Path Ways

The Johns Hopkins Medical Institutions | Department of Pathology | Volume 5, Issue 4, April 1, 2003

Director's Corner

J. Brooks Jackson, M.D., M.B.A.

Since the last Pathways newsletter in the Fall, the Department has been doing well in a number of areas. For the first 7 months of this fiscal year, funded research is running 14% ahead of last year which is on target with the Dean's stated goal of a 7% increase for the School of Medicine. The departmental hospital operating margin is 10% above what has been budgeted this year, and professional fee collections are 4% ahead of last year. Articles published in peer reviewed journals primarily authored by Pathology faculty numbered 199 in calendar year 2002.

Dr. J. Brooks Jackson

Our recruitment efforts have been very active in the last several months in the Residency and graduate student programs. The number of resident applications nearly doubled this year and we interviewed 78 applicants compared with 57 last year. The reason for this significant increase is hard to pinpoint, but in my applicant interviews, several factors are

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Inside...

Neuropathology Division in Highlight

INTRODUCTION

The Faculty of the Neuropathology Division are recognized internationally for their experimental studies, diagnostic skills, and consultations concerning disorders of the central and peripheral nervous systems. Pathologists, clinicians, and medical examiners from around the world contact our pathologists for help with diagnoses of tumors and traumatic lesions of the brain and spinal cord, forensic neuropathology, neurodegenerative disorders, and progressive neurologic disease in children. We consult with pathologists and referring physicians on issues related to patient care and can also offer family members information about the causes or the genetic components of diseases of the brain. Moreover, we have established an outstanding research program focusing on neurodegenerative diseases and experimental therapeutics. Finally, over the years, we have trained many House Officers and Investigators who are major contributors to the field.

RESEARCH

Over the past several years, the major research efforts of investigators in the Division of Neuropathology have focused on several human neurodegenerative diseases and on genetically engineered mouse models, which have proved to be of extraordinary value for studying disease mechanisms and for experimental therapeutics. In collaboration with a variety of colleagues at Johns Hopkins University School of Medicine, our group has made very substantial progress with regards to Alzheimer's Disease (AD), Parkinson's Disease (PD), Amyotrophic Lateral Sclerosis (ALS) (Lou Gehrig's Disease), and the trinucleotide repeat diseases, like Huntington's Disease (HD).

ALZHEIMER'S DISEASE

The strategies and discovery process are well illustrated by studies of AD, a late-life neurodegenerative disorder characterized by progressive memory and cognitive impairments leading to dementia. Some individuals inherit the disorder as an autosomal dominant and this familial form of the illness (FAD) has been linked to mutations in three genes encoding: the Amyloid Precursor Protein (APP), presenilin 1 (PS1), or prese-

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Director's Corner

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apparent. First, the reduction in the requirement for board certification from 5 to 4 years is partially responsible. Second, a number of specialties such as surgical specialties have experienced dramatic decreases in reimbursement rates compared with Pathology. Third, the headache of arguing with HMOs and third party payers over patient care issues combined with less time to spend with patients is resulting in a shift away from family practice, pediatrics, and internal medicine. Fourth, I believe the greater flexibility of work schedules in Pathology is becoming more attractive especially to the increasing number of female medical students. We will be taking 9 residents next year (8 through the Match). The graduate student program also experienced a 34% increase in applicants this year. We will be offering 6 positions in the program for next year which will mean we will have 21 students in the program next year. Our first two graduates of the program (Jon Brody and Laura Richman) successfully completed the program earlier this year.

The two areas that continue to pose challenges are the increasing number of regulations and the need for more space. The latest regulatory requirement imposed by the government is the HIPAA act (Health Insurance Portability and Accountability Act) which requires that a written authorization be obtained from patients before disclosing private health information either internally or externally unless one is directly involved in the patient's care. This requirement also applies to research subjects (and their specimens) as well as to the use of health information to identify potential donors. It is very important that faculty, fellows, residents and staff become acquainted with these regulations through the University/Hospital websites and conferences on this subject. Failure to comply can result in civil and criminal penalties.

Office space and clinical/research laboratory space continues to be very tight. We are scheduled to have 13,500 additional space in the Cancer Research Building (CRB2) next to the Bond Street building when it is completed in the Fall of 2004. In the meantime, the Broadway Research building is scheduled to open this summer and then occupied in the fall. Pathology will then receive 5000 sq ft of temporary space in Jefferson (old Oncology building) until we can move into the CRB2. This temporary space, which is primarily research laboratory space, will be used for new faculty recruitment and for those faculty who need additional space for specific projects. Planning for the new Acute Care Tower and Women and Children's Hospital is now underway in full. A number of departmental faculty and staff are involved in this interdepartmental effort. These buildings will be built on the site of the Jefferson Building and the site of the laundry on the corner of Orleans and Wolfe Streets. The plan is to build these two hospital buildings simultaneously and have them completed within the next 5 years. I will be holding periodic meetings with faculty and staff to obtain feedback and keep you informed of the progress on these projects.

In the meantime, please be patient as we are continuing to make progress in a number of different areas.

Pathology Alumni

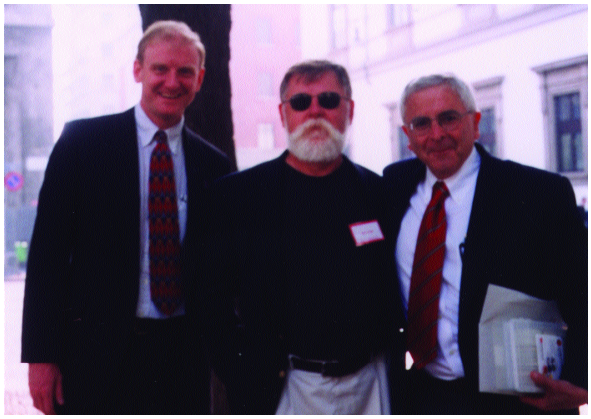
We are interested in updating our Alumni records.

Please send us your preferred mailing address and preferred email address.

Email your information to **pathology@jhmi.edu**

"Where in the world is Pete Lund?"

Have you ever been out of town and had the experience of running into an old friend, relative, or co-worker completely by chance? Well, it seems that Pete Lund, our recently retired Director of Pathology Photography, has a knack for this. In September 2001, Norm Barker was visiting Holyrood Castle in Edinburgh, Scotland and had a real surprise when he bumped into Pete while touring the grounds. More recently, Drs. Askin and Hruban were walking in a square in Milan, Italy after lecturing in the Hopkins-Milan Surgical Pathology Course, when they heard "hey Fred, hey Ralph." When they turned around, much to their amazement, there was Pete Lund. Pete was on a vacation tour of Italy with his wife Sandy, and just happened to be in the same square as Drs. Askin and Hruban. So if you are traveling abroad, keep an eye out for Pete. You never know where he will pop up next!



Awards / Recognition

Pathobiology Graduate Program's First Graduate Wins National Prize

Jonathan Brody, Ph.D. is ranking up a number of firsts. He is the first member of the first class of the Graduate Program in Pathobiology to earn a Ph.D. degree. He was the first graduate student to serve as Chief Graduate Student, representing student interests to the Program and Department leadership. This April, in another first, Brody will receive the prestigious predoctoral Experimental Pathologist-in-Training Award from the American Society for Investigative Pathology and present his findings at the Chugai Symposium at the Society's annual meeting as part of EB2003 in San Diego.

The Experimental Pathologist-in-Training Award is given to the individual submitting the most meritorious work in any given year. To earn the award, Jonathan Brody submitted part of his dissertation work performed in the laboratory of Dr. Gary Pasternack. This work focused on how members of the pp32 gene family exert an anti-tumor effect by seeming to help cells decide whether to remain immature and proliferative, or to differentiate and stop dividing. Brody dissected the pp32 molecule and identified the functionally important regions. He then went on to make key observations about pp32 and differentiation, showing that it apparently acts through histone acetylation, a sort of molecular language mark-up for genes that determines whether or not they will be active.

Jonathan Brody has been a Ph.D. since completing all requirements last October. He will officially receive his hood and his diploma at commencement this coming May. Although he has graduated, he hasn't gone too far away. After a few months spent tying up loose ends, Brody began a postdoctoral fellowship with Dr. Scott Kern in February.

11th annual Martin Luther King Jr. Community Service Awards

A medical lab technician in the School of Medicine's Pathology Department, John Matthew has been recognized for his efforts with the non-profit organization Kairali of Baltimore. Matthew helped found and is currently president of the Indian organization, which has worked with Habitat for Humanity and sponsors youth soccer tournaments and other endeavors.

Congratulations to John Matthew for receiving the Martin Luther King Jr. Community Service Award honoring his demonstration of community service with a spirit of volunteerism and citizenship.

Jung Whan Kim, DVM –
Recipient of a 5-year Predoctoral Fellowship from the Howard Hughes Medical Institute.

Jens Koopman, M.D. –
2003 GlaxoSmithKline Outstanding Scholar-in-Training Award from the AACR

Paul M. Ness, M.D. –
Appointed Editor of Transfusion for the American Association of Blood Banks

Anthony Parker, Ph.D.–
Post Doctoral Fellow in Dr. James Eshleman's lab received a Scholar in Training Award from the AACR

Bin Yang, Ph.D. –
2003 Pathologist-in-training Award from the Hans Popper Hepatopathology Society

Robert Pu, M.D. –
2003 Stowell-Orbison Award

Primary Faculty Changes - Since September 2002

New Faculty

Alex Rai, Ph.D.,	Instructor	Chemistry
Hongxiu Ji, M.D, Ph.D.,	Assistant	Gynecologic Pathology
Tong Li, Ph.D.,	Research Associate	Neuropathology
Christine Iacobuzio-Donahue, M.D., Ph.D,	Assistant	G.I. Pathology
Shiwen Peng, Ph.D.,	Research Associate	Gynecologic Pathology

Departures

Darryl Carter, M.D.,	Assistant Professor	Qual Tech
Ellen S. Pizer, M.D., Ph.D.,	Associate Professor	Washington Pathology Consult, Seattle, WA
Jankowsky, Ph.D.,	Research Associate	Caltech, Pasadena, CA

Promotions

Angelo M. De Marzo, M.D., Ph.D.	Associate Professor	Kidney/Urologic
Richard Roden, Ph.D.,	Associate Professor	Gynecologic Path
Chien-Fu Hung, Ph.D.,	Assistant Professor	Gynecologic Path
Nicole Parrish, Ph.D.,	Assistant Professor	Microbiology
Zhiping Qian, M.D.,	Assistant Professor	Immunology

Neuropathology Division in Highlight

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nilin 2 (PS2). Characteristic features of the brain pathology in AD are: extracellular amyloid deposits, comprised of a 4KD peptide (termed Aβ), generated by β- and γ-secretase cleavages of APP; and neurofibrillary tangles and neurites, which represent intraneruonal accumulations of modified tau proteins in the cell bodies and distal terminals, respectively.

Investigations in the Neuropathology Laboratory, led by Dr. David Borchelt, have taken advantage of information from genetics, biochemistry, and neuropathology of the human disease. The group has produced transgenic mice that overexpress one or two of the genetic mutations associated with FAD. These animals develop Aβ amyloidosis in the brain. Dr. Alena Savonenko, an oustanding behavioral neuropsychologist in our Department, has demonstrated that mice carrying two FAD-linked mutations develop memory impairments as demonstrated on working memory tasks. These deficits worsen with age and appear to be related to the presence of accumulations of the Aβ42 peptide in the brains of these mice. The animals exhibit Aβ-containing neuritic plaques, but do not show neurofibrillary tangles, possibly because the mouse tau is somewhat different from human tau. As described below, these transgenic models are of great value for experimental therapeutics.

Drs. Phil Wong, Huaibin Cai, and Tong Li, have knocked out some of the genes postulated to be critical in the generation of the Aβ peptide. First, Drs. Wong and colleagues, including Dr. Samuel Sisodia, now at the University of Chicago Medical School, knocked out *PS1* and showed that *PS1* null mice die in late embryogenesis because PS1 is a component of γ-secretase, which makes one of the cleavages critical for releasing toxic Ab into the brain. More recently, Dr. Li has knocked out another gene, termed *Nicastrin*, and has shown that, it too is part of the γ-secretase complex. Mice lacking Nicastrin, exhibit an embryonic lethal phenotype because this gene product, like PS1, is critical for signaling by Notch1, a key participant in a pathway essential for cell fate decisions important during development. Significantly, cells from *PS1* or *Nicastrin* null mice, because they lack γ-secretase activity, cannot generate Aβ.

However, the most exciting discoveries have come from recent gene knockout work carried out by Drs. Wong, Cai and colleagues. They have demonstrated that a protease, termed β APP Cleaving Enzyme (BACE1), makes the first and rate-limiting cleavage that ultimately leads to the release of toxic Aβ. Cultured cells lacking BACE1 are unable to make Aβ. Moreover, in vivo, mice lacking *BACE1* do not form Aβ in their brains, even when two FAD-linked mutant transgenes are also expressed in the brains of these mice. Significantly, preliminary studies by Drs. Savonenko and Fiona Laird have shown that these mice do not appear to develop age-associated memory deficits. This work is extraordinarily exciting because it demonstrates that BACE1 is a very attractive target for anti-Aβ therapy and that inhibition of BACE1 could potentially have an impact not only on the biochemical and structural pathology in the brain, but on the memory performance of individuals with AD.

Drs. Sheng and Koliatsos have recently published a study in which they show that Aβ amyloid exists in a dynamic state in the brain (i.e. there is a balance between formation of Aβ and its clearance). In *APPswe* and *APPswe/PS1TgΔE9* mice, they showed that amyloid deposition in the hippocampus, is dramatically reduced when specific synaptic inputs are removed. These findings demonstrate for the first time that amyloid plaques are dynamic structures, whose persistence may depend on constant supply of APP. This discovery is very encouraging for therapeutics, in that blocking of the formation of the toxic Aβ42 peptide may reduce the Aβ burden and perhaps lead to recovery of functions.

The studies in Alzheimer's Disease demonstrate the extraordinary value of transgenic and gene targeting studies with regards to analyses of mechanisms of the disease and the identification of targets for therapy. Work by Drs. Troncoso, Borchelt and colleagues provide another illustration of the value of these mice for experimental therapeutics. Following the lead of a biotechnology company, Dr. Troncoso and his colleagues have immunized mice with Aβ and Freud's adjuvant have shown that vaccination reduces amyloid burden in the brain. Moreover, following passive transfer of Aβ antibodies into the mutant mice, Drs. Troncoso and Savonenko have demonstrated that memory deficits in these mice can be quickly and transiently reversed.

PARKINSON'S DISEASE

Similar progress is being made by Drs. Michael Lee, Dr. Y. Xu, and colleagues who are studying Parkinson's Disease. This common late-life neurodegenerative disorder, associated with slow movements, rigidity and tremor, is, in some cases, inherited in an autosomal dominant fashion. One of the mutant genes encodes α-synuclein (α-syn), a neuronal protein which appears to function at synapses. When Dr. Lee and coworkers introduced the A53T α-*syn* into mice, the mice developed a motoric disorder, similar to those seen in cases of PD. Moreover, the brains of the mice contained N- and C-termini and truncated α-syn peptides. Significantly, the presence of clinical signs and brain pathology in the mice appeared to track with the presence of the cleavage products. Drs. Neva West, Lee and colleagues, working with Dr. J. Troncoso, are attempting to determine whether similar fragments occur in PD. Finding that these fragments occur in the human disorder would suggest that proteolytic cleavages of α-syn, like the BACE1 and γ-secretase cleavage of APP in AD, may generate toxic peptides that are important in the pathogenesis of PD. Again, like the BACE1and γ-secretase stories, inhibition of the enzymes cleaving, α-syn might provide a new mechanism-based treatment of PD.

MOTOR NEURON DISEASES

Mutations in Cu/Zn superoxide dismutase (SOD1) cause autosomal dominant familial ALS. By introducing mutant SOD1 transgenes into mice, Dr. Wong and colleagues have developed a mouse model for

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Neuropathology Division in Highlight

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familial ALS and have shown that mutant SOD1 causes disease through a dominant gain of adverse property. The nature of this toxic property remains unclear. Using these SOD1-mutant mice, Dr. Jamuna Subramanian, has examined the hypothesis that SOD1 mutant mediated toxic copper chemistry causes motor neuron disease. Because free copper can be toxic in cells, the delivery of copper to specific proteins within various compartments of the cell is tightly regulated through specific copper chaperones. The delivery of copper to SOD1 is mediated through a soluble protein called CCS (copper chaperone for SOD1). We have generated CCS-deficient mice and demonstrated that CCS is necessary to deliver copper to mammalian SOD1; these null mice show no SOD1 activity. To test whether Cu in mutant SOD1 is required to cause motor neuron degeneration, Dr. Subramanian crossbred CCS deficient mice to a series of mutant SOD1 mice. The onset, progression and pathology of the disease observed in a series of mutant SOD1 mice lacking CCS are similar to these features occurring in mutant SOD1 mice on either the CCS+/+ or CCS+/- background. Significantly, copper incorporation into mutant SOD1 in spinal cords of FALS mice lacking CCS was defective. Taken together, these results do not support a role for the toxicity of copper in the pathogenesis of mutant SOD1-induced motor neuron disease.

Recently, a new gene, termed *ALS2*, on chromosome 2 has been linked to several families with juvenile ALS. *ALS2* encodes a protein termed alsin, which shares homology to GTPase regulatory proteins. Because mutations in *ALS2* is inherited as an autosomal recessive and that the identified mutations all lead to a premature truncation of the majority of the protein, it is hypothesized that the disease mechanism is associated with a loss of ALS2 function. Dr. Huaibin Cai has now ablated the gene encoding ALS2 in ES cells and generated chimeric mice in order to develop a mouse model of this rare form of ALS. Dr. Cai will use this model to clarify the mechanisms whereby loss of ALS2 leads to selective degeneration of motor neurons, and to elucidate of the functional role of ALS2 and its relationship to the more common mutant SOD1-linked ALS or to sporadic ALS.

Dr. Lee Martin and his colleagues are investigating the mechanisms whereby neurons die, either by necrosis or apoptosis. In a variety of model systems, including mice with motor neuron disease, they have begun to define the roles of specific molecules and pathways in models and in human disease. A fuller understanding of death effects on mechanisms should help in the design of therapies to prevent or ameliorate all degeneration.

Finally, in an effort to develop replacement therapies for neural repair, Drs. Yan and Koliatsos are working with different types of neural stem cells in several models. For example, they have begun to replace motor neurons that have degenerated after their axons and are cut. Following implantation of stem cells, some of these precursors enter into the neuronal lineage and extensively migrate throughout the gray matter and nerve roots. Some of these cells acquire mature neuronal phenotypes, extend into the motor roots, and form synapses.

CLINICAL SERVICE

EXPERIENCE

Our diagnostic expertise in neuropathology includes such specialties as adult and pediatric brain and spinal cord tumors; cerebrovascular disease; trauma; forensic neuropathology; AIDS; and neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease, amyotrophic lateral sclerosis and progressive supranuclear palsy.

EXPERTISE

Expert consultation

Director of Neuropathology Surgical Consultations Services, Dr. Peter Burger is one of the world's leading authorities in the interpretation of surgical specimens of brain and spinal cord tumors in adults and children. He is co-author of the AFIP *Atlas of Tumor Pathology, Tumors of the Central Nervous System*, and has authored two major textbooks in central nervous system tumors. Currently, he is the review pathologist for several clinical trials studying new therapies for patients with brain tumors. Dr. Burger personally oversees all diagnostic evaluations sent to the service. Dr. Charles Eberhart, M.D., Ph.D., who specializes in the pathology and biology of is tumors of the central nervous system, has developed a research program utilizing genetically-based models of neoplasia in he brain.

Dr. Barbara Crain is an expert in autopsy neuropathology with an emphasis on epilepsy and cerebrovascular disease. She is vice chair of the Neuropathology Committee of the College of American Pathologists.

Dr. Juan Troncoso has a research program on neurodegenerative diseases, including Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease and plays a key role in our NIH funded Centers for these diseases. He established the Brain Resource Center, which is the repository for brain tissue specimens at Johns Hopkins University, and, along with Dr. Crain, analyzes this case material. In addition to his research and service efforts, Dr. Troncoso has served as neuropathologist for the Office of the Chief Medical Examiner of Maryland for more than 15 years.

Special capabilities and services

Our laboratory is fully equipped to perform the special diagnostic tests needed to study diseases of the brain, particularly the neurodegenerative disorders, and has vast experience with the methods required for these studies. Members of our group are skilled in interpreting stereotactic needle biopsies of brain lesions and can perform in-situ hybridization, immunohistochemistry, light microscopy, immunofluorescence, and electron microscopy, as necessary. The Department's Molecular Diagnostics Laboratory performs molecular testing for the diagnosis of certain types of brain tumors.

Donald L. Price, M.D.
Director, Division of Neuropathology
Professor of Pathology, Neurology and Neuroscience

FUNDING OUR FUTURE

Generous Support from Dr. Elizabeth Williams

In April 2000, Dr. Peter Argani created the Johns Hopkins Gallbladder and Bile Duct Cancer web site (http://pathology2.jhu.edu/gbbd). Modeled after the pancreatic cancer web site created by Dr. Ralph Hruban, this was designed with several purposes in mind. First and foremost, it was designed to help patients and family members of patients with this deadly disease gain a better understanding of the disease process, signs, and symptoms. Numerous medical illustrations by Jennifer L. Brumbaugh, M.A. make many of the difficult anatomic and physiologic relations of the biliary tree easy to understand. Second, the site was designed to provide a forum for patients and family members of patients with this disease to communicate through the on-line discussion board (chat room). Third, it provides easy access for patients to specific physicians at Hopkins who specialize in the treatment of biliary cancer, so that patients can easily identify an expert to see at the time of diagnosis. Fourth, it provides updates on the most current research on biliary cancer performed at Johns Hopkins and abroad.


Dr. Elizabeth Williams

Elizabeth Williams, Ph.D., was one of the first to find The Johns Hopkins Pathology Gallbladder and Bile Duct Cancer web site. She immediately made a lasting impact on biliary cancer treatment and research here. Elizabeth was one of the most active participants in the chat room, and her willingness to share her experiences with others led to reciprocation by other patients and overall increased communication in this aspect of the site. When Elizabeth initially entered the chat room, it was not uncommon for no correspondences to occur in a given day. Now, there are typically 5 or more different correspondences each day. The increased visibility and activity of the web site led others, such as the family of Margaret Lee (see previous issue of Pathways), to visit the site and become affiliated with Johns Hopkins Pathology. Elizabeth also brought her passion for finding a cure for this deadly disease to Johns Hopkins. In a brief period of time, Elizabeth learned a remarkable amount about her disease, and began the search for potential therapies. Elizabeth frequently emailed Dr. Argani and Dr. Ralph Hruban to discuss advances in research and visited The Johns Hopkins Gastrointestinal Pathology research labs (including that of Dr. Anirban Maitra) on multiple occasions in 2001. All of us were struck by the depth of her understanding of her disease, and how advanced her knowledge of research in this area. Indeed, several of Elizabeth's suggestions led to projects in biliary cancer at Johns Hopkins, including several which will be presented at this year's USCAP Meeting in March.

Unfortunately, Elizabeth A. Williams succumbed to bile duct cancer early in 2002. To the end, she remained dedicated to finding a cure for all patients with this disease, and remained convinced that only through further cutting-edge research could the seeds for a cure be sown. In her will, Elizabeth Williams donated $500,000 to The Johns Hopkins Pathology Biliary Cancer Research Fund established by Drs. Argani and Maitra. This remarkable donation is a tribute to the remarkable person whom we were privileged to have known.

Generous Support from the Roy L. Jeannotte Foundation

In January 2000, Dr. Elizabeth Montgomery created the Barrett's Esophagus web site (http://pathology.jhu.edu/beweb). The web site is a collaboration between patients and the physicians and scientists of Johns Hopkins. It grew out of a shared passion to improve the quality of information and resources available. The Jeannotte family found the web site in their search for a better understanding of Barrett's Esophagus and its treatment and the research being done with esophageal cancer.

On June 28, 2002, the Roy L. Jeannotte family came to Hopkins to visit Dr. Elizabeth Montgomery to see the research being done in the labs and to form a partnership with the Department of Pathology. Every dollar generated by the Foundation directly funds research to isolate the genes associated with the development of esophageal cancer. In September 2002, the family held the Roy L. Jeannotte Memorial Golf Classic in Finchburg, Massachusetts to honor Roy's passion for golf and to support Dr. Montgomery's research. To date, $60,000 has been donated by the Roy L. Jeannotte family. This remarkable donation exemplifies the wonderful partnerships that have been established between private donors and department investigators in the battle against human suffering.

The Joseph C. Eggleston Fund in Surgical Pathology


Joseph C. Eggleston

The Joseph C. Eggleston Fund in Surgical Pathology honors Joseph C. Eggleston, M.D., '62, former Director of Surgical Pathology and Professor of Pathology. Dr. Eggleston touched many of our lives with his dedication to excellence in Surgical Pathology and his outstanding teaching. The income from this endowed fund will be allocated each year to a surgical pathology resident or junior faculty member in the Division of Surgical Pathology for projects that support their career development in surgical pathology. We are pleased to announce that Dr. Mohammed Ansari-Lari is the first recipient of an award from the Joseph C. Eggleston Fund. Dr. Ansari-Lari received the award for his work in hematopathology.

The Yener S. Erozan Fellowship in Cytopathology

The Yener S. Erozan Fellowship in Cytopathology honors Yener S. Erozan, M.D., Director Emeritus of the Cytopathology Institute and past President of the American Society of Cytopathology. Dr. Erozan is a much loved teacher and diagnostician who continues to have a wonderful influence on the Division of Cytopathology and on the Department. Income generated from this endowment will be allocated to a fellow in Cytopathology to support the development of their career.

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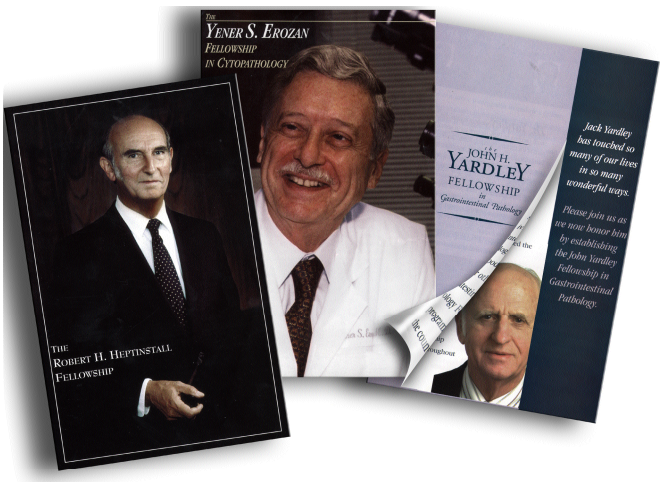

FUNDING OUR FUTURE

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The Robert H. Heptinstall Fellowship

The Robert H. Heptinstall Fellowship honors Robert H. Heptinstall, M.D., former Baxley Professor and Director of Pathology. Dr. Heptinstall is well known to all of us for his text book, his scientific accomplishments and for his wonderful personality – his impatience with pretension, his wit and humor, and his vivid storytelling. The Robert H. Heptinstall Fellowship will promote research activities and clinical training of outstanding young pathologists pursuing careers in research.

The John H. Yardley Fellowship in Gastrointestinal Pathology

Thanks to your generous support, we are pleased to announce that over $850,000 has already been raised for The John H. Yardley Fellowship in Gastrointestinal Pathology. This Fellowship will promote the research activities and/or clinical training of promising pathologists pursuing advanced training in the study of gastrointestinal liver disease in the Department.

The recipient of the John H. Yardley Fellowship for the Academic Year 2003-2004 is Dr. Parry Dilworth. Dr. Dilworth completed her residency training at the University of Minnesota. The John H. Yardley Fellowship is a wonderful example of how private giving can both honor our treasured faculty and, at the same time, support the careers of young pathologists.

We ask that you consider supporting these funds and fellowships annually. What a wonderful way to honor these great physicians. We are enclosing a self-addressed return envelope to facilitate your contribution this year. Please contact Dr. Ralph Hruban at 410-955-9132 or rhruban@jhmi.edu for additional information. If you would like to use a separate envelope, you may send your tax-deductible contribution payable to The Johns Hopkins University to:

Attn: Mabel P. Smith
Department of Pathology
Johns Hopkins Hospital
Carnegie 428
600 North Wolfe Street
Baltimore, MD 21287-6417

Thanks to all of you that have made this support a reality for our young pathologists. ■

New Grants and Contracts Awarded to Pathology Faculty Through December 31, 2002

FACULTY MEMBER	AWARD TYPE	AGENCY	DATES	TOTAL FUNDING
Baldwin, William	R21/R01 Grant	NIH/NHLBI	08/01/02-07/31/07	1,635,000
Berg, Karin	Subcontract	University of Alabama- Birmingham	08/01/02-07/31/03	148,667
Borchelt, David	Grant	Alzheimer's Association	08/01/02-07/31/04	250,000
Borowitz, Michael	Contract	Wyeth Pharmaceuticals	06/27/02-06/26/03	18,368
Eberhart, Charles	Grant	Children's Brain Tumor Fdtn.	11/01/02-10/31/04	100,000
Haas, Mark	Grant	National Kidney Foundation-MD	07/01/02-06/30/03	8,179
Hamad, Abdel	Inst. Grant	JHU/IRG	08/01/02-07/31/03	20,000
Hung, Chien-Fu	Grant	American Cancer Society-IRG	11/01/02-10/31/03	20,000
Jackson, Brooks	Subcontract	Family Health International	08/01/02-01/31/03	100,000
Jackson, Brooks	U01 Supplement	NIH/NIAID	09/30/02-02/29/04	1,800,000
Kickler, Thomas	Contract	Sysmex Corporation	06/30/02-12/31/02	17,000
Koliatsos, Vassilis	Inst. Grant	JHU Center for ALS Research	07/01/02-06/30/04	169,097
Kurman, Robert	Grant	DoD - Army	08/01/02-07/31/05	2,319,646
Maitra, Anirban	Grant	Cancer Research Foundation	01/15/03-01/14/05	80,000
Merz, William	Contract	Merck & Co.	07/01/02-12/31/02	10,000
Ness, Paul	U01 Grant	NIH/NHLBI	09/01/02-08/31/07	1,499,867
Pasternack, Gary	Grant	James S. McDonnell Foundation	08/01/02-07/31/03	150,000
Price, Donald	Grant	Adler Foundation	07/01/02-06/30/03	35,000
Racusen, Lorraine	Grant	National Kidney Foundation-MD	07/01/02-06/30/03	10,000
Roden, Richard	Grant	American Cancer Society	07/01/02-06/30/06	774,000
Rose, Noel	R01 Grant	NIH/NHLBI	09/01/02-08/31/06	1,471,500
Rosenthal, Dorothy	Contract	Tripath Imaging	06/21/02-06/20/03	55,560
Schneck, Jonathan	R21 Grant	NIH/NHLBI	09/01/02-08/31/05	735,750
Shih, Ie-Ming	R21 Grant	NIH/NCI	07/01/02-06/30/03	163,387
Sokoll, Lori	Contract	Roche Diagnostics	06/10/02-12/31/02	17,000
Sokoll, Lori	Contract	Roche Diagnostics	09/01/02-03/31/03	24,000
Su, Gloria	K01 Grant	NIH/NCI	09/01/02-08/31/07	726,982
Torbenson, Michael	Contract	Maxim Pharmaceuticals	09/01/02-08/31/03	9,560
Tuder, Rubin	Grant	Alpha-1 Foundation	07/01/02-06/30/04	200,000
Wong, Phil	R01 Grant	NIH/NINDS	07/01/02-06/30/07	1,941,565
Wong, Phil	R01 Grant	NIH/NINDS	12/01/02-11/30/07	1,941,565
Total				$16,451,693

Ella H. Oppenheimer (1897-1981)

Associate Professor Emeritus (1963 – 1981)
Associate Professor of Pathology, JHSOM (1945 – 1963)
The Johns Hopkins University School of Medicine (Class of 1924)

If you sit in the Johns Hopkins Pathology Library facing the fireplace, eyes in a portrait over the mantle instantly engage you. They are those of a smiling mid-aged woman, at once benevolent and critical. The plaque under the large photograph identifies her as Ella H. Oppenheimer, M.D., 1897-1981. In a department that boasts the heritage of noted pathologists William H. Welch and William G. MacCallum, we had never heard of Dr. Oppenheimer; yet her portrait hangs in a special room dedicated to her memory. We were compelled to discover who she was. More than a "triple threat", Ella was a scientist dedicated to describing mechanisms of serious pediatric diseases, a great teacher of residents and medical students, a respected clinical colleague, plus a woman successfully involved with her family.

Ella Oppenheimer was born into the famous Baltimore Hutzler family, known for the downtown department store of the same name. For nearly a generation, Hutzler's was the place to shop in Baltimore, but her modesty never allowed her to mention this family connection. Ella was not a challenged student and took summer courses during high school, finishing earlier than usual. Despite her boredom, she performed sufficiently well to be accepted into Goucher College in Towson, where she was awarded an A.B. degree in 1918. In 1973, Goucher would recognize her lifetime accomplishments by awarding her an honorary Doctor of Science degree. During an era in which women were expected to marry young and to stay at home, Ella entered the Johns Hopkins School of Hygiene in 1919. Her professors encouraged her to transfer into the medical school, and in 1921 she followed this advice to obtain her M.D. in 1924. Upon graduation, she considered a career in pediatrics, but Professor MacCallum helped her decide that pathology was to be her profession. During that period, she met and married her husband, Henry Miller, a native Baltimorean, a stockbroker, and for years the treasurer of Associated Jewish Charities. Their personal collaboration would last for 35 years and would produce two children, and six grandchildren.

Following the trajectory of Dr. Oppenheimer's career at Hopkins is instructive for the tenacity and patience that faculty, especially those that were female, had to possess in order to ascend through the Hopkins hierarchy. After completing medical school, Dr. Oppenheimer joined the faculty of the Pathology department as an Assistant. In 1925 she was promoted to Instructor and would hold that position for 20 years! Not until the end of World War II, in 1945, would she be promoted to the level of Assistant Professor. As is the case today, many faculty held positions both in the hospital and University systems. From 1941-1949 Dr. Oppenheimer held the titles of Assistant Pathologist, Associate Pathologist, and Pathologist of the hospital. Thirty years after joining the faculty, Dr. Oppenheimer was promoted to Associate Professor, the highest rank that she would achieve. In 1963, she became Associate Professor Emeritus.

According to her daughter, Patsy Perlman, Ella was "never a liberated woman." She loved what she did, and did what she wanted to do. She admired other women and was modest about her own accomplishments; so much so, that she returned her salary back to the Pathology Department. Imagine one of today's physicians doing the same! For years she was the only woman physician in the pathology department, a fact that can be verified by viewing the annual departmental photographs along the walls of the 4th floor corridor of Carnegie Building. Dr. MacCallum recognized her dedication early in her career, and gave her the task of compiling the diagnostic index of the autopsy files. Before computerization this was an immensely tedious chore. The value of this index cannot be underestimated. Without it, all of the rich autopsy case material from Dr. Welch forward would not have been accessible or available for research, and therefore, essentially lost. In addition, she scheduled the courses for undergraduate medical students, and assembled and reviewed with them the teaching collections, both gross and microscopic.

Ella H. Oppenheimer (1897-1981)

Her greatest contributions and personal stress occurred during World War II when many of the young pathologists were serving in the war effort. Ella held the department together, especially the teaching of medical students. John (Jack)Yardley, M.D., now professor of pathology, but once a second year medical student (1950-51), reminisced during her memorial service about her teaching style. "Students thrived on her decisive, no-nonsense approach. She created both interest and desire to learn. There was awe of her – and let us face it – a certain amount of fear, too. Not that fear is always a bad thing pedagogically when it is so obviously mixed with the underlying warmth and understanding which Dr. Oppenheimer also imparted. She had that rare attribute of knowing how to both comfort the afflicted and to afflict the comfortable."

True to the Hopkins tradition, Ella was dedicated to Discovery, and contributed significantly to our understanding of Cystic Fibrosis. She first began publishing on Cystic Fibrosis in 1940 and developed a particular interest in pancreatic lesions in these patients. She would continue work on this disease until her death, publishing at least 25 articles in this area (1,2,3). Much of her early research (beginning in the 1920's) dealt with the culturing and study of

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Ella H. Oppenheimer (1897-1981)

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Vaccinia virus (4). Her keen interest in infectious diseases would broaden to include a number of studies on Rubella (5) and Syphilis, with publications on these topics spanning some 60 years. Dr. Oppenheimer also carried out a number of studies on the heart, including ones on myocarditis and congenital cardiac abnormalities. These studies on the heart provided her with the opportunity to collaborate with another famous female Hopkins physician, Dr. Helen Taussig (6). Her fascination with pediatric and congenital illnesses was clear; regardless of the research avenue, Dr. Oppenheimer was usually focused on childhood aspects of disease.

While her contributions were significant during her tenure as a faculty member, much of her work would begin in her "second career" following the death of her husband and her "retirement." Prior to this time, travel by faculty members was not encouraged. In her role of Emeritus, she worked tirelessly for 18 years. She discovered the joys of travel and sharing ideas with colleagues at scientific meetings. As a result of these interactions, she was a founding member of the Pediatric Pathology Club and would become its President at the age of 78. This club became a national organization and was the mother organization of the modern Pediatric Pathology Association. At age 83, Dr. Oppenheimer was still exploring areas in medicine that had occupied her throughout her career. In fact, at the time of her death, she had three papers in press on Cystic Fibrosis (7), Syphilis, and Rubella!

But Ella's dedication to Discovery did not stop at the microscope. She traveled the world collecting seashells, and catalogued her collection with the same zeal devoted to the index of autopsies. According to Yardley, "Everything I saw Dr. Oppenheimer do, she did with huge vigor and enthusiasm. This applied not only to her efforts as a practicing pathologist, teacher, and scientist. It was also evident in her many other interests and hobbies, including, in addition to her grandchildren, such diversified activities as gardening, golf, needlepoint, and shell collecting. I also remember that she was a devoted Orioles fan, deriving tremendous pleasure not only from the game, but from the stockholders' meetings, which she thought were a gas."

This very complex woman accomplished what few of us can. She earned the enormous respect of her peers during an era in which discrimination of women was rampant; maintained the freedom to pursue her diverse hobbies; and allocated the energy to raise a family and sustain a marriage. Arnold Rich, M.D., and Ella were colleagues who admired each other greatly. As part of an internal departmental document that summarized events during the years 1931-1965, Dr. Rich gave tribute to the role Ella played in the department. "There is no doubt whatsoever in my mind that the quiet, efficient, unselfish devotion of this remarkable lady to these supposedly mundane but actually essential tasks has been the major factor in the continuing excellence of this Department. Through the years, many members of the staff have come and gone, some to become internationally famous for their research and academic accomplishments. All are in her debt and, furthermore, all know it and admit it. Dr. Oppenheimer has remained, holding the Department on course, and giving it substance, dependability, and continuity." Ella had the opportunity to return the praise in a published eulogy to Arnold Rich in 1979 (8).

Her last departmental chair, Robert H. Heptinstall, M.D., spoke fondly during her memorial service. He recalls "Ella continued to come into her office every day up until the day she died, and did a great deal for the residents and young people in the Department, giving them guidance and advice with their cases and projects. She was a great source of wisdom to me, and the more senior people, and we constantly got her opinion when trying out anything new. Those of you who knew Ella well, will realize this was often done to get her permission, rather than her opinion."

Sitting in the Pathology Library in the 21st Century, Ella's portrait reminds us that dedication to your own beliefs and commitment to purpose are the most important personal attributes. She transcended the culture of her era and that of a very chauvinistic institution, and left both much better because of her example. We are much better for having investigated her life.

We are grateful to Dr. Oppenheimer's daughter, Patsy Perlman; to Mabel Smith, administrator of the Pathology department; and the staff at Johns Hopkins Alan Mason Chesney Medical Archives, for sharing their memories and momentoes of Ella Oppenheimer.

Dorothy Rosenthal, M.D.
Michael Viglione, M.D.

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7. Similarity of the Tracheo-bronchial mucous glands and epithelium in infants with and without Cystic Fibrosis. Hum Pathol. 12 (1): 36-48, 1981

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Department of Pathology Incoming House Staff, 2003-2004

Shien Micchelli

Shien Micchelli was born in Minneapolis, Minnesota. She received her BS in zoology and psychology from the University of Wisconsin and remained there to earn an MS in molecular entomology (yes, bugs). Before going to medical school, Shien worked as a pharmacy technician. She comes to us from Tufts University School of Medicine. She is an avid photographer who enjoys cooking and Chinese language and culture. (AP/CP)

Jeffrey Schowinsky

Jeffrey Schowinsky was born in Zanesville, Ohio. He received his BA in biology from the University of Chicago. After college, Jeffery worked on diabetes research at the Ben May Institute of Cancer Research. He went to the Medical College of Wisconsin where he was an active volunteer for Habitat for Humanity, and in a local health clinic. He enjoys traveling, especially to National Parks and Scrabble. (AP/CP)

Joshua Wisell

Joshua Wisell was born in Denver, Colorado. He attended the Univeristy of Colorado School of Medicine after attending Colorado State for his BS in biology. During college, he worked at the National Jewish Medical Center as a research assistant examining the role of airway smooth muscle relaxation and contraction in asthmatics. In medical school, he did research in gynecologic pathology. He enjoys playing the guitar and skiing. He has also climbed many of Colorado's peaks that rise over 14,000 ft. (AP/CP)

Marc Lewin

Marc Lewin was born in Johannesburg, South Africa and comes from a long line of pathologists. He graduated from Tulane University with a degree in Cellular and Molecular Biology. As an undergraduate researcher, he studied bioremediation of 2,4,6-trinitrotoluene. He was a student volunteer in the Jackson Free Clinic for the Homeless while in medical school at the University of Mississippi. He enjoys traveling, yoga and athletics. (AP/CP)

Kathryn Johnson

Kathryn Johnson was born in Philadelphia, Pennsylvania. She graduated from Virginia Tech with a BS in chemistry. She earned a PhD in Polymer Sciences studying zwitterionic surfactants at the University of Southern Mississippi. After earning her PhD, Katheryn enrolled at the Medical College of Virginia as a member of the Army Medical Corps. She is interested in traveling, ancient culture, caving and rock climbing. (AP/CP)

Jeffrey Iding

Jeffrey Iding was born in Cincinnati, Ohio. He completed his undergraduate training at Ohio State where he received a BS in psychology. He attended the University of Cincinnati College of Medicine where he was a Basic Sciences tutor, a Biochemistry group leader and a Gross Anatomy teaching assistant. In addition to his teaching responsibilities, he also worked on virtual colonoscopy. He enjoys book collecting and snorkeling (AP/CP).

Donna Hansel

Donna Hansel was born in Fridley, Minnesota. She is a Hopkins "lifer." She received her undergraduate, PhD and MD degrees at Hopkins. Her dissertation work involved amidated neuropeptides in neural precursor cell proliferation. After graduating from medical school, she completed one year of residency at Erasmus Universiteit in Rotterdam, Netherlands. In her free time, she likes to travel and swim. (AP)

Matthew Georgy

Matthew Georgy is from Williamsport, Pennsylvania. He earned a BS in Biology from Lycoming College in Pennsylvania. There he researched green fluorescent protein and used site directed mutagenesis to study its spectral properties. From there, he went to Case Western Reserve University School of Medicine. As a medical student, he researched mismatch repair in colon cancer. His interests include tennis, baseball and astronomy. (AP/CP)

Ashlie Burkart

Ashlie Burkart comes from Columbus, Ohio. She went to Brown University where she earned her BA in Biology. During undergraduate work, she was involved in numerous research projects in neuroscience and signal transduction. She spent a year after college assessing cancer treatment issues at Beth Israel in New York City. Ashlie is an accomplished artist with interests in multiple media including photography, sculpting, painting and animation film. (AP/CP)

On the Web…

Core Competency Conference for Residents

Our Pathology Residency Program now offers a unique, resident-driven didactic online module. During these sessions, commonly encountered histologic entities are presented and formally discussed with our entire housestaff by senior level residents. This direct mentoring system provides junior level housestaff with the basic tools required for their training and aids in the professional development of our graduating residents.
http://pathology2.jhu.edu/rescomp/

Updates from the Disease-Specific Web Sites

Total Pancreas Cancer Donations top $1 million

We are pleased to announce that to date over 1 million dollars has been donated to pancreatic cancer research at Johns Hopkins by the users of the Pancreas Cancer web site. Since1995 over 4700 donors have contributed. Some have given as little as $5 and others over $250,000. Almost all were given to honor a friend or loved one who either is battling pancreatic cancer or who lost the battle against this disease.
http://pathology.jhu.edu/pancreas/

Bikers Hit the Road to Benefit Johns Hopkins Research

The Monastra family exemplifies the commitment of our web site audience. Their most recent fundraising event, Ride to Make a Difference for Pancreatic Cancer Research, was a clear success with some 150 registered motorcycle riders plus their passengers. The event took place outside of Atlanta, GA, in October 2002. Approximately $40,000 was raised for the Joseph Monastra Foundation to benefit pancreatic cancer research at Johns Hopkins University and Roy Milligan won a beautiful 1999 Harley Davidson FXD Super Glide. Roy was riding in memory of his best friend who died of Pancreatic Cancer in October. The Monastra's next fundraiser will be held on April 5, 2003 in Hudson, Ohio.

http://pathology2.jhu.edu/pancreas/monastra.htm

Speaking Out… in Another Language

It is critical to get the word out about ovarian cancer, so why not start with the most populous nation on earth? Thanks to Amanda Lietman and our translator, Yanqin Yang, the Chinese version of the Ovarian Cancer web site is now available online **http://ovariancancer.jhmi.edu/chinese**. This website provides important information to empower Chinese-speaking women worldwide.

More languages will follow and we'd be very grateful for any offers of translation by native Spanish speakers. Please contact Amanda Lietman at **alietma@jhmi.edu** if you are interested in translating.

Grrrl Power!!
Raises Money and Awareness for Ovarian Cancer

Close to 60 women and men participated in the first annual HERA Ovarian Cancer Climb for Life fundraiser this past September in Salt Lake City, Utah to help focus attention on this under-recognized threat to women's health and to help raise money for research. Black Diamond in Salt Lake City hosted the actual event while another 375 people raised money climbing at their own crags and gyms all over the United States and as far away as Antarctica.

The event was organized by Sean Patrick, who founded the women's cancer foundation, HERA (Health, Empowerment, Research and Advocacy) and co-founded the Johns Hopkins Ovarian Cancer Web Site. The events' proceeds go to the Johns Hopkins Ovarian Cancer Initiative to sponsor research and to help women undergoing treatment with travel assistance. "Because of the generosity of our sponsors over 95% of the money raised goes directly to the cause," Patrick stated. Close to $45,000 was raised with an additional $35,000 given in in-kind services.

In the last half of 2002, private donations to the Johns Hopkins Ovarian Cancer Research Initiative totaled more than $50,000. We are grateful for everyone's contributions, and the first Research Fellowship awards will be given in memoriam of Dr. Rick Montz.

Next year's event is currently being planned. Visit us online for updates and to browse beautiful photo galleries of the events.
http://ovariancancer.jhmi.edu/climb/

Department members interested in developing new departmental web sites or updating existing pages should contact Jennifer Brumbaugh at 410-614-7912.

Calendar

April 9-12, 2003	4th Annual Mastering the Challenges of Cytopathology Baltimore Marriott Waterfront Hotel
April 20-26, 2003	National Medical Laboratory Week "Laboratory Professionals: Exceptional People - Exceptional Work"
April 21, 2003	Pathology Young Investigators' Day including a lecture by Dr. Stanley Hamilton at noon in the Tilghman Auditorium in the Turner Building
May 1-3, 2003	Johns Hopkins Medical and Surgical Association Biennial Meetings, Johns Hopkins University School of Medicine
May 2, 2003	Pathology Biennial Grand Rounds 9AM, Wood Basic Science Building, West Lecture Hall Speaker: Angelo M. DeMarzo
May 28-29, 2003	Critical Issues in Laboratory Medicine, Renaissance Hotel, Baltimore, MD
May 30-31, 2003	Critical Issues in Surgical Pathology, Renaissance Hotel, Baltimore, MD
June 8, 2003	Department of Pathology Employee Appreciation Day The Baltimore Zoo

Trading Posters for Running Shoes

You might think of Mitch Heinz as the person who prepares posters in PathPhoto. But when late July has rolled around for the last couple of years you would have found him lacing up his running shoes for the St. Jude Children's Research Hospital in Memphis. For the past 2 summers Mitch has taken his vacation and participated in the St. Jude Memphis to Peoria, IL Run. The concept is to drive to the St. Jude Children's Research Hospital in Memphis and then to run back to Peoria, IL, relay-style, to the St. Jude Midwest Affiliate in Peoria, IL. This has come to be one of the foremost charity running events in the nation. Each year since 1982, runners have made the 465-mile event that has raised over $7.7 million for St. Jude kids. All of the overhead expenses for the event are paid for by corporate sponsorships, allowing all of the money that the runners collect to go directly to the care of the children at St. Jude. Each runner has to raise a minimum of $2000 in donations each year to participate. Last year, Mitch raised just over $5000 and hopes to raise more than that for this years run which is July 30 – August 2. More information about this event can be found at the run website: www.stjuderuns.org
Employees, doctors, and nurses from the St. Jude Hospital in Memphis also participate in this event.

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