It was one of those perfect English autumnal days which occur more frequently in memory than in life.

P. D. James

Dear Pathology Faculty, Trainees and Staff:

We had ~300 applicants to the 2006 Pittsburgh MSTP. The quality of the applicants continues to be stellar challenging our Selection Committee. As the admissions process requires an immense amount of time from faculty, staff and students, we expedited applications this year, decreasing the number of interviews from 80 to 50. Even after this reduction, we still found ~35 applicants who would make excellent matches with our MSTP. To further focus our efforts on applicants specifically interested in Pittsburgh, we delayed the Placement Weekend to the end of March at which time we worked with 15 applicants to identify labs for their first lab rotation, a mere seven weeks away! All of our efforts paid off with the June 1st matriculation of 12 stellar students (11 new students and one 2nd year medical student). While it is still early to predict, a quarter of these new students appear to be headed to pathology.

To help the incoming class define future lab rotations and graduate programs for their thesis work, Dr. Geoff Murdoch and I coordinated a new summer course entitled “Molecular Medicine.” This course met for two hours every Tuesday and Thursday evening. Each week a different graduate program introduced an important biomedical problem from the unique perspective of their field. The new students had abundant opportunity to work closely with a broad spectrum of mentors, while each graduate program has the opportunity to showcase its best research and superb faculty. Meeting as a class for four hours a week went a long way to building esprit de corps before the chaos of medical school began.

We barely had time to catch our breath before the summer undergraduate program began. Again this year we are hosting eight undergrads from around the country for nine weeks of lab work and professional development. Each undergraduate is paired with one of our senior MSTP graduate students who have generously offered to mentor these nascent physician scientists in their laboratory.

And just when we thought the program was under a full head of steam, we got a call from NIH NIGMS. Surprise! They want to come (site) visit us. Years ago this would have been a tough hurdle to clear, but not in 2006. Instead it became an opportunity to once again showcase the Pittsburgh MSTP. And it worked very well indeed! We received a priority score of 161 and a recommendation to triple our current funding. Now with NIH in the financial doldrums, we will not see all of that money, but it is good to know others think we are worth it!

Clayton A. Wiley, M.D./Ph.D.
ASSOCIATE DEAN, DIRECTOR OF MSTP
**HIGHLIGHTS**

Adriana Zeevi, Ph.D. Elected as Councillor at Large of the American Society of Transplantation.

Marie DeFrances, M.D. Ph.D. was selected by the Association of American Medical Colleges (AAMC) to attend the “Early Career Women Faculty Professional Development Seminar” in July 2006. She also gave an oral presentation entitled, “Negative regulation of PI3K by PIK3IP1, a novel p110 interacting protein: implications in cell growth and tumorigenesis” at the FASEB Summer Research Conference “Liver Growth, Development and Disease” at Snowmass, CO, in July 2006.

Bruce Rabin, M.D., Ph.D., will appear on WTAE Channel 4’s Healthy 4 Life Special - Success Starts Early. October 8 at 1:00 p.m.

Samuel Yousem, M.D., will serve as Vice President of the Medical Staff for PUH. Is also the recipient of the UPMC ACES award.

Dr. Shi-Yuan Cheng has been invited to serve as a member of the Tumor Progression and Metastasis Study Section, Center for Scientific Review for the term July 1, 2006-June 30, 2010.

**PRESENTATIONS**

Federico A. Monzon, M.D.
Specialty Labs Informatics: Opportunities and Challenges in Clinical Laboratories That Do Not Fit the AP/CP Paradigm. APIII 2006. Vancouver, BC.

Lawrence Nichols, M.D. gave a presentation on June 27, 2006 at the mini Med School series; title of lecture is “The Value of Autopsies”. The title of the whole evening presentation is “Learning from the Dead.”

Please submit newsworthy items as they happen to Szalkuskict@upmc.edu. The next newsletter will go out November 20, 2006. Deadline date for items is November 10. Thanks.
WELCOME NEW PATHOLOGY

Jeffrey Fine, M.D., Assistant Professor of Pathology at Magee Womens Hospital. Dr. Fine completed a Pathology/Oncology Informatics Fellowship in July, 2006. His primary focus is in the area of surgical pathology and informatics related to women’s health.

Olga Navolotskaia, M.D., Assistant Professor of Pathology at Magee Womens Hospital. Dr. Navolotskaia cytopathology fellowship at Magee in July, 2006. Her primary focus is in the area of surgical pathology and cytopathology.

PATHOLOGY PHD GRADUATE TRAINING PROGRAM

I am pleased to announce that eleven students have recently joined the Cellular and Molecular Pathology Graduate training program. Four MD/PhD students are included in this new class. The students and mentors are:

<table>
<thead>
<tr>
<th>Student</th>
<th>Mentor</th>
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<tr>
<td>Lauren Drowley</td>
<td>Johnny Huard, Ph.D.</td>
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<tr>
<td>Arlee Fafalios</td>
<td>Beth Plug, Ph.D.</td>
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<tr>
<td>Paulina Huang</td>
<td>Luyuan Li, Ph.D.</td>
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<td>Corrine Kliment, MD/PhD student</td>
<td>Tim Oury, M.D., Ph.D.</td>
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<td>Abagail Lade</td>
<td>Jean Latimer, Ph.D.</td>
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<td>Rebecca Leman, MD/PhD student</td>
<td>Jennifer Grandis, M.D.</td>
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<tr>
<td>Bowen Liu</td>
<td>George Michalopolous, M.D., Ph.D.</td>
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<td>Jiangxia Liu</td>
<td>Zoltan Oltvai, M.D., Ph.D.</td>
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<tr>
<td>Michelle Manni</td>
<td>Tim Oury, M.D., Ph.D.</td>
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<tr>
<td>Cyrus Raji, MD/PhD student</td>
<td>Bill Klunk, M.D., Ph.D.</td>
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<tr>
<td>Michael Thompson, MD/PhD student</td>
<td>Paul Monga, M.D.</td>
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Leadership Change

As Director of the Cellular and Molecular Pathology Graduate Training Program for the past eight years, I have had the pleasure to lead our PhD program through numerous changes both within the program and in the institution. From a change in the name of the program to the development and formation of the Interdisciplinary Graduate Training Program at the School of Medicine, we have seen our program grow from only a few students to more than 30. It’s now time to hand the baton to a colleague that has been the Associate Director during the past year. Wendy Mars, Ph.D., will be Director of the CMP Graduate training program effective October 1, 2006. Wendy is currently the Director of our summer undergraduate training program and the course Director of the departmental journal club, a required course for all our students. Please join me in welcoming Wendy as our new Program Director. I will assume the role of Associate Director during the next few months to assist Wendy in this transition.

Robert Bowser, PhD – Director
Dear Pathology Faculty, Trainees and Staff:

The major news from the Residency Program is two changes in staff:

After three years as Program Director, I have stepped down from this position and accepted a position as a Consulting Pathologist at the British Columbia Cancer Agency and the University of British Columbia School of Medicine. We are pleased to announce that the new Program Director will be Dr. Trevor Macpherson.

The second change in staff is that Trish Zrimsek has been promoted to Academic Manager of the Residency Program. Recruitment is underway to find a new Administrative Coordinator.

Finally, it is the time of year when recruitment begins. We are currently receiving applications through the ERAS system and will be scheduling interviews in the near future.

I enjoyed working with the residency program. Best of luck to all of you.

Gregory Naus, M.D.
Professor of Pathology

This year’s Pathology Summer Undergraduate Research Program (SURP) was a tremendous success. Sixteen students (our maximum capacity!), working with fifteen different faculty members, were Pathology participants. Four of these students were specifically placed with UPCI faculty, due to funding provided from the private sector that was specifically targeted to both UPCI and Pathology.

For those of you who are not familiar with the Pathology SURP program, it is part of a small consortium within the School of Medicine Interdisciplinary Biomedical Graduate Program. The other participants are Cell Biology/Physiology, Immunology, Biochemistry/Molecular Genetics, Molecular Virology/Microbiology, and Pharmacology. Students are matched with graduate faculty mentors who agree to assist them with a specific research project. Whereas some activities are done as a whole (~50 students total), others, such as the Pathology retreat, are specific for the Pathology SURP students. The program is 10 weeks long and ran from May 30 to August 4, with the students giving formal presentations of their research in a mini-symposium format on the last two days.

SURP is one of our school’s most successful recruitment tools. Of the 62 students that have participated in Pathology SURP from 2000-2005, 14 have matriculated into MD, PhD, or MD/PhD tracks at Pitt. Another 16 are known to have gone elsewhere to programs such as Duke, Vanderbilt and Johns Hopkins, so we are clearly doing something right! Furthermore, the quality of our students continues to grow—with the average GPAs in the high 3’s and our applications now coming from throughout the world. This year we had three students from South America (1) and Asia (2)!

If you are interested in hearing more about SURP, please let me know.

Wendy M. Mars, Ph.D., Director, Pathology SURP
(wmars@pitt.edu)
NIH NRSA Pre-doctoral Fellowship. Award period March 2006 to March 2008. Title: ER Stress and Its Role in Type I Diabetes (TID). **Sheila Marie Schreiner**, Pathology Ph.D. candidate, mentor is Dr. Jon D. Piganelli.

Awarded an American Heart Association's pre-doctoral fellowship this summer "A novel role for type 1 plasminogen activator inhibitor (PAI-1) in Type 2 Diabetes.

**Gina Randa** (CMP Program) predoctoral student in lab of Dr. Jon Piganelli.

**GRANTS**

**Federico A. Monzon** (Principal Investigator) Sponsored Research Agreement - Federico A. Monzon Pathwork Informatics LLC. Validation of PathWork Oncology Suite: Tissue of Origin Test,

Dates of Proposed Project 5/1/06 – 4/30/07 Annual Direct Costs $233,965

It has been demonstrated that gene expression-based methods can increase the successful identification of the primary tissue of origin for metastatic tissue specimens. The PathWork Oncology Suite: Tissue of Origin (POS:TOO) test has been developed as an in vitro diagnostic test using gene expression to evaluate the tissue of origin for metastatic tumors. POS:TOO is a suite of 15 one-against-all tests, each of which reports an independent Similarity Score. The physician is expected to interpret the 15 individual scores to draw a final conclusion as to the likely tissue of origin for the specimen. This project will validate the use of a gene expression microarray based diagnostic test (POS:TOO) to determine the tissue of origin in primary or metastatic moderately and poorly differentiated tumors.

**Eric Lagasse, Ph.D.** The American Association for Cancer Research announced the first 11 recipients of the new Jeannik M. Littlefield-AACR Grants in Metastatic Colon Cancer Research. The awards, ranging to $250,000, were established in February 2006, to support innovative research projects designed to accelerate the discovery and development of new agents to treat metastatic colon cancer. Grant awards were selected through a rigorous and highly competitive process by a committee of accomplished senior scientists. AACR is currently distributing a total of $2,644,977 to the successful investigators.

"Among the 114 applications submitted, these 11 awardees were judged to have the most merit," said David Irwin, Ph.D., managing director of the Science and Education Division of the AACR. "We offer our sincere congratulations to the investigators, and anticipate they will make substantial contributions to this field of cancer research."

The Jeannik M. Littlefield-AACR Grants in Metastatic Colon Cancer Research are sponsored by Jacques and Sandy Littlefield of Portolo Valley, California, who donated $3 million to the AACR in late 2005. They are named for Mr. Littlefield's mother.
TESTIMONY Of Stephen Strom, Ph.D.
“Amniotic Epithelial Cells”
Before the Labor/Health and Human Services/Education and Related Agencies Appropriations Committee Of the Senate Appropriations Committee
The Honorable Arlen Spector, Chairman June 27, 2006

Stem Cell Characteristics of Amniotic Epithelial Cells

Our laboratory has been active in the area of regenerative medicine for nearly 15 years. We believe that some liver diseases currently treated by whole organ transplantation might be corrected, by the transplantation of isolated liver cells in a procedure which is simple, safe, less invasive and less costly than whole organ transplantation. We were the first group in the US to treat liver failure and metabolic liver disease by the transplantation of isolated liver cells. So far our group has treated approximately 25 patients with this cellular therapy. While still experimental, the results suggest that liver cell transplants can support life in patients with terminal liver failure and correct metabolic diseases of the liver (1).

Just as with whole organ transplants, there is a shortage of donor livers for liver cell isolation. Approximately 3 years ago we became somewhat reluctant stem cell biologists and decided to try to generate liver cells for our transplants from stem cells. For a number of reasons we decided to focus on the amnion layer of the placenta as a possible stem cell source. We began to search for cells with characteristics similar to those reported for embryonic stem cells. The results were clear, the amnion of human placenta contains cells with cell surface markers and a gene expression profile which is very similar to those found on embryonic stem cells.

Last November in the Journal Stem Cells, we reported that amniotic epithelial (AE) cells isolated from human term placenta express surface markers normally present on embryonic stem and germ cells including stage specific embryonic antigens (SSEA) 3 and 4 and Tumor rejection antigens (TRA) 1-60, 1-81. Like embryonic stem cells, amniotic epithelial cells express the genes thought to be the basis of pluripotency including the expression of octamer-binding protein 4 (Oct-4), and nanog. Based on immunohistochemical and genetic analysis, we were able to demonstrate that in a culture dish, amniotic epithelial cells have the potential to differentiate to all three germ layers—endoderm (liver, pancreas), mesoderm (cardiomyocyte), and ectoderm (neural cells). Under specific culture conditions, amniotic epithelial cells display the capacity for self renewal.

We believe that stem cells derived from human amnion display several characteristics that suggest that they will be useful for cell transplantation and regenerative medicine:
Amnion expresses markers of pluripotency suggesting that they may have the capacity to become every cell type in the body. Amnion does not require feeder layers for maintenance of the stem cells. Amnion-derived stem cells do not form tumors when transplanted. Amnion is freely available because it is normally discarded following a live birth. Amnion is abundantly available from the over 4 million live births each year in the US. Amnion-derived stem cells are obtained from term placenta, and only following a live birth of a baby. Thus, we believe that there will be no social, ethical or religious opposition to the use of stem cells from this source. We conclude from our initial studies that amnion derived stem cells may be a useful and non-controversial source of stem cells for cell transplantation and regenerative medicine. We urge the United States Congress to support this promising area of research in every way possible.

References
Submitted June 26, 2006. Stephen C. Strom, Ph.D. and Toshio Miki, MD, Ph.D., Department of Pathology and McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, PA 15261.
“Molecular and Cellular Mechanisms of Steatohepatitis: Apoptosis as the Critical Mediator”

Gregory J. Gores, M.D.
Professor of Medicine and Physiology
Chief, Division of Gastroenterology and Hepatology
Mayo Medical School
Rochester, MN
Wednesday, October 11, 2006—noon
1105 UPMC Conference Center

“Glomerular Filtration Barrier Failure: A Molecular Perspective”

Matthias Kretzler, M.D.
Associate Professor of Internal Medicine
Department of Internal Medicine
Department of Physiology and Nephrology
University of Michigan
Ann Arbor, MI
Wednesday, October 18, 2006—noon
1105 B/C UPMC Conference Center

“Core Binding Factor and the Pathogenesis of Acute Leukemias”

Mondira Kundu, M.D., Ph.D.
Hematopathology Fellow
University of Pennsylvania
Philadelphia, PA
Wednesday, October 25, 2006—noon
1105 B/C UPMC Conference Center

“Pathologists and Detection of Bioterrorism Agents”

Jeannette Guarner, M.D.
Center for Disease Control
Atlanta, GA
Wednesday, November 1, 2006—noon
1104 UPMC Conference Center

“What is a Small Round Blue Cell”

Annual Totten Lecture
Lester Thompson, M.D.
Southern California Physicians Medical Group
Woodland Hills, CA
Wednesday, November 8, 2006—4:00 p.m.
Lecture Room 5 Scaife Hall

PUBLICATIONS


Man YG, Zhao CQ, Wang J, XL Chen. A subset of prostate basal cells lacks corresponding phenotypic markers. Pathology-Research & Practice, 2006 July 12 (Epub ahead of print)


ADMINISTRATIVE STAFF UPDATE

The Pathology Central Administrative Office would like to extend a welcome to the following new staff members. These positions will serve an important role in augmenting the administrative services to the faculty and programs of the department – please join us in welcoming them!

Cassandra Russell – Pre-Award Grants Support - Cassie will be assisting Department administrative staff and faculty with grant submissions, contracts, sponsored projects, material transfer agreements and compilation and reporting of Department pre-award activity.

Shari Tipton – Administrative Assistant – Shari will be providing central office support functions, including call direction, scheduling appointments and supply orders. She will also be responsible for coordinating the administrative needs of the Department’s Graduate, PIRT PPRTP and SURP programs.

Grace Hafner – Post-Award and Purchasing Support – Grace will be helping to process the Department’s growing volume of University purchase orders, as well as assisting with research account reconciliations and SPAR maintenance for faculty and staff.

Michael Batyi and Zelda Newman – Coder I – Both Mike and Zelda joined our department’s Billing Office at the beginning of FY07 and will be providing much needed ICD-9 and CPT coding support for the department.

Brian Rudolph, MHA/MBA
Administrative Director
I would like to remind everyone that the payroll deadlines for each month are very early in the month. The paperwork is due one week prior to deadline in the Dean’s office for processing. If we miss this deadline we are charged a service fee to process for the check. If this happens, I will be asking you to supply an account number to cover this expense. Otherwise, the employee will not receive a paycheck until the following month. The deadlines for November and December payroll: Student timesheets are due no later than November 3rd to meet the November payroll deadline and on November 21st in order to meet the December deadline. Adjustments will be made in the following month.

REMEMBER
SUPERVISORS OF WORK STUDY/STUDENT WORKERS: All timesheets for your students are due into my office on the 10th of each month. Students should project the hours they will work up to the 15th of each month. Adjustments will be made the following pay period. IT IS YOUR RESPONSIBILITY TO SEE THAT STUDENT WORKERS HOURS ARE TURNED IN ON TIME! If a student does not turn in their hours on time, they will not be paid until the following month! Payroll submissions have been delayed in the past due to the time it takes to “track down” timesheets.

VISA UPDATE
Nicole Paterline will handle all staff and faculty visa issues for the department. Her telephone number is 648-1230 and her e-mail is: lucarellina@upmc.edu. Please contact her directly if you have any questions or need to have your current visa extended. You must contact her four months prior to the expiration of your J-1 visa and six months prior to your H-1B expiration.

REASONS TO VISIT THE PAYROLL OFFICE
To get your pay stub – Even though you may have direct deposit, your stub provides proof of income and provides a list of your deductions. These are available on the last working day each month in Room S-417 BSTWR between the hours of 1-4:00 p.m.

Change in name or address – If you change your name due to marriage or divorce, you must change it with Social Security first. Bring your updated card to the Payroll Office. Forms are available if you should change your address.

Resignation - Faculty should submit a resignation letter to Dr. Michalopoulos and Division Director. Staff should give a copy to your supervisor, which should include your final date of employment. This should be done within 24 hours after you have informed your Supervisor in order to process your paperwork. Be sure to include your forwarding address in order for your W-2 form to be forwarded to the correct address.

To Hire New Employees - Faculty wishing to hire staff positions should initiate this process through the Payroll Office. This includes foreign recruits also.

Medical Leaves - If you are going on leave or have just returned from a leave (personal or FMLA) you must let me know in order to get your paperwork in order.

Tracking of Vacation/PH/Sick Time - For staff, turning in your time sheet each month is mandatory for accurate vacation and sick time records. Timesheets are currently being sent via e-mail for all employees. If you are not receiving these, please contact me immediately to verify your e-mail address.

To Change your W-4 - This will make tax time go more smoothly, and is often necessary if your status changes (e.g. marriage, divorce, children). You may also need to change your deductions or have additional funds withheld.

Foreign Faculty/Staff/Students - You should come by my office if:
- You have received your Permanent Resident “green” card
- You have recently received your authorization to work cards
- Your current visa has been extended. Please bring copies of the approval notice or new IAP-66

Direct Deposit - Direct deposit is a convenience, however, difficulties arise caused by the following:
- You have closed your account without canceling your direct deposit with the University. If this happens, the bank may refuse the deposit and it could take 1-2 weeks before the University can issue your check.
- You have terminated your employment without cancellation of your direct deposit
- Please keep in mind that the payroll deadlines are very early in the month and the sooner you tell me about new hires and changes, the better.

I can be reached at 648-1038 if you have any questions/concerns. Please call my office first to schedule an appointment before “stopping by.” This will ensure that I’ll be available to discuss your issues/concerns. Thank you.

Carolyn Nolte, Payroll Coordinator