recent molecular and immunohistochemical markers.” In May, he traveled to Taiwan, and spoke on a similar topic at the Department of Pathology in National Cheng-Kung University Medical College. During the same trip, he was also invited to give a seminar at Genome Research Center, Academia Sinica, speaking on “Cancer-Testis (CT) antigens: Potential targets for therapeutic cancer vaccines.”
Keynotes
continued

(Dr. Knowles can’t)
This discussion led to a series of recommendations which will be forwarded to the Council of the Association of Pathology Chairs for further consideration. In addition, Dr. Daniel Knowles continues his activities as Chief Medical Officer of the Weill Cornell Physician Organization. Lastly, he has been appointed Chairman of the Internal Advisory Board charged with developing the administrative, clinical and scientific infrastructure necessary to eventually develop an NCI-designated Comprehensive Cancer Center at the Weill Cornell Medical Center. Other members of the Department of Pathology and Laboratory Medicine involved in this effort include Dr. Ethel Cesaran and Dr. Mark Rubin, who will serve as an Associate Director of the Cancer Center.

Dr. Scott Ely traveled to Mumbai, India to teach a workshop on AIDS-related hematopoietic cancers in January of 2007, as part of an NIH effort to help Indian physicians begin research in the face of their burgeoning AIDS epidemic. In March, Dr. Ely taught a 5 hour overview of hematopathology at the New York University Dental School. In June, he traveled to Kos, Greece, to the Xth Annual International Myeloma Workshop, to present work done in collaboration with Drs. Knowles, Chen-Kiang, and Mathew on the mechanisms of BIRD therapy, the role of the retinoblastoma protein in cell cycle regulation, and del(13q) pathogenesis in multiple myeloma.

During the last several months, Dr. Domenick J. Falcone has been busy with curricular activities and medical education. He served on a task force that established guiding principles for the educational activities at the Qatar campus by faculty in New York. He also serves on a task force that is recommending financial models to fund and reward medical education. Finally, he was invited by the Core of Basic Sciences Committee to participate in the evaluation of the pharmacology curriculum, and recommend new approaches to teaching pharmacology during the first and second year. Dr. Falcone continues to serve as Associate Director of the Human Structure & Function course and Director of the Host Defenses course. During the convocation exercises in May, Dr. Falcone received the First Year Teaching Award from the Class of 2010.

Dr. Syed Hoda lectured on various surgical pathology and breast pathology-related topics in multiple national and international venues including: School of Breast Oncology in Atlanta, GA in November 2006; The Mexican Cytology Society in Queretaro, Mexico in December 2006; M.D. Anderson Cancer Center Grand Rounds in Houston, TX in March 2007; ASCP’s Weekend of Pathology in Chicago, IL in March 2007; USCAP Practical Pathology Seminar in Cancun, Mexico in May 2007; Pathology Update at Royal Siraj Hospital in Bangkok, Thailand in June 2007, and Pathology Conference at the Institute of Pathology, New Delhi, India in August 2007. In March 2007, Dr. Hoda together with Dr. Suzanne Brandt and Dr. Gloria Young, presented “The Rosen Triad: Tubular Carcinoma, LCIS and Columnar Cell Change” at the USCAP Annual Meeting in San Diego, CA. Dr. Syed Hoda’s cytology textbook entitled “Fundamentals of Pap Test Cytology” was published by Human Press in early 2007.

Dr. Joan Jones was elected President of the New York Pathological Society for the 2007-2008 term. This follows a two year term in which Dr. Jones served as Vice President of the Society and Program Chair. Since 2006, Dr. Jones’ research has focused on the identification and prognostic significance of tumor microenvironment for metastasis (TMEM) in human breast cancer samples. Data has been presented at the International Association for Breast Cancer Research, the United States and Canadian Academy of Pathology, and the American Association for Cancer Research. The Department’s Immunopathology Laboratory was instrumental in developing the triple immunostain which is required for identification of TMEM. Preliminary analysis of cases with known outcomes suggests that TMEM quantitation is an independent predictor of long-term metastatic outcome.

Dr. Davide Larone conducted Clinical Mycology Workshops for the Southern California branch of the American Society for Microbiology in November, 2006 and for the Maryland Society for Clinical Laboratory Sciences in March, 2007. In April, she served as Visiting Professor in Clinical Pathology at the University of Michigan; while there, she presented four lectures, including Pathology Grand Rounds entitled “Morphologic Features of Fungi in Tissue.” During April she also spoke on “Galactomannan and Beta-Glucan Tests for Fungi” as a participant in the Infectious Disease Advanced Topics Program at Memorial Sloan Kettering Cancer Center. At the American Society for Microbiology National Meeting in Toronto, Canada in May, 2007, she presented a lecture on “Methods of Detection of Klebsiella pneumoniae carbapenemase (KPC) in New York City Isolates.” At the ASM meeting in Toronto, she also presented two posters: one with Dr. Rosanny Espinal-Witter on “Detection of Klebsiella pneumoniae Carbapenemase (KPC) by Vitek 2 AST GN Card Using Ertapenem as the Indicator” and the other, with Dr. Claudia Cohen, entitled “Comparison of Pro-Lab Diagnostics Prollex Streptococcal Grouping Latex Kit and BD BBL StreptocardTM Enzyme Latex Test for Lancefield Grouping of Streptococcal Isolates.”

Dr. Edyta Pirog served as a moderator for a gynecologic pathology platform sessions at the 96th Annual Meeting of The United States & Canadian Academy of Pathology, San Diego, CA, 2007. In addition she was a senior author of two posters presented at the meeting: “Estimated false negative results of H2C2 HPV testing as correlated with consensus Pap Test diagnosis” and “The Bethesda System 2001 recommendation of reporting endometrial cells seen in Pap tests of women age 40 years and older is overly conservative.” In addition, Dr. Pirog presented a talk entitled: “Correlation between Human Papilloma Virus detection and histologic features of vulvar carcinoma,” at the HPV and Cancer International Meeting, Besancon, France, 2007.

Dr. Hanna Rennert presented a poster entitled “Development of a Novel and Rapid Molecular Genetic Test for Mutation Screening in Autosomal Dominant Polycystic Kidney Disease (ADPKD)” at the Nature Genetics Nephrogenetics meeting in February 2007. This work described the development of a novel method for identification of sequence variations in large genes, using a mismatch-specific DNA endonuclease and DHPLC. She is now continuing work to develop an algorithm for evaluating the pathogenic potential of non-synonymous sequence variants. At the annual meeting of the Pan American Society for Clinical Virology in Clearwater, FL, in May 2006 Dr. Rennert presented a poster entitled “Evaluation of a quantitative real-time PCR assay for EBV in plasma specimens.” In July 2007 she was invited to present her work about the use of genetic testing to identify patients with polycystic kidney disease at the Hypertension and Polycystic Disease Department’s seminar series at the Rogosin Institute. In September 2007 she was invited to present her work concerning genetic analysis of MSR1 and RNASEL genes in Asian-Indian Hormone-Refractory Prostate Cancer in the DOD Innovative Minds in Prostate Cancer Today (IMPaCT) meeting.

Dr. Surya V. Seshan served as an abstract reviewer for “Renal Pathology: Basic/Experimental pathology,” American Society of Nephrology (ASN) annual meeting at San Diego, CA in November 2006 and was the moderator for the “Angiotensin and RAS in renal inflammation” session at the ASN. She was an invited speaker in the Postgraduate Course – Basic renal pathology on “Renal lesions in SLE” at the ASN. Also in November, Dr. Seshan was invited to speak at the international symposium in Pathology/Romanian division of IAP at “Victor Babes” National Institute, Bucharest, Romania on “Tubulo-interstitial lesions in immune disorders” and “Renal lesions in dysproteinemias.” In the winter and spring months, she gave grand rounds in the Departments of Medicine, Pathology, Rheumatology and Nephrology in various area hospitals in New York and New Jersey on renal diseases, lupus nephritis, hepatitis-C associated renal disease and amyloidosis. She served on the research grant review committee sponsored by Kidney and Urology Foundation of America (KUFA) and Renal Pathology Society in February 2007. In May 2007, she was an invited speaker at “Pathology potpourri – An evening for nephrologists” for KUFA, New Brunswick, NJ.

Dr. Sandra Shin served on a multidisciplinary expert panel discussion for the 6th Annual Breast Cancer Evening Update sponsored by the Lean on Me Breast Cancer Network, in Roslyn, N.Y. on November 15, 2006. On February 10, 2007, she was the guest speaker for an all-day CME accredited seminar for the Duckworth Pathology Group and Methodist-University Hospital in Memphis, TN. This seminar consisted of several lectures including “Needle Core Biopsy of the Breast,” “Ductal carcinoma in-situ,” and “Diagnostically Problematic or Unusual Lesions of the Breast” Digital image unknown and glass slide unknown sessions were also conducted.

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Dr. Shin was invited to serve as a scientific grant reviewer for the Department of Defense (ODD) for a third consecutive year. She was a reviewer for the Breast Cancer Concept Award, Pathobiology 1, in March of 2007 and subsequently, for the Breast Cancer Research Program (BCRP), Pathobiology 1, in August of 2007. She served as a co-moderator for the Breast Platform Session at this year's United States and Canadian American of Pathology (USCAP) meeting in San Diego, CA (March 24-30, 2007). During this meeting, she gave a platform presentation entitled “Characterization of diagnostically problematic spindle cell lesions arising in papillary tumors of the breast” and a poster presentation entitled “Malignant spindle cell tumors of the breast demonstrating overlapping immunoprofiles for cytokeratin and myoepithelial markers.” Dr. Paul Rosen was a co-author for both presentations. This fall, she will be serving her 2nd year as an USCAP abstract reviewer (Breast Section) for the upcoming 97th annual meeting in Denver, Colorado.

Dr. Wayne Tam was the Grand Rounds lecturer at the Department of Pathology and Microbiology, University of Nebraska Medical Center on December 6, 2006. The title of his talk was “PRDM1, Plasma Cell Differentiation, and Lymphomagenesis.” He gave a platform presentation entitled “MicroRNA-mediated Translation Repression of PRDM1 alpha expression in Hodgkin/ Reed-Sternberg Cells: A Potential Pathogenetic Lesion in Hodgkin Lymphoma” at the 48th ASH Annual Meeting in Orlando, Florida in December, 2006. He was invited to lecture on “Pitfalls in Lymphoma Diagnosis” and give a slide seminar at the sixth Asia Pacific International Academy of Pathology Congress in Singapore held in May, 2007.

Dr. Rita K. Upmacis was an invited speaker at the New York Medical College in Valhalla in April and presented a talk entitled “Nitrogen oxide interactions with cytooxygenase: implications in atherogenesis.” In May 2007, Dr. Upmacis participated in the Experimental Biology Meeting in Washington DC. The title of her presentation was “Contribution of inducible nitric oxide synthase to protein nitration and bioperoxidation in ApoE-null mice. In September 2007, Dr. Upmacis was invited to give a lecture at the University of Nottingham, U.K. at a symposium in honor of the 60th birthday of her PhD advisor, Dr. Martyn Poliakoff. In her talk, entitled “Of Mice and Men, and Martyn,” she reminisced about her time at Nottingham, but also discussed her studies involving nitric oxide-related chemistry that may occur under physiological and pathophysiological conditions.

Dr. Madeline F. Vazquez led the first Expert Cytology Panel review of lung cancers detected in the International-Early Lung Cancer Action Project [I-ELCAP] during the 16th International Conference on Screening for Lung Cancer held at Weill Cornell Medical Center in April 2007 and gave a lecture entitled “Histopathologic subtypes of adenocarcinoma resulting from CT screen-
Welcome to Our New Residents

Joanna Chan, MD  Adam Gersten, MD

Katherine Maloney, MD  Nicole Panarelli, MD

Dara Rosenman, MD  Steven Salvatore, MD

Jeremy Segal, MD, PhD

Resident's Corner
by Debra G.B. Leonard, MD, PhD

Highlights from Our Graduating Residents

Three of our residents completed Anatomic and Clinical Pathology training in July 2007, and have left the program for fellowship positions. Dr. David Czuchlewski, who was our Chief Resident in 2006-2007, is at the University of New Mexico in a Hematopathology Fellowship. Dr. Steve Rohan, who received the Distinguished House Staff Award in 2007, has an interest in Genitourinary Pathology; he is currently an Oncologic Pathology Fellow at Memorial Sloan Kettering Cancer Center, where he will continue as a GU Fellow for 2008-2009. Dr. Matthew Bramlage also is an Oncologic Pathology Fellow at Memorial Sloan Kettering Cancer Center this year, and will continue as a Cytopathology Fellow in 2008-2009. We wish David, Steve and Matt all the best!

Information about Our Current Residents

- **Dr. Bijal Amin** is currently our Chief Resident. She attended George Washington University in Washington D.C., where she earned both her undergraduate degree in painting and art history and her medical degree. After completing an internship in internal medicine at the University of Washington, she returned to the east coast and has been enjoying continuing her fine arts education during residency. She is very happy to have such a wonderful group of residents to work with during her Chief year and is looking forward to her Dermatopathology fellowship next year.

- **Dr. Garron Solomon** is one of our PGY-4 residents and is headed for a career in Dermatopathology. He recently accepted a fellowship position for 2008-2009 at the Ackerman Academy of Dermatopathology in New York City.

- Originally from Tennessee, **Dr. Emily Loyd** attended undergraduate school at Indiana University in Bloomington and medical school at The University of Tennessee, Memphis. She left the Mississippi River for an excellent training program in pathology at NewYork-Presbyterian Hospital-Weill Cornell Medical College, and to experience New York City. She is thrilled to be staying at Weill Cornell for the fellowship in Gastrointestinal Pathology and looks forward to an academic career.

- **Dr. Patrick Wagner** attended college at the University of Pittsburgh (in the Cathedral of Learning) and medical school at Harvard. Next year he plans to resume his surgery residency after completion of his Anatomic Pathology training. Exciting events in his life this year were getting married to Natasha and cutting off almost all of his hair!

- **Dr. Molly Dyrsen** is currently a second year AP/CP resident with an interest in Dermatopathology. She graduated from University of Alabama in May 2002 as a Presidential Scholar with a B.S. in Biology. She received her medical degree in May 2006 from the University of Louisville, where she graduated magna cum laude and was a member of Alpha Omega Alpha. She has worked on several projects with Dr. Cynthia Magro, Director of Dermatopathology. Two of these projects were presented at the 2007 USCAP meeting. Additionally two manuscripts generated by Drs. Magro and Dyrsen have been accepted for publication in the Journal of Cutaneous Pathology. Molly recently completed her third marathon and is especially proud of the trophy she received.

- **Dr. Brian Robinson** is currently a second year resident in Anatomic Pathology. He attended Washington University in St. Louis for his undergraduate degree, where he majored in Biology and Spanish, and then entered Cornell University for medical school. He plans to specialize in genitourinary pathology.

We honored our departing housestaff on May 29th at Dock’s Restaurant. At the dinner, the Housestaff presented Dr. Syed Hoda with the M. Desmond Burke Teaching Award.

Above, left to right: Drs. David Czuchlewski, Matthew Bramlage, Stephan Rohan, Wenyong Zhang. Below: Dr. Syed Hoda
Welcome to Our New PGY-1 Residents

We are very pleased to welcome our seven new first year residents who joined the Pathology Residency Training Program in July 2007.

- **Dr. Nicole Panarelli** is a native New Yorker. She received a Bachelors of Arts degree in Government studies from Georgetown University in 2003. She then attended New York Medical College from which she received her medical degree in 2007.

- **Dr. Joanna Chan** received her BA in biology in 2002 from Johns Hopkins University and her MS in cellular/molecular biology in 2003 from the same institution. Joanna graduated in May 2007 with her medical degree from the Milton S. Hershey Medical Center, Pennsylvania State University.

- **Dr. Adam Gersten** received his BA in biological sciences in 2002 from Cornell University in Ithaca. He graduated in June 2007 with his medical degree from the Albert Einstein College of Medicine in New York.

- **Dr. Katherine Maloney** graduated this past June from the University of Massachusetts Medical School in Worcester, MA. She attended the College of American Pathologists (CAP) annual meeting this October in Chicago, and presented an abstract and poster on her research entitled, Expression of Vascular Endothelial Growth Factor Subtypes in Mammary Invasive Ductal Carcinoma and their Relationship to Tumor Progression.

- **Dr. Dana Rosenman** grew up in Plainview, New York. She graduated from Boston University with a BA in Biochemistry and Molecular Biology in 2003 and then continued her education at Boston University School of Medicine where she received her medical degree in 2007.

- **Dr. Steven Salvatore** received his BS in May 2003 from Wake Forest University and his medical degree from Saint Louis University in May 2007. This summer, Steve and his wife were married in northern Denmark and have enjoyed the transition to living in New York.

- **Dr. Jeremy Segal** received his BA in biophysical chemistry in 1997 from Dartmouth College. In June 2006, he received his PhD from Rockefeller University as part of the Cornell MD/PhD program. In May 2007, he will receive his medical degree from Cornell University Medical College. Dr. Daniel M. Knowles was Jeremy’s academic advisor.

References


Faculty On The Move Upward...

It is a bittersweet delight to see our faculty move onward and upward in their careers. We bid farewell to Drs. Muller and Peerschke, both of whom are moving on and climbing the academic ladder of success.

After 20 years as a Cornellian, Dr. William Muller has accepted the position of Chairman, Department of Pathology, Northwestern University Feinberg School of Medicine and Pathologist-in-Chief, Northwestern Memorial Hospital (both in Chicago, IL). We wish Dr. Muller the best of success and thank him for his numerous significant contributions to our department. Dr. Muller will maintain an adjunct appointment in our Department.

After 11 years on our faculty, Dr. Elinor I.B. Peerschke will become Professor of Pathology at the Mount Sinai School of Medicine where she will hold the positions of Associate Director for Clinical Laboratories; Chief, Division of Translational Research; Director, Clinical Microscopy and Director, Coagulation. We wish her all the best and look forward to maintaining an active relationship with Dr. Peerschke, as she will also maintain an adjunct appointment at Cornell.

We also bid farewell to Dr. Ximing Yang who will be returning to Northwestern University and Dr. Sun Chung who is pursuing a career at a commercial laboratory.

Left to right: Dr. Peerschke, Dr. Burke, and Dr. Knowles at the reception.

Focus

continued from page 7

She was co-first author on a Cancer Research paper describing for the first time the interstitial loss associated with the gene fusion. This study required developing analysis tools with members of the Broad Institute of M.I.T. and Harvard. Francesca was also the lead author on the first paper to demonstrate the aggressive natural history of fusion prostate cancer in a Watchful Waiting cohort from Sweden. These observations also lead to the development of the first National Cancer Institute (P.I. Rubin) and Prostate Cancer Foundation (P.I. Demichelis) funded grants on gene fusion prostate cancer that help support the detailed mapping of chromosome 21 in the region between ERG and TMPRSS2 using both SNP arrays and developing chromosome specific tiling arrays to characterize the breakpoint(s).

As a co-discoverer of this landmark biologic observation, she will continue to participate in the on-going development of clinical tests (FISH and Urine based) with Gen-Probe (San Diego, Ca.), which has licensed the rights to develop these assays commercially. Therefore, from discovery to clinical application, Francesca has been a member of a translational research team and played an important role throughout this process. As part of this team effort between the University of Michigan and Harvard, she was a co-recipient of the Inaugural American Association for Cancer Research Team Science Award for the discovery of Gene Fusion Prostate Cancer (AACR Meeting, Anaheim, CA. 2007).

She recently joined the Weill Cornell Medical College as Instructor in Pathology and Laboratory Medicine with a secondary appointment at Institute for Computational Biomedicine, where she is an Institute Fellow. She will serve as the lead computational biologist for the Prostate Cancer Working Group.

References

Faculty Publications in 2007


Faculty Publications in 2007 continued


Newly Awarded Grants in Pathology

National Institutes of Health
National Cancer Institute
Title: Towards Understanding Prostate Cancer Heterogeneity
Principal Investigator: Mark Rubin, MD
Period of Support: 08/01/07-07/31/11
Total Direct Costs: $ 922,132

Starr Cancer Consortium
Research Grant Award
Title: Tumor Development and Treatment of EBV-associated Lymphomas in Immune Competent Humanized Mice
Principal Investigator: Ethel Cesaram, MD, PhD
Period of Support: 11/01/07-10/31/09
Total Direct Costs: $380,000

National Institutes of Health
National Institute of Allergy and Infectious Diseases
Title: Regulation of Antibody Production by Innate Immune Cells
Principal Investigator: Andrea Cerutti, MD
Period of Support: 05/01/07-04/30/08
Total Direct Costs: $100,000 (Supplemental Award)

Cancer Research Institute
CRI Tumor Immunology Predoctoral Fellowship
Title: The Role of Innate Immune Signals in Normal and Neoplastic B Cells
Principal Investigator: Paul Santini (Dr. Andrea Cerutti’s Lab)
Period of Support: 06/01/07-05/31/09
Total Direct Costs: $25,000

Multiple Myeloma Research Foundation
Seniors Award
Title: Cell Cycle Based Combination Therapy for Multiple Myeloma
Principal Investigator: Selina Chen Kiang, PhD
Period of Support: 06/01/07-05/31/09
Total Direct Costs: $100,000

AIDS Malignancy Consortium/EMMES Corporation
Research Grant Award
Title: Targeting SRC Family Tyrosine Kinases in AIDS-Related Lymphoma
Principal Investigator: Y. Lynn Wang, PhD
Period of Support: 01/01/08-13/01/08
Total Direct Costs: $181,818

CME Conference Update

Tutorial on Neoplastic Hematopathology January 27-February 1, 2008 Boca Raton Marriott Boca Raton, Florida

This course is designed to update physicians on the latest advances in Neoplastic Hematopathology. It will be conducted under the direction of Daniel M. Knowles, MD.

Conference Agenda

SUNDAY JANUARY 27

7:00-8:00 am ..... Registration
8:00-9:00 am ..... The Classification of Non-Hodgkins Lymphomas
Chairperson: John K.C. Chan, MD
9:00-9:15 am ..... Questions
9:15-10:15 am ........ Diffuse Aggressive B Cell lymphomas
John H.C. Chan, MD
10:15-11:00 am Questions
11:00-11:15 am .... Break
11:15-11:30 am .... Immunophenotypic Analysis in the Diagnosis and Classification of Lymphoproliferative Disorders
Nancy L. Harris, MD
12:00-1:30 pm ...... Lunch
1:30-2:15 pm ......... The Classification of Normal B Lymphocytes
Daniel M. Knowles, MD
2:15-2:30 pm ....... Questions
2:30-4:15 pm ........ Peripheral T Cell lymphomas and Angioimmunoblastic T Cell lymphomas
Elaine S. Jaffe, MD
4:15-4:30 pm .......... Questions
4:30-5:15 pm ......... Small B Cell lymphomas
Nancy L. Harris, MD
5:15-6:00 pm .......... Questions
6:00-8:00 pm ....... Registration

MONDAY JANUARY 28

7:45-8:00 am ..... Introductory Remarks
Daniel M. Knowles, MD
Morning Session
8:00-9:00 am ..... Normal T/Lymphoid Tissue: Structure and Function
Nancy L. Harris, MD
9:00-9:15 am ..... Questions
9:15-10:15 am ........ Reactive lymphoidpathoses
Lawrence Vellis, MD
10:15-11:00 am Questions
11:00-11:15 am .... Break
11:15-12:00 pm .... Questions
12:00-2:00 pm ...... Lunch
3:00-3:15 pm ....... Questions
3:15-4:30 pm .......... Break
3:30-4:45 pm ......... Molecular Analysis in the Diagnosis and Classification of lymphoproliferative Disorders
Adam Bagg, MD
4:45-5:00 pm .......... Questions
5:00-5:15 pm .......... Reception

TUESDAY JANUARY 29

Morning Session
Chairperson: Adam Bagg, MD
8:00-9:00 am ..... The Classification of Non-Hodgkins Lymphomas
Nancy L. Harris, MD
9:00-9:15 am ..... Questions
9:15-10:15 am ........ Diffuse Aggressive B Cell lymphomas
John H.C. Chan, MD
10:15-11:00 am Questions
11:00-11:15 am .... Break
11:15-12:00 pm .... Questions
12:00-1:00 pm ...... Lunch
2:00-3:00 pm ....... Flow Cytometric Analysis in the Diagnosis and Classification of Hematologic Neoplasia
Steven Koff, MD
3:00-3:15 pm ....... Questions
3:15-3:30 pm .......... Break
3:30-4:45 pm ......... Molecular Analysis in the Diagnosis and Classification of lymphoproliferative Disorders
Adam Bagg, MD
4:45-5:00 pm .......... Questions
5:00-5:15 pm .......... Reception

WEDNESDAY JANUARY 30

Morning Session
Chairperson: John H.C. Chan, MD
8:00-9:00 am ..... Hodgkin lymphomas
Jennifer L. Burke, MD
9:00-9:15 am ..... Questions
9:15-10:15 am ........ Immune-Deficiency Associated Lymphoproliferative Disorders
Amy Chadbourn, MD
10:15-11:00 am Questions
11:15-12:00 pm .... Pathology of Acquired Immune Deficiency Syndrome
Daniel M. Knowles, MD
12:15-1:15 pm ....... Lunch
3:00-3:15 pm ....... Questions
3:15-4:30 pm .......... Break
3:30-4:45 pm ......... Questions
4:45-5:00 pm .......... The Spleen
Jerome S. Burke, MD
5:00-5:15 pm .......... Questions

THURSDAY JANUARY 31

Morning Session
Chairperson: James Vardiman, MD
8:00-9:15 am ..... B and T Cell Chronic Lymphoproliferative Disorders
Kathy Foscar, MD
9:15-9:30 am ..... Questions
9:30-10:30 am ........ Flamma Cell Dendritics
Robert W McKeever, MD
10:00-10:45 am Questions
10:45-11:00 am ... Break
11:45-12:15 pm .... Bone Marrow Manifestations of lymphomas and lymphoma-like Conditions
Galen Peterson, MD
12:15-1:15 pm ....... Lunch
5:00-5:15 pm .......... Questions

FEBRUARY 1

Morning Session
Chairperson: Lucene Peterson, MD
8:00-9:00 am ..... Chronic Myelogenous Leukemia
John Anasti, MD
9:00-9:15 am ..... Questions
9:15-10:15 am ........ Other Myeloproliferative Disorders
John Anasti, MD
10:15-10:30 am Questions
10:30-11:15 am .... Break
11:15-12:00 pm .... Questions
12:00-1:00 pm ...... Lunch
5:00-5:15 pm .......... Questions

Target Audience
Pathologists, pathologists-in-training and medical oncologists/hematologists.

Accreditation
35.6 AMA PRA Category 1 Credit(s)™

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Design JBRH Advertising & Design, Inc.
The Pathologist is a bi-annual publication of the Department of Pathology and Laboratory Medicine

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Volume 14 • Fall 2007