COLUMBIA PATHOLOGY AND CELL BIOLOGY REPORT

Volume 1, Issue 1 Winter 2008

From the Chairman

It is time that the Department of Pathology and Cell Biology had a Newsletter. We are a big department, recently made larger by the merger with the Department of Anatomy and Cell Biology. I think it is important that links be made between our pathology services and our basic scientists and the Newsletter will, I hope, help this process. People with seemingly disparate interests, once they meet each other or even know about each other, often find productive common ground. I envisage other important functions. The current issue of the Newsletter explains the structure of the Department and the people who are responsible for its important divisions. The Newsletter will serve to introduce new members of the department, including, in the current issue Dr. Carlos Cordon-Cardo and Dr. Lara Harik. The Newsletter will keep us informed about new residents, fellows and graduate students. Our residency and Ph.D programs are changing and we will all be informed about what improvements are contemplated.

The Newsletter will serve to congratulate our faculty for their accomplishments and will duly note new promotions, grants, awards, and publications. The achievements of our students, residents and fellows will be marked with great pleasure. The Department of Pathology and Cell Biology has many administrators who make the department run. The Newsletter will not neglect their efforts and achievements.

Our review of Newsletters from sister departments reveals a potential to be self-congratulatory. Well, we will do some of that, but we will include an article of sub-

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Members of Pathology and Cell Biology may not understand the organization and activities of their Department. The Department's relations with the Taub Institute and the Institute for Cancer Genetics will be covered in a future issue. In the meantime, taking our cue from Julius Caesar, the Newsletter offers the following:

ALL PATHOLOGY IS DIVIDED IN THREE PARTS

ANATOMIC PATHOLOGY | CLINICAL PATHOLOGY | CELL AND MOLECULAR BIOLOGY

Anatomic Pathology *By Charles Marboe, Vice Chair*

In the early days of anatomic pathology as studied by Bichat in Paris or Virchow in Germany, the profession established that disease was based in the tissues and correlated lesions with symptoms. This 19th century pathology usually happened at autopsy so it could rarely be said that pathologists did their patients any good. So obsessed were pathologists with these correlations that the French school of pathologists was criticized for being therapeutic nihilists. The best that can be said is that many of the techniques of histology that we now use were pioneered in those days and diseases that we now treat – think Hodgkin's disease or Addison's disease - were defined. Times have changed and now pathology is essential to the well being of our patients. The field has specialized such that anatomic pathology at Columbia now has seven subdivisions, employs 36 pathologists and examines more than 67,000 cases per year. Although the division does about two hundred autopsies a year, most of our examinations are from patients in the course of treatment.

The divisions of Anatomic Pathology are: surgical pathology, headed by Kathleen O'Toole; neuropathology, directed by James Goldman and Ob-Gyn pathology, which is lead by Thomas Wright. Bachir Alabeid is in charge of hematopathology, Guo-Xia Tong is the interim director of cytopathology, and Vivette D'Agati leads renal pathology. The autopsy service is the responsibility of Benjamin Tycko.

The faculty has active research interests that include basic research, translational studies and clinical-pathologic correlations. Many members of the division are involved in projects using the most current molecular techniques to determine prognosis and to guide therapy in malignancies. The division of neuropathology has expertise in diagnosis and research in nerve and muscle disease, neurodegenerative disorders, brain tumors and developmental anomalies. In-depth studies of the relationship of human papillomavirus to cervical cancer are performed by the division of ob-gyn pathology. The renal pathology laboratory, one of the largest in the country, has major research interests in the pathological mechanisms of focal-segmental glomerulosclerosis, HIV-associated nephropathy, lupus nephritis and drug toxicities. There are multiple active

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COLUMBIA UNIVERSITY MEDICAL CENTER

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collaborations focused on the treatment and pathology of heart, lung, kidney, and liver transplants. These are only a few examples and in future issues of the Columbia Pathology and Cell Biology Report, we will discuss some of these efforts in detail.

Clinical Pathology

(Laboratory Medicine)
By Steven Spitalnik, Vice Chair

Clinical Pathology is composed of eight subdivisions and employs nearly 20 pathologists who, on a yearly basis, perform nearly 6,000,000 diagnostic tests from living patients. These include both routine and STAT tests on both common analytes (e.g. calcium levels) and esoteric analytes (e.g. quantitative real-time PCR assays). In addition to providing professional interpretations on a wide variety of tests such as serum protein electrophoresis and pre-natal cytogenetics, laboratory medicine physicians also provide direct care for patients in the Therapeutic Apheresis area and oversee the preparation of hematopoietic stem cells in the Cell Therapy Laboratory.

Clinical Pathology's eight divisions and their heads are: Microbiology, Phyllis Della-Latta, PhD; Transfusion Medicine & Cellular Therapy, Harold Kaplan MD; Core Laboratory, Alexander Kratz, MD, PhD (Interim Director); Cytogenetics, Brynn Levy PhD; Special Chemistry, Michael Pesce, PhD; Special Hematology/Coagulation, Jeffrey Jhang, MD; Immunogenetics and HLA Laboratory, Nicole Suciu-Foca, PhD; Molecular Diagnosis, Mahesh Mansukhani, MD.

Clinical Pathology faculty members pursue scholarly efforts in developing new diagnostic methods and in ongoing clinical, basic science, and translational research programs. These include developing new molecular methods for the diagnosis of human malignancies and human infectious diseases, developing new molecular cytogenetic methods for identifying inherited genetic disorders, investigating the detailed mechanisms of viral invasion of host cells, studying cellular metabolism of sphingolipids and cholesterol, and developing mouse models of hemolytic transfusion reactions. These are only a few examples. The Columbia Pathology and Cell Biology Report, will provide more depth in future issues.

Division of Cell and Molecular Biology

By Richard Vallee, Vice Chair

Studies of cell and molecular biology have been alive and well for many years in at least two Columbia departments, Anatomy and Cell Biology and Pathology. The departments have now merged, and Cell and Molecular Biology has a single home. A noteworthy feature of the merged department is the combination of disease and basic research. At some level the effort to understand and treat human disease has driven most NIH-funded research. The prospect of "doing something about it" has become increasingly real, and the department is particularly well-situated to meld an understanding of the workings of the cell with clinical research.

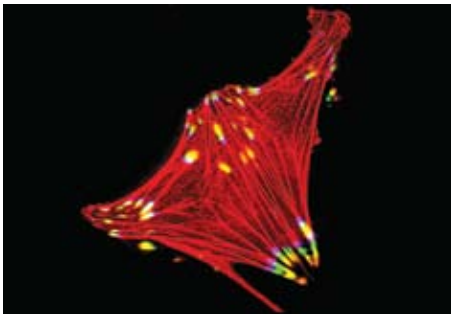
With previous good fortune and astute recruiting the new department has inherited a number of areas of expertise. One prominent theme has been the role of the cytoskeleton in normal and abnormal cell biology. This area has grown with the recruitment of Yinghui Mao, who studies the role of microtubule-interacting proteins in cell division. Mao received his postdoctoral training from Don Cleveland, where he did pioneering work on mitotic checkpoint proteins. In particular, he showed that the microtubule motor protein, Cenp-E activates the protein kinase activity of the mitotic checkpoint protein BubR1. This finding provides some of the first and best evidence linking the behavior of chromosomes to the cellular surveillance system designed to leave no chromosome behind during mitosis. *(See the figure on page 4).* Mao's lab uses Xenopus cytosolic extracts for most of their experiments. Mitotic spindles can be induced to form in vitro in this system, in which chromosome segregation can be studied cytologically and even biochemically. Cell synchrony is a given and genetics is replaced by the ability to subtract and restore individual proteins with ease. The work of Mao's lab relates to that of many in the department studying cancer and cell migration.

There is also a long history of contributions to normal and disease neurobiology by members of the joint department. Here, too, we have been very fortunate in our recruiting. Dr. Gil Di Paolo did his postdoctoral work with Pietro De Camilli at Yale on the role of phosphoinositides in synaptic transmission. Phosphoinositides are involved in many aspects of cell function, and Gil has also rapidly become a valued colleague. Remarkably, he has a past acquaintance with those ubiquitous cellular polymers, microtubules, which have been studied by so many others in the department.

Cell biology holds a curious position in modern research: everyone needs it, but few can define it. An old school of thought encourages the study of "cells, not gels." A more current view and an appropriate subtitle for the Division of Cell and Molecular Biology would be "Cells and Gels." Cells are beautiful, especially seen live and/or in the remarkable multicolored cell images now routinely generated in labs such as ours. Equally pleasing for many of us, of course, is the clean gel band, though, in this case, of course, context is everything.

If Cell Biology refers to questions that can be answered entirely at the cellular level, then a substantial fraction of Cell Biology at Columbia is now concentrated within our merged department. This is an exciting development, and the hope is that Cell Biology will flourish and grow in this environment.

The Art of Cell Biology



The composite image shows actin filaments (red) and focal adhesions (rainbow of colors) in a living stationary fibroblast. The image was produced by pseudocoloring the focal adhesions imaged at different times and shows that these sites of attachment to the substratum slip. Courtesy Prof. Greg Gundersen (Smilenov, L. et al. Science 286, 1172 (1999).

The Case of the Enlarged Liver: A Tale of Two Signals (At Least)

Jay H. Lefkowitch, MD

The Clinical Problem:

A middle-aged patient consulted a gastroenterologist because of bloating and abdominal fullness. The physical exam showed no obesity or stigmata of chronic liver disease, but the liver was markedly enlarged, without splenomegaly. Alcohol intake was reportedly several drinks per week, but had been discontinued 3 months previously. Serum liver tests were normal except for mild elevations in aminotransferase, alkaline phosphatase and gamma glutamyl transferase levels. Hepatitis virus serology and autoantibodies were all negative. A CT-guided liver biopsy was obtained.

The Histopathologic Evaluation:

In comparison to normal liver tissue (Fig. 1A), the patient's liver biopsy showed marked scarring, with the worst fibrosis in centrilobular regions and extending outward to interconnect to portal tracts (Fig. 1B). The extensive fibrosis was prominently associated with proliferating bile ductular structures (Fig. 1b, Fig. 2c). Some hepatocytes were swollen and contained clumped eosinophilic material consistent with Mallory bodies (Fig. 2A), which was confirmed with immunostaining for ubiquitin (Fig. 2B). However, only rare fat vacuoles were seen in hepatocytes. Immunostaining for p21 was also performed and showed extensive positivity in hepatocyte nuclei (Fig. 2D and Inset).

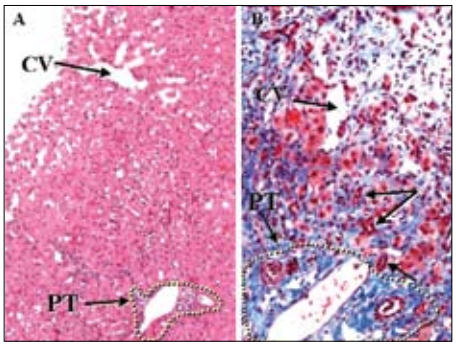


Fig. 1 Panel A: Hematoxylin and eosin stain of a normal liver biopsy showing central vein (CV) and portal tract (PT) with cords of hepatocytes radiating between the two regions. Panel B: The liver biopsy from this case stained with trichrome for connective tissue (in blue) shows extensive fibrosis around the central vein (CV) and extending between the liver cords (perisinusoidal fibrosis) outward to bridge to the portal tract (PT). Note the prominent bile ductular structures ("ductular reaction") derived from periportal progenitor/stem cells which have formed in periportal regions and within the fibrosis (arrows).

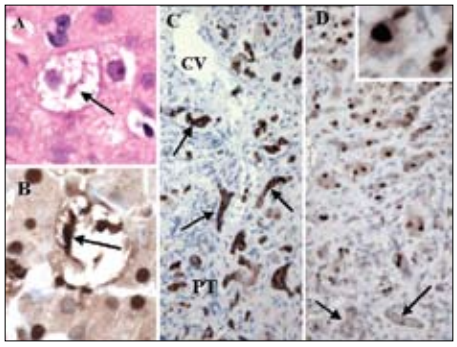


Fig. 2 A: A ballooned hepatocyte contains eosinophilic material consistent with a Mallory body (arrow). B: Immunostain for ubiquitin shows positive staining of another hepatocyte containing a Mallory body (arrow). C: Immunostain for cytokeratin 7 highlights the numerous bile ductular structures (arrows) growing along the fibrosis linking central vein (CV) to portal tract (PT). D: Immunostain for p21 shows positive dark nuclear staining of most hepatocytes in the center and upper part of the field, indicating senescence. Note the lack of significant staining of the newly formed ductular structures at bottom (arrows). Inset: Positive nuclear immunostaining for p21 in a senescent hepatocyte.

The Pathologic Diagnosis:

Marked hepatic fibrosis following alcoholic steatohepatitis (ASH)

The features seen on light microscopy in this case demonstrated advanced fibrosis in the centrilobular and perisinusoidal pattern typical of alcoholic liver disease. However, establishing the diagnosis was challenging because only minimal classic changes of steatohepatitis were present (likely because alcohol consumption had stopped several months earlier). Immunohistochemistry was not only diagnostically critical for identifying the rare Mallory bodies present by their ubiquitin positivity (1), but it also showed extensive evidence of hepatocellular senescence as manifested by the strong positivity for p21 in hepatocyte nuclei. p21 is an inhibitor of cyclin-dependent kinases (the latter are critical to the process of cell division and regeneration). Expression of p21 results in cell arrest in the G1 phase of the cell cycle and diminished regenerative capacity. In the current case, the extensive p21 positivity indicated widespread hepatocellular senescence (presumably an effect of alcohol use). The inability to regenerate caused activation of periportal progenitor/stem cells. Similar findings were also recently reported in another fatty liver disease, nonalcoholic steatohepatitis or NASH (2). Ductular proliferation is associated with progressive fibrosis, as previously described in chronic hepatitis C (3).

References

1. Lefkowitch JH. Morphology of alcoholic liver disease. *Clin Liver Dis* 2005; 9: 37-53.

2. Richardson MM, Jonsson JR, Powell EE et al. Progressive fibrosis in nonalcoholic steatohepatitis: association with altered regeneration and a ductular reaction. *Gastroenterology* 2007; 133: 350-352.

3. Clouston AD, Powell EE, Walsh MJ, et al. Fibrosis correlates with a ductular reaction in hepatitis C: roles of impaired replication, progenitor cells and steatosis. *Hepatology* 2005; 41: 809-818.

From the Chairman

Continued from page 1

stance in each issue. In the current one, Dr. Jay Lefkowitch, describes a complex diagnosis concerning a patient with an enlarged liver. Dr. Rich Kessin has agreed to edit the Newsletter, which will appear 3 times a year, so if you have ideas or contributions to make, please contact him.

In closing, let me say that this is a sad time for the Department. In the past weeks we have lost three of our members, Dan Fink, MD, Associate Professor of Clinical Pathology, Gabriel Godman, MD, Professor Emeritus of Pathology and Dr. Joseph G. Fink, Assistant Professor of Clinical Pathology. A tribute to Dan Fink by Steve Spitalnik is included in this issue. He was a wonderful colleague and friend. Gabriel Godman had a productive scientific career that spanned the half century from 1950–2000. He was a reserved man who made substantial contributions to the cell biology of viral replication, to the actions of the cytochalasins and to the biology of Alzheimer's Disease. He possessed an encyclopedic knowledge of anatomic pathology and contributed enormously to the autopsy service over his years at Columbia. Dr. Godman remained active at Columbia until about three years ago. We are all grateful for his contributions to our department over the years.

Honors

Greg Gunderson, thesis advisor and Ellen Ezratty, winner of the Harold Weintraub Graduate Student Award

Ellen Ezratty The Harold Weintraub Graduate Student Award, given annually to 12 to 15 students from around the world, recognizes outstanding achievement during graduate studies in the biological sciences. Ellen Ezratty, a graduate student in the cell biology program who graduated with distinction in 2007 after completing her research in Dr. Gregg Gundersen's laboratory, won the Weintraub Award. Ellen is now with Dr. Elaine Fuchs, at Rockefeller University.

The Newsletter is pleased to announce that Professors **Carol Mason** and **Lloyd Greene** have been elected Fellows of the American Academy for the Advancement of Science.

Dorothy Warburton

The American Society of Human Genetics gave the William Allan Award to Dorothy Warbarton at its annual meeting in October. Previous recipients of the William Allen Award have included Bert Vogelstein, Joseph Goldstein and Michael Brown, Mary Lyon, David Botstein and Ray White. Dr. Warburton received the award for her pioneering work in the field of cytogenetics. Dr. Warburton directed the CUMC Cytogenetics Laboratory for 35 years and taught medical students, residents and graduate students.

New Faculty

Carlos Cordon-Cardo, MD, PhD

The Newsletter extends a belated welcome to Dr. Cordon-Cardo, professor of pathology and urology, vice chair of the Department of Pathology in P&S, and co-leader of the Genitourinary Malignancy Program. Dr. Cardon-Cardo is associate director for research infrastructure in the Herbert Irving Comprehensive Cancer Center. Over the past 20 years, Dr. Cordon-Cardo has played an instrumental role in moving cancer pathology from a discipline focused on the appearance of cancer cells to one that assesses molecular changes leading to the tumor's biological and clinical behavior. The integration of molecular techniques into pathology has improved diagnosis and prognosis of cancer, but also has increased understanding of cancer and uncovered new therapeutic targets.

As director of the Division of Molecular Pathology at Memorial Sloan-Kettering Cancer Center where Dr. Cordon-Cardo spent the last 24 years, he helped create an infrastructure for translational research that harmoniously integrated physicians and scientists from different disciplines. At CUMC, he envisions a similar structure that builds bridges between basic scientists and physicians.

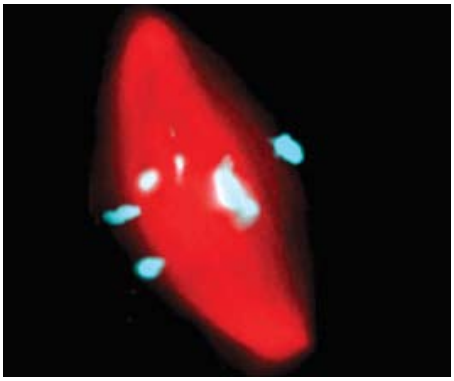
Among the most highly cited researchers in clinical medicine, Dr. Cordon-Cardo has more than 350 peer-reviewed publications. He received his M.D. from the Autonomous University of Barcelona and his Ph.D. in cell biology and genetics from Cornell.

Lara Harik, M.D.

Dr. Lara Harik graduated from medical school at The American University in Beirut in 2000. After her graduation she did a combined anatomic and genitourinary fellowship at Emory University under the direction of Dr. Mahul Amin. Following her fellowship, Dr. Harik moved to Memorial Sloan Kettering as an oncologic pathology fellow and then obtained more training in genitourinary medicine. Her research interests span all of the organ systems of genitourinary pathology with a particular focus on the bladder. Dr. Harik looks forward to continued translational research in the Department of Pathology and Cell Biology. The Department welcomes Dr. Harik.

Other new faculty members include: Anjali Saqi, M.D., Livio Pellizzoni, Ph.D, Xiaowei Chen, MD and Shine Sun Yun, MD. The Newsletter will provide more background in a future issue.

Mayhem in Mitosis



Accurate chromosome segregation requires successful attachment of every chromosome to mitotic spindle microtubules. The image shows a metaphase spindle in Xenopus egg extracts with unattached chromosomes characteristic of chromosome-microtubule attachment failure. (red) Spindle microtubules; (blue) Chromosomes. From Yinghui Mao (Asst. Professor) and Jiayin Zhang.

Department of Pathology Incoming Clinical Fellows 2007

Neuropathology

Ada Baisre-de-Leon, M.D. received her medical degree from the Superior Institute of Medical Sciences of Havana, Cuba. She trained in pathology for two years in the "S. Allende" Hospital in Havana, and then for four years in AP/CP at UMDNJ-New Jersey Medical School. She completed a one year Oncologic Pathology Fellowship at Memorial Sloan-Kettering and is now concluding a year as a Diagnostic Molecular Pathology Fellow at Memorial. She also is interested in motorcycles.

Hematology

Darryl Alan Oble, M.D., Ph.D., received his doctorate from the University of Manitoba and his Ph.D. (Immunology; working with murine models of scleroderma and psoriasiform disease) from the University of British Columbia. He has just completed the Anatomic Pathology Residency Program at Massachusetts General Hospital where he has continued to work on immunologic aspects of lung disease, immunotherapy of solid tumors, and lymphomas.

Hematology

Deborah W. Sevilla, M.D., received her B.S., with distinction in Biology, from Duke University, and her M.S. (Biomedical Sciences) and M.D. from Eastern Virginia Medical School, Norfolk. She has just completed the Anatomic Pathology Residency Program at Duke University Medical Center, having served as Chief Resident for the past year. She has multiple presentations and publications on topics in hematopathology.

Incoming Residents 2007

Nike Beaubier
(AP/NP)
B.S. University of Texas, Austin, Molecular Biology

Beta Beta Beta Honor Society

M.S. Stanford University, Cell and Molecular Biology

M.D. Columbia University College of Physicians & Surgeons

Nike studied mathematics at the University of North Carolina for 3 years prior to transferring to UT. She has worked at Deltagen and Affymetrix, has been conducting research with Carol Troy of our department, was President of Bard Hall Players, volunteers at a free clinic, competes in triathalons, and is fluent in French.

Richard Francis
(CP)

B.A. Johns Hopkins University, Behavioral Biology

Phi Beta Kappa

Curt P. Richter Award for Outstanding Achievement in Behavioral Biology

Ph.D. Columbia University, Pathology (Institute for Cancer Genetics)

Thesis Title:
Modeling DNA Double-Strand Break Repair in Hematopoietic Cells

M.D. Columbia University College of Physicians & Surgeons

Richard has also been active in the Big Brothers Big Sisters program in New York.

Shafinaz Hussein
(AP/CP)
B.S. California State University, Long Beach, Biology

Phi Beta Kappa, magna cum laude

M.D. New York Medical College

Shafinaz has worked with the supernature.cc Film Production Company, has been very active in AMWA and the Free Clinic Project at New York Medical College, is an active artist, and is proficient in Burmese and Malay.

Rachelle Retoma
(Oral Pathology)

B.A. University of Maryland

D.M.D.
Temple University School of Dentistry

Rachelle received her B.A. from the University of Maryland Baltimore County and her D.M.D. from Temple University. She has practiced dentistry for ten years, most recently in Tacoma, Washington, has traveled extensively and is also interested in motorcycles.

Anthony Sireci
(AP/CP)
B.A.
New York University, Chemistry

Phi Beta Kappa, NYU

Presidential Scholar,
Phi Lambda Epsilon, summa cum laude

M.D. Johns Hopkins University School of Medicine

Anthony has worked as a teaching assistant in chemistry at NYU, has research experience and publications in neurotoxicity and neuroprotection, has been co-president of the gay and lesbian student group at Hopkins, has been active in local community testing and counseling for HIV, and is fluent in Italian.

Faculty Promotions

The Department is pleased to announce the promotions that occurred in 2007:

Professor

Karen Duff, Ph.D.
Professor of Pathology and Cell Biology

Wei Gu, Ph.D.
Professor of Pathology and Cell Biology (in the Institute for Cancer Genetics)

Ramon Parsons, M.D., Ph.D.
Avon Foundation Professor of Medicine and Pathology (in the Institute for Cancer Genetics and in the Herbert Irving Comprehensive Cancer Center)

Liza Pon, Ph.D.
Professor of Pathology and Cell Biology

Benjamin Tycko, M.D., Ph.D.
Professor of Pathology and Cell Biology (in the Institute for Cancer Genetics and in the Taub Institute)

Associate Professor

Cathy Lee Mendelsohn, Ph.D.
Associate Professor of Urologic Sciences (in Urology, the Institute of Human Nutrition and Pathology) with tenure.

Asa Abeliovich, M.D., Ph.D.
Associate Professor of Pathology and Neurology with tenure.

Associate Professor of Clinical Pathology

Bachir Alobeid, M.D.
Associate Professor of Clinical Pathology

Govind Bhagat, M.D.
Associate Professor of Clinical Pathology

Retirements

May Parisien, MD, Associate Professor of Clinical Pathology, is retiring following 32 years in the Department. A full appreciation of Dr. Parisien's career will appear in the next issue of the Newsletter.

New Grants

Last year the Department's faculty obtained new grant support, as listed below. These numbers do not include grants to members of the Institute for Cancer Genetics (ICG) or the Taub Institute, with which the Department is closely associated. The total new support for this year, combining direct and indirect costs, is more than $2,500,000. The total departmental spending derived from government and non-government support and gifts is more than $18,000,000. The department ranks 4th or 5th nationally. The Chair and the Newsletter congratulate the faculty and students who worked so hard to continue our research and teaching programs.

Asa Abeliovich
Novel Therapeutics for Parkinson Disease
American Parkinson Disease Foundation

Asa Abeliovich
Targeting the PTEN, mTor, Autophagy Pathway in Parkinson Disease
Michael J. Fox Foundation

Gilbert Di Paolo
A Novel Approach for Rapid Chemically Induced Modulation of PIP2 Synthesis at the Synapse
The McKNight Endowment Fund for Neuroscience

Gilbert Di Paolo and Belle Chang
The Regulation of PIP2 Metabolism in Nerve Terminals
NIH

Fiona Doetsch
Neural Stem Cells and Their Niche in the Adult Mammalian Brain
Spunk Fund

Michael Gershon
Microenvironment in Enteric Neuron Development
NIH

Greg, G. Gundersen
Mechanisms of Integrin Microtubule Crosstalk
NIH

Christopher Henderson
Role of FAS Death Receptor Signalling in Motor Neuron Degeneration
NIH

Richard H. Kessin
A Strain Repository for *Dictyostelium discoideum*
NIH

Tae-Wan Kim
Identification of Small Molecule Inhibitors of BACE1-mediated APP Cleavage
NIH

Tae-Wan Kim
Role of Phosphoinositides in AB-oligomer Associated Synaptic Dysfunction
NIH

Anne-Judith Silverman
Synaptic Interactions between GIRH and GNRH Neurons
NIH

Steven Spitalnik
Epitope Masking Reagents in Transfusion Medicine
NIH

Carol, M. Troy
Novel Molecular Therapeutic Interventions in Cerebral Ischemia
American Heart Association

Richard Vallee
Molecular Genetics of Cytoplasmic Dynein
NIH

Hyneck Wichterle and Estaban Mazzoni
Anterior-posterior Pattern of Hox Gene expression in ES-Cell Derived Motor Neurons
Damon Runyon Foundation

Hyneck Wichterle
Establishment of Segment Identity in Embryonic Stem Cell Derived Motor Neurons
NIH

In Memoriam

Dr. Daniel J. Fink spent his entire professional career at Columbia University Medical Center. After receiving BS and MS degrees in engineering from Cornell and MIT, respectively, he enrolled as a medical student in the Columbia University College of Physicians & Surgeons, graduating with an MD degree in 1975. Following an internship in internal medicine at Montefiore Hospital, he pursued residency training in clinical pathology at CUMC and graduate training in public health at the Mailman School. He joined the faculty at CUMC as an Assistant Professor of Clinical Pathology in 1979, received an MPH in 1980, and was promoted to Associate Clinical Professor of Pathology in 1987. During his 27 years as a faculty member he served admirably in many key clinical and administrative functions, most importantly as the founding Director of the Core Laboratory at New York Presbyterian Hospital and as the founding Director of the Center for Advanced Laboratory Medicine at Columbia University. He was active in teaching medical students and pathology residents.

Dan's scholarly interests focused on issues related to informatics, public health, and quality initiatives. As such, he developed the first laboratory information system at CUMC and was instrumental in the strategic vision and day-to-day operation of the current and future systems. His interest in public health was most evident by his active participation and leadership role in the long-term, NIH funded program to study the effects of the Chernobyl accident on thyroid cancer and other thyroid diseases. His interest in quality improvement led him to be involved in the evaluation of new laboratory test instruments, in the support of large clinical trials, and in his participation and leadership roles in important national and Hospital committees, such as the NYPH Quality and Patient Safety Committee. In particular, he ably and enthusiastically led many inspection teams sponsored by the College of American Pathologists charged with evaluating the accreditation of pathology departments around the country.

He was especially pleased to have just recently received a plaque honoring his long years of service to the Columbia University College of Physicians & Surgeons and was actively looking forward to future challenges and endeavors. He leaves behind his wife, Yvonne, and daughter, Leslie (P&S Class of 2009). He was a wonderful husband, father, leader, mentor, colleague, and friend, and we all miss him terribly already.

Steven Spitalnik

Pathobiology and Molecular Medicine *A Revised PhD Program*

There are more than 350 Ph.D students in basic science on the CUMC campus. Originally divided into 10 programs they are now reorganized into four graduate programs with specific tracks within each program. There are therefore graduate programs in Cellular, Molecular, Structural and Genetic Studies, Neuroscience and Behavior, Biomedical Informatics and Mechanisms of Health and Disease. Members of the department participate in several of these programs, including the Graduate Program in Cellular, Molecular, Structural and Genetic Studies which has a specific Track in Cell Biology. One of our prime responsibilities is in the Graduate Program in Mechanisms of Health and Disease, particularly in the track Pathobiology and Molecular Medicine. The Track is directed by Dr. Ronald Liem. The motivating thought in this new Pathobiology and Molecular Medicine Track is that the distinction between basic and clinical science is artificial. The members of the Mechanisms of Health and Disease Graduate Program realize that in some graduate programs students receive an excellent education in basic science, without also learning about great clinical problems. It is to span this gap that the Track in Pathobiology and Molecular Medicine has been created.

Dr. Ronald Liem
Director of
Graduate Studies

The Newsletter is pleased to introduce the following first-year Ph.D students in Pathobiology and Molecular Medicine:

Angela Jia:
Angela received her B.S. from the University of Toronto in June 2007. She has worked on cellular oncology projects as an undergraduate student and is interested in continuing disease oriented research in oncology.

Celia Keim
Celia graduated from Pennsylvania State University in May 2007 with a major in Biochemistry and Molecular Biology. Celia worked in several laboratories as an undergraduate and is interested in research in Virology and Cancer Biology.

Mai Sato
Mai received her B.A. from Pomona College in May 2006. She did research on DNA repair and recombination for her Senior Thesis and spent a year in her native Japan before starting her graduate studies at Columbia. She is interested in cancer research.

Nsikan Akpan
Nsikan graduated from Bard College with a B.A. in Biology in 2006. Following graduation, he worked as a Research Intern at Tufts University for one year prior to enrolling in the graduate program. Nsikan is interested in neurodegenerative diseases.

Led by faculty who are at the forefront of the profession, our students pursue thesis research in several areas:

- Cancer Biology
- Neurodegenerative diseases
- Cellular and molecular neurobiology
- Cell motility, cytoskeleton and intracellular trafficking
- Virology
- Neuronal stem cells

The Pathobiology and Molecular Medicine Track takes pride in the scientific education of its graduate students. It creates courses and seminars to keep students abreast of the latest issues. We train students in basic skills such as writing and speaking that are important to a scientific career. As a result, our graduates have gone on to important positions in academia and industry. We believe the new focus will keep our graduate offerings vibrant.

A Note on Publications

The members of the department contributed approximately 260 peer reviewed publications in the years 2005-2007. The newsletter suggests that interested parties search the websites of the individual faculty members at http://pathology.columbia.edu/

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