

THE ROCKEFELLER UNIVERSITY HOSPITAL

UPDATE

SUMMER • 2005

Dr. Barbara O'Sullivan Becomes Administrative Leader of The Rockefeller University Hospital

by Dr. Barry S. Coller

With Dr. Emil Gotschlich's transition to Emeritus status on July 1, 2005, Dr. Barbara O'Sullivan succeeded him as the administrative leader (Chief Executive Officer) of The Rockefeller University Hospital.

Dr. O'Sullivan, who trained in Internal Medicine and Critical Care Medicine, has served with distinction as the Hospitalist for The Rockefeller University Hospital for the past three years. In addition to her medical contributions, she has also made major administrative contributions. She has chaired the Hospital's Pharmacy and Therapeutics (P&T) Committee, and has served on the Medical Records Review Committee, Medical Staff Credentials Committee, Medical Staff Executive Committee, and Isotope Human Use Subcommittee.

As Chair of the P&T Committee, she developed a novel mechanism of quality assessment and improvement for detecting potential medication errors by attending nursing sign-out sessions. The information obtained from this program has led to changes in procedures to further strengthen our medication safety program. Dr. O'Sullivan has also led the implementation of our patient and staff surveys, which have provided extremely valuable information for identifying our strengths and areas that need additional attention. She has also taken a

lead role in updating our disaster plan and the Medical Staff Bylaws and Rules and Regulations.

In addition, she has taken an active role in insuring that our medical, nursing, and administrative policies and procedures meet or exceed all of the requirements of the regulatory agencies that oversee the hospital's functions, including the Joint Commission on the Accreditation of Health Organizations (JCAHO). Finally, Dr. O'Sullivan has had extensive experience in medical systems re-engineering, having led a major re-engineering project at Mount Sinai Hospital. We are especially fortunate to have her continue to serve as Hospitalist, in addition to her new administrative responsibilities.

To assist Dr. O'Sullivan in her new role, Ms. Susan Richer will take on expanded administrative responsibilities as Director of Finance and Hospital Administration, assisting department leaders and insuring the financial stability of the hospital. Ms. Richer has served with distinction as the administrator of the General Clinical Research Center (GCRC) grant, which provides major funding for the hospital. Last year, she provided exceptionally valuable leadership in preparing for both the GCRC grant renewal submission and the subsequent site visit that resulted in an additional five years of funding.

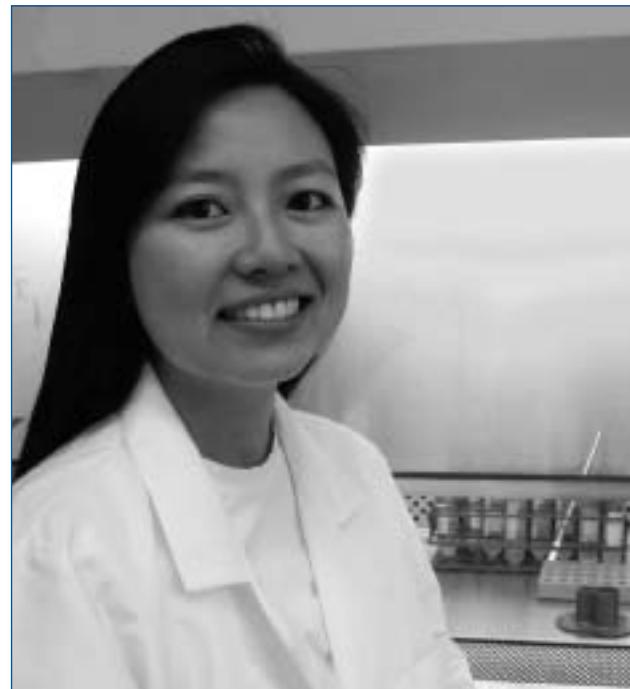
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Dr. Barbara O'Sullivan and Dr. Emil Gotschlich

Staff Honored at Nurses' Recognition Day

by Melissa Offenhartz, R.N.



Mayu Frank, M.S., A.N.P., of the Laboratory of Molecular Neuro-oncology, received the 2005 Award for Excellence in Clinical Research at Nurses' Recognition Day in May. This award is presented to a Rockefeller University nurse who exemplifies and embodies the highest level of clinical research nursing. The winner is chosen from among nominees submitted by members of our research community. Ms. Frank helps conduct clinical trials using dendritic cells in the treatment of prostate cancer. Her expert clinical skills and dedication to the research nursing profession are widely acknowledged by those who work with her.

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Mayu Frank, M.S., A.N.P.

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Understanding EBV-Associated Malignancies

by Kevin N. Heller, M.D.

Laboratory of Viral Immunobiology

Dr. Christian Münz, Head



Kevin N. Heller, M.D

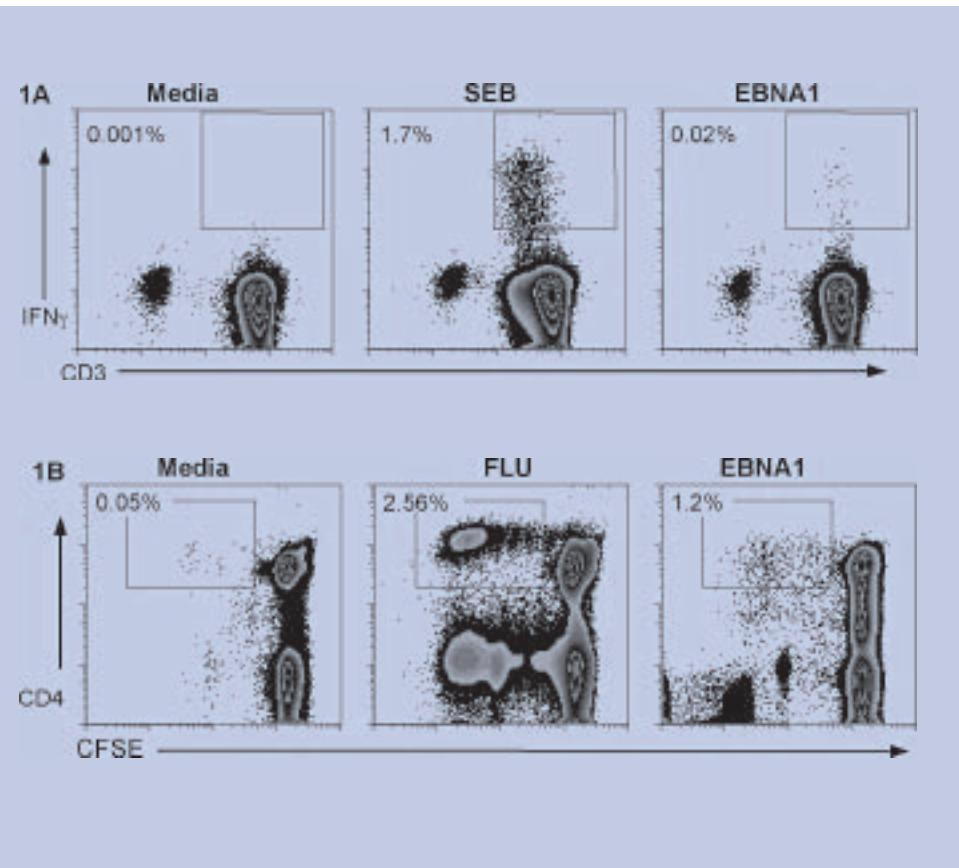


Figure 1: EBNA1 specific CD4+T cell responses can be analyzed by intracellular IFN γ staining and proliferation. A. CD4+ T cell responses from fresh blood from a healthy volunteer in response to media (no stimulus), Streptococcus enterotoxin B (SEB), and EBNA1 peptides are shown. Whole blood assay gating on CD4+ T cells; value is percent of CD3+ and CD4+ T cells expressing IFN γ in response to indicated antigens. The 0.02 percent of CD4+ T cells responding to EBNA1 is typical of the significantly small, but relevant, population of CD4+ T cells in the peripheral blood of normal individuals. B. Lymphocyte proliferation from the same healthy volunteer in response to media (no stimulus), influenza infection (FLU), and EBNA1 peptides. All lymphocytes are shown; CD4+ T cells appear above all other lymphocytes (y-axis represents CD4-positivity). Value is percent of CFSE dilute (proliferating) CD4+ T cells. This is representative of 20 healthy EBV-carriers.

The Laboratory of Viral Immunology is studying the immunobiology of the persistent and sometimes cancer-causing Epstein-Barr virus (EBV). EBV is commonly known as the virus that causes infectious mononucleosis in adolescents. This virus establishes persistent infection in more than 90 percent of the human adult population, and although most people remain completely healthy, a small minority of infected individuals develop spontaneous EBV-associated malignancies. We believe that people remain healthy because the immune system exerts a protective control over EBV.

When this immune control fails, individuals can develop EBV-associated malignancies, such as Hodgkin's disease, nasopharyngeal carcinoma, and Burkitt's lymphoma. These EBV-associated malignancies may arise either in patients without predisposing conditions, or in those with poor immune function, such as transplant recipients or patients co-infected with HIV. The greatly increased incidence of malignancy in these immunosuppressed patients underscores the important role of the immune response in controlling EBV proliferation, and thereby ultimately preventing an EBV-associated malignancy.

The research in our laboratory focuses on the differences between the immune response to EBV among healthy EBV carriers and those suffering from EBV-associated malignancies. We believe that healthy carriers of the EBV virus have a protective immune response capable of preventing the virus from proliferating to a point that it may cause malignant changes. The immune response to one protein that is common to all EBV infections, "EBNA1," has become the primary focus of our investigations. We propose that the critically important agents of immune control responsible for the EBV-protective immune phenotype are EBNA1-specific T cells. These cells even exert immune control over the EBNA1 expression program that is present exclusively in Burkitt's lymphoma. We suggest that patients may have a decreased number or altered surface markers (phenotype) of such EBNA1-specific T cells.

To assess the immune response to EBNA1, we evaluate the CD4+ T cells from patients and healthy volunteers. By exposing a volunteer's blood sample in the laboratory to EBNA1 antigens, and then evaluating the cells for activation, we can assess the number and phenotype of EBNA1-specific CD4+ T cells. In one method, EBNA1-specific T cells can be demonstrated by flow cytometry as cells that produce interferon- γ (IFN γ) when stimulated with EBNA1 (figure 1A). We also developed assays to determine EBNA1-specific CD4+ T cell proliferation, which calculates proliferation based on the dilution of a cell surface label, "CFSE" (figure 1B).

Preliminary results revealed that 90 percent of healthy carriers have this specific CD4+ T cell response. We have begun to characterize the "healthy" immune response to EBNA1 by determining the phenotype of CD4+ T cells that respond to EBNA1. Comparative studies of EBNA1-specific T cells from patients relative to our findings in healthy volunteers have begun to reveal subtle differences. Understanding these differences is the primary goal of our research.

A deficiency in EBNA1-specific T cell response may permit the development of EBV-associated tumors. Enhancing the immune response to EBNA1 may therefore be therapeutically effective. It is also conceivable that in patients suffering from an EBV-associated malignancy, the tumor itself influences the phenotype of EBNA1-specific T cell immunity. Regardless of the mechanism that leads to defective EBV-specific immune control, immunotherapies against EBV-associated malignancies could attempt to restore the protective EBNA1-specific T cells and complement current antineoplastic therapies.

Kevin Heller completed his undergraduate studies at Yale University, where he earned a Bachelor of Science degree in Molecular Biophysics and Biochemistry. As an undergraduate, he pursued interests in tumor biology and tumor immunology by participating in research at the Cold Spring Harbor Laboratory and the National Cancer Institute. He attended medical school at the George Washington University School of Medicine in Washington, D.C., and completed his residency training in pediatrics at the Children's Hospital of Buffalo. While in Buffalo, Dr. Heller had the opportunity to partake in patient care at the Roswell Park Cancer Institute, and ultimately went on to fellowship training in Pediatric Hematology and Oncology at Memorial Sloan-Kettering Cancer Center. Because of his interest in tumor immunology, he decided to work with Dr. Christian Münz in the Laboratory of Viral Immunobiology at The Rockefeller University. Upon the completion of his fellowship training at Memorial Sloan-Kettering, Dr. Heller joined The Rockefeller University as a Clinical Scholar in the Laboratory of Viral Immunobiology. Dr. Heller's current research was recognized with the Henry Christian Award by the American Federation for Medical Research.

Integrin α IIb β 3: A Mediator of Platelet Aggregation

by Beau Mitchell, M.D.

Laboratory of Blood and Vascular Biology

Dr. Barry Coller, Head

The broad long-term objectives of the Laboratory of Blood and Vascular Biology are to enhance our understanding of blood cell adhesion phenomena, and to translate that knowledge into improved diagnosis, treatment, and prevention of vascular disease. My work focuses primarily on the structure, function, and biogenesis of an adhesion molecule: integrin α IIb β 3. This protein is expressed exclusively on the surface of platelet precursors (megakaryocytes) and mature platelets, and is the primary mediator of platelet aggregation. Platelet aggregation, in turn is required to prevent bleeding from damaged blood vessels.

Patients with congenital absence of this receptor have the inherited bleeding disorder called Glanzmann thrombasthenia, and are at risk for life-threatening bleeding. The α IIb β 3 receptor is also a target of highly successful antiplatelet therapies such as abciximab, a chimeric mouse-human antibody against α IIb β 3 that has been clinically proven to reduce mortality after percutaneous coronary interventions.

The goal of my project is to identify the molecular mechanisms responsible for the intracellular processing of both normal α IIb β 3 and thrombasthenia-causing mutants of α IIb β 3. I am determining which proteins assist this complex, multi-domain, multi-subunit protein in folding and assembly inside the cell before it is sent to the cell surface. We have taken the approach of chemically blocking specific protein functions and then assaying for an effect on α IIb β 3 biogenesis. We have identified several key proteins and have developed a model for α IIb β 3 processing in the endoplasmic reticulum (the cell's protein factory). (See illustration.)

These studies of normal and mutant integrin biogenesis have been performed largely in cell lines that lack the megakaryocyte's protein trafficking and processing machinery. A high priority has therefore been to study the biogenesis of α IIb β 3 in its native cell, the human megakaryocyte. To this end, we have developed a culture system to generate megakaryocyte-lineage cells from discarded units of human umbilical cord blood. We are currently embarking on a project to develop megakaryocytes from human embryonic stem cells, which will allow for greater experimental manipulation and provide more insight into the developmental regulation of α IIb β 3 production.

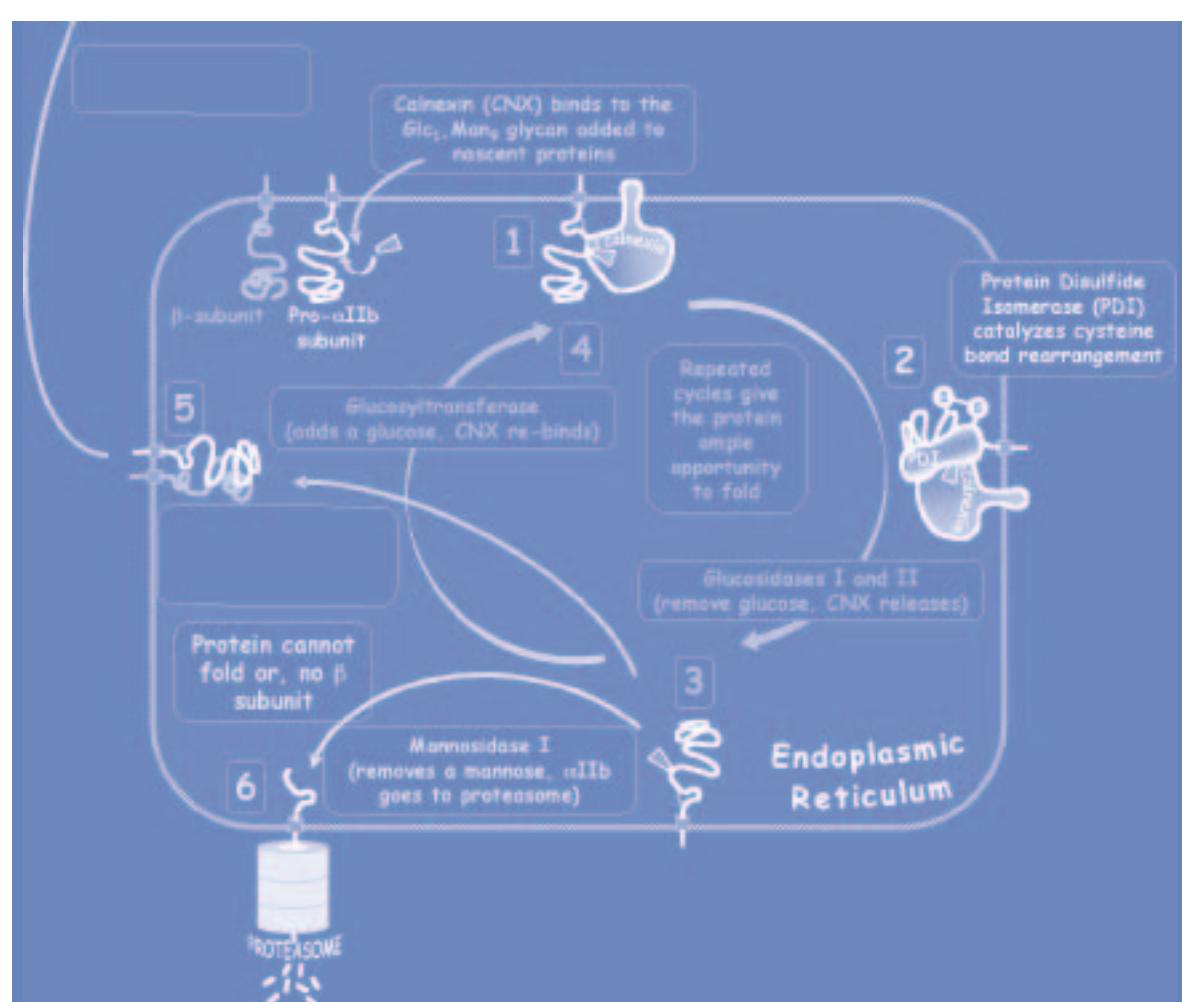
We hope these projects will significantly advance our understanding of the biogenesis of integrin receptors. Although our primary focus will be on the megakaryocyte integrin, α IIb β 3, our findings may also provide insight into the biogenesis of other integrin receptors. Since these receptors play important roles in developmental biology, tumor growth and metastasis, and many important cell adhesion and signaling phenomena, our data may have implications for a wide range of normal physiology and disease states.



Beau Mitchell, M.D.

Beau Mitchell received his bachelor's degree from Oberlin College and his medical degree from Tufts University, and completed his pediatrics training at Boston City Hospital. He joined the laboratory of Dr. Deborah French at the Mount Sinai School of Medicine in 2000 during his fellowship in Pediatric Hematology/Oncology. His first project was studying structure-function relationships in the α IIb β 3 integrin by analyzing the effects of mutations found in patients with Glanzmann thrombasthenia, and the current project grew out of those studies. Dr. Mitchell is the recipient of a KO8 award, a five-year mentored NIH grant aimed at supporting junior researchers in the transition to becoming independent researchers. Dr. Barry Coller is Dr. Mitchell's mentor on this grant, which is in its third year. Dr. Mitchell is on the faculty of the Division of Pediatric Hematology/Oncology at the Mount Sinai School of Medicine, and is currently at The Rockefeller University as a Visiting Research Associate. His clinical focus is coagulation disorders, and he plans to continue to integrate his clinical and research interests.

Schematic of α IIb β 3 biogenesis



New Nursing Personnel Introduce Themselves



Sarah Pollak, R.N., B.S.N.



Rhonda McCurchin, N.A.



Melissa Offenhartz, R.N., M.A.



Celeste Nelson, R.N., F.N.P.

Sarah Pollak, R.N., B.S.N.

I began working as a Clinical Research Nurse last January. The majority of my nursing experience has involved taking care of medical surgical patients. I was fortunate to have had the experience of traveling nursing, working in various hospitals all over the U.S., including Washington, D.C., San Diego, Denver, and San Francisco. The last couple of months here at Rockefeller have been very educational, as I have been exposed to various active protocols on the inpatient unit. I took this position to further my knowledge of the research process and to become involved in the care of patients enrolled in studies.

Rhonda McCurchin, N.A.

I work as a Nursing Assistant on the inpatient unit, located on the third floor. My past several months at Rockefeller have been a great experience for me. I am very happy to acknowledge that I am now a more advanced nursing assistant. Most of all, I've met a lot of wonderful people. I plan to attend school to further my nursing career.

Melissa Offenhartz, R.N., M.A.

I joined The Rockefeller University Hospital last January as the new Nurse Manager of the Outpatient Clinical Research Center. I was fortunate to have the expert guidance of retiring Nurse Manager Peggy Hemptstead through mid-February. I received my B.S.N. in 1993 from Indiana University, and my M.A. in nursing education from NYU in 2000. I worked as a staff nurse at Lenox Hill Hospital for seven years. My clinical experience includes medical/surgical, HIV/AIDS, and cardiac intensive care nursing. After receiving my master's degree, I worked as a critical care educator at Lenox Hill Hospital and as a cardiac clinical specialist at Mount Sinai Hospital. I was also an adjunct faculty member at the NYU Division of Nursing, teaching undergraduate pathophysiology, health assessment, nursing fundamentals, and medical/surgical nursing.

I have always had a very strong interest in research, having been a doctoral student in molecular genetics in my pre-nursing days. Working at The Rockefeller University Hospital affords me the unique opportunity to practice nursing in a research setting, and I look forward to gaining expertise in this very exciting area of nursing practice.

Celeste Nelson, R.N., F.N.P.

I am happy to come to The Rockefeller University Hospital as the new Research Coordinator for Dr. Peter Holt in the Strang Cancer Prevention Center. Dr. Holt is currently conducting colon cancer prevention studies. I graduated from Lafayette College with a B.A. in biology and from Pace University with a B.S.N. and M.S.N. I have ten years of clinical experience as a family nurse practitioner, having practiced in Manhattan for the past five years at the Allergy and Asthma Associates of Murray Hill with Drs. James Rubin and Paul Ehrlich. I gained research experience at the Marion Bessin Liver Research Center at the Albert Einstein College of Medicine under the direction of Dr. Allan Wolfson. My husband, Daniel Nelson, Ph.D., also works here at Rockefeller, in the Fischetti/Gotschlich Laboratory.

New Hospital Programmer Introduces Herself



Claudia Peissert

Claudia Peissert

I joined the Rockefeller University last January to work in the hospital as a scientific database programmer. I am developing a Web-based interactive study design, operation, and management module. I've been designing databases and developing database applications for more than nine years. For the last four years, I worked as a Senior Consultant in a software company in Berlin. I look forward to contributing to the Rockefeller University Hospital's efforts.

Patients Rate Hospital Highly in NRC/Picker Survey

by Dr. Barbara O'Sullivan

Most volunteers who have responded to The Rockefeller University Hospital's recent Patient Survey rated the overall care they received here as very good or excellent. Moreover, nearly 97 percent reported they would recommend the hospital to others. A large percentage of survey respondents also indicated that Rockefeller's reputation was the primary reason they chose to participate in the survey.

This is just some of the good news that is coming out of the latest NRC/Picker Survey, which was reported to the Hospital Committee of the Board of Trustees at their March meeting.

"Our volunteers are so grateful for the services they receive here that they have been very anxious and willing to participate in our Patient Survey," reports Cindy Seidman, Director of Regulatory Affairs at The Rockefeller University Hospital. "They see it as an opportunity to praise the staff members they regard so highly. Working with our research participants on this survey is the best part of my job."

The Picker survey has been under way for over a year, and is yielding useful and encouraging feedback. More than 350 research volunteers have consented to participate in the survey.

The survey was developed by the Picker Institute in collaboration with the National Institutes of Health (NIH) Clinical Center after a decade of research that included over 8,000 interviews with patients and healthcare providers. Through this process, the surveyors identified the areas, or "dimensions," of care that matter most to patients and healthcare professionals alike.

In contrast to the patient satisfaction surveys of yore, this type of survey yields data about specific activities and behaviors that can be measured and acted upon. It moves beyond gathering satisfaction ratings and paints a fuller picture of the patient's experience.

Specific questions – such as, "How long did you wait to see the physician?" and "Did you have all of your questions answered?" – identify areas for improvement that we can address. In addition to questions about clinical care, the survey also includes questions that evaluate research-specific areas, such as the consent process and comfort with protocol participation.

The Hospital's Physician-in-Chief, Dr. Barry Coller, first heard about the survey at an NIH Board of Governor's meeting in 2002, where the NIH

presented its results and experience with the new survey. The NIH used the survey to benchmark with academic medical centers, but identified the need to benchmark with a similar research hospital in the areas specific to clinical research. Dr. Coller suggested that The Rockefeller University Hospital participate in the survey, and benchmark relevant research-related items with the NIH.

Ms. Seidman lead the team that worked with the NIH group to develop a survey that offered customized questions, while maintaining enough congruity with the NIH survey to enable benchmarking on important research areas of common interest.

At Dr. Coller's suggestion, this survey instrument was presented to the IRB for their review of issues relating to privacy and confidentiality. At the IRB's suggestion, the survey was structured as an investigational protocol, requiring that the volunteers consent to participate. This approach offers the opportunity to publish findings from the survey that may be applicable to other hospitals.

The survey also fulfills an important regulatory requirement. One of the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) standards requires the hospital to collect data and monitor performance improvement activities in the areas of patient safety, pain management, and continuity of care. The survey instrument enables the hospital to perform this function.

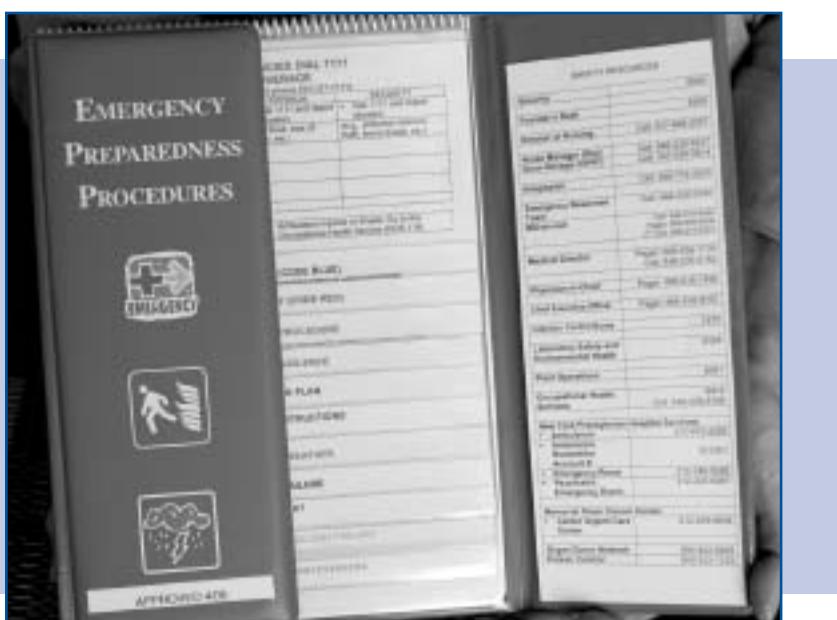
With a year of data available, the Senior Staff Hospital Committee has developed an action plan and timeline to address areas for improvement. We will continue to measure our patient's perceptions of care, and assess the impact of these changes. We will also strive to maintain the level of performance that was reflected in our first survey period.

It is important to put strong emphasis on the hospital's strengths and to ensure that every employee understands what is most important to our patients. We recognize that patient volunteers are critical members of the clinical research team. Their input about hospital services is vital to improving our operations and service. And their expression of appreciation for the work we do here is...priceless.

Be Prepared!

by Kelly McClary, R.N.

Fire. Bomb threat. Hazardous material spill. Serious IT failure. Needle-stick injury. What should you do? The answer is...reach for the new red Emergency Preparedness Binder, which contains the answers to these questions, and many more. The contents of the binders were fastidiously developed by members of the Environment of Care Committee, which coordinates the Safety Program at The Rockefeller University Hospital.



Included in the binder is valuable information on:

- Safety: an overview of how to get emergency assistance from the University, with an emphasis on dialing 1111 from an in-house extension or 212-327-7111 from a cell phone or outside line
- Cardiac Arrest/Code Blue: the code called in our hospital when a patient's health status is deteriorating rapidly
- Fire Emergency/Code Red: the code called in our hospital to inform staff members that there is a fire on the unit

- Evacuation Plan and Route: the essentials of who, what, where, when, and how to evacuate patients from the patient care areas
- Hazardous Materials and Waste Management: the essentials of what to do in the event of a hazardous materials spill or exposure
- Inclement Weather: The Rockefeller University telephone number to call for information in the event of inclement weather (212-327-7200) and the responsibilities of staff members during a storm
- Information Technology Failure: the essentials of how to obtain assistance if a hardware or software failure should occur, and a synopsis of what to do in the event of complete failure while you are working on any patient care computer
- Needle Stick Injury Procedure: what to do in the event of a needle stick injury
- Utility Failure: how to contact essential personnel if a utility failure occurs
- Workplace Violence: the essentials of the University's policy on workplace violence, and how to obtain help if you observe or experience workplace violence

On the left and right flaps, respectively, are the following:

- Bomb Threat Procedure & Checklist
- Contact Numbers: essential contact numbers listed in alphabetical order for key responders or agencies that may need to respond to a safety event

Binders have been placed in all high traffic areas, including the Nurses' Stations, Bionutrition, Hospital Information Services, and Pharmacy, as well as in the offices of other key responders. The binders will be updated as necessary, and at least annually. The binders are also used as a teaching tool during new employee orientation for our hospital-specific safety program.

The next time you are in the hospital, find a binder and take a look at its contents, so you will know where to get essential information in the event of an emergency.

Nurses' Recognition Day 2005 Has an International Flavor

by Melissa Offenhartz, R.N.



National Nurses' Week begins each year on May 6th and continues through Florence Nightingale's birthday, May 12th. This weeklong celebration and recognition of the work done by professional nurses was officially sanctioned in 1982, when President Reagan signed a proclamation declaring May 6th to be "National Recognition Day for Nurses." From that one day, the celebration evolved into National Nurses' Week. On May 10, 2005, The Rockefeller University Hospital recognized its own nurses as part of this National Nurses' Week celebration.

The theme chosen for this year's celebration was "Nursing around the World," in recognition of the diversity within our nursing staff, as well as the international experiences that many of The Rockefeller University nurses have had. This theme also dovetailed with a multicultural educational initiative undertaken this year throughout the hospital.

Members of the nursing staff prepared poster exhibits displaying their personal experiences of international nursing. Marian O'Rourke, clinical research nurse in the inpatient unit of the hospital, shared photographs and recollections of nursing in Ireland and Saudi Arabia. Jill Culiner, nurse practitioner in the Breslow lab, offered reminiscences and images of her nursing school experiences at Oxford, in the United Kingdom. Kathy Bell, research nurse in the Kreek lab, recognized the "global" aspects of nursing in New York. And Juanita Hickman, nurse manager of the inpatient unit, served up some "MREs" (meals ready to eat), as well as photos of her experiences as a military nurse in Saudi Arabia and Iraq. A poster highlighting the global nursing shortage was presented by Melissa Offenhartz, nurse manager of the outpatient unit.

The celebration began with a welcome speech by Director of Nursing and Patient Care Services Kelly

McClary, R.N. Ms. McClary described the specialized role of the clinical research nurse, and advocated for the recognition of this profession as a defined nursing specialty. She also highlighted the important contributions made by the clinical research nurses to the overall mission and functioning of The Rockefeller University Hospital.

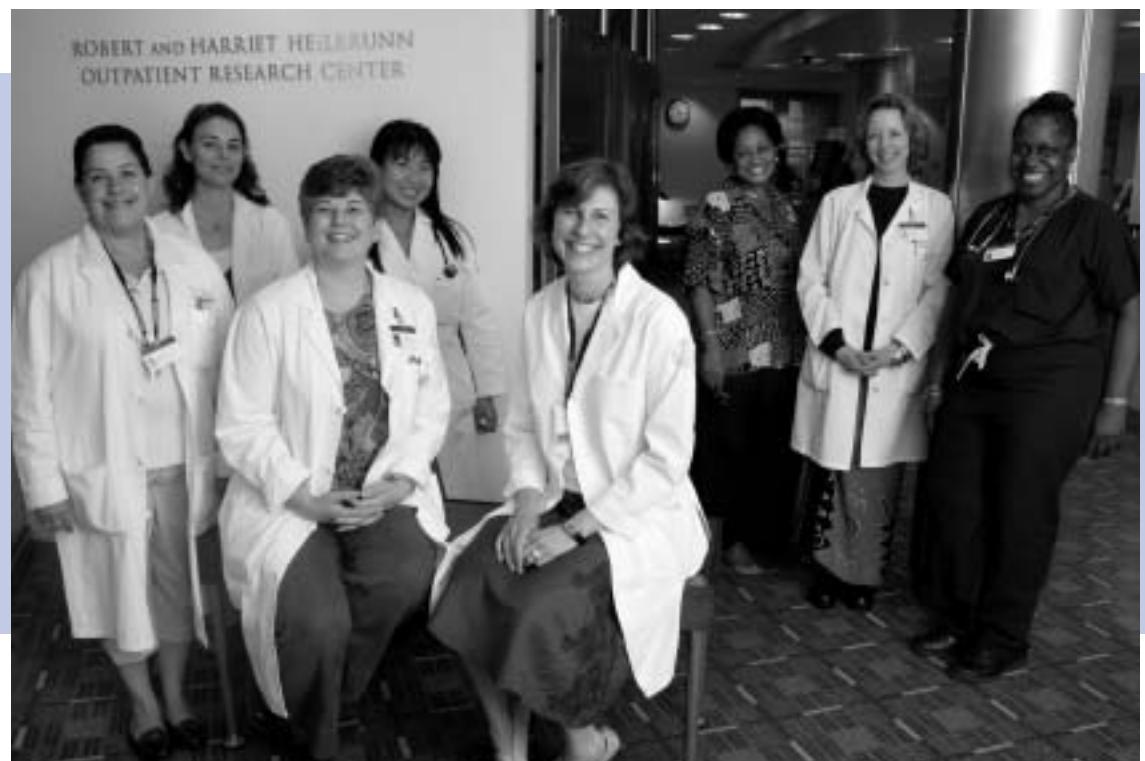
Ms. McClary also presented the annual awards for excellence in Research Nursing (see related article).

Karen Zaremba-Soto, Arts, Recreation, and Special Events Coordinator, and Bryan Whitefield, Coordinator for Nursing and Patient Care Services, produced a documentary of Oscar-winning quality on Nurses' Week, soliciting commentary and scripted "factoids" about nurses, nursing, and nurses' week from a broad cross-section of The Rockefeller University community. Contributors included Dr. Barry Coller – donning a hard hat and bow tie – members of the nursing, bionutrition, security, and maintenance staffs, and Rockefeller University President Paul Nurse, who delighted everyone with his observations about being "Doctor Nurse."

Finally, Dr. Barry Coller offered his perspective on clinical research nursing, including observations on how vital and challenging regular patient care nursing is, and how doubly vital and challenging it is to integrate both patient care nursing and participation in the clinical research team's efforts to obtain important new scientific knowledge. He emphasized that the research nurse plays a crucial role by having dual responsibilities as patient comforter and patient advocate. He thanked The Rockefeller University nurses for their important contributions to the research activities of our institution.

Staff Honored *continued from Page 1*

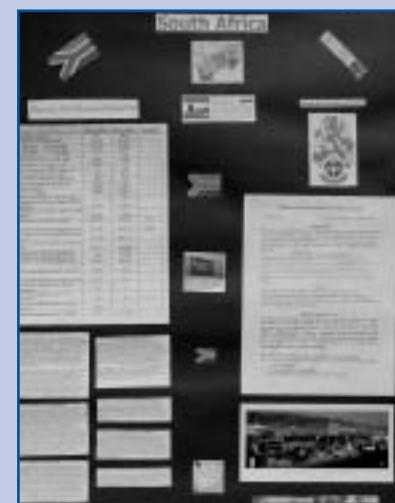
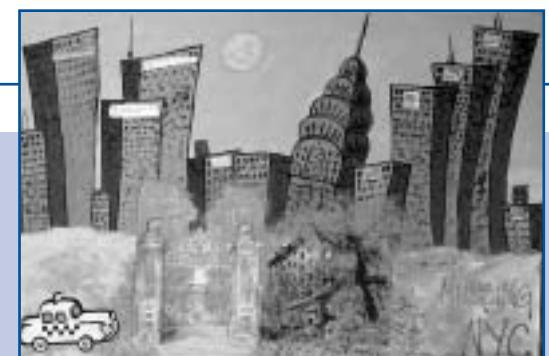
The nurse managers of the inpatient and outpatient units presented special awards to members of their nursing staffs for their contributions to Rockefeller University hospital nursing. Juanita Hickman selected Marian O'Rourke for special recognition on the inpatient day shift. Alex Buenaventura honored Ellen Martin on the evening shift and Vedanta Sharma on the night shift. The entire outpatient unit staff was acknowledged by their new nurse manager, Melissa Offenhartz, for their expertise and teamwork. In addition, all of the clinical research nurses received gifts of hats, bags, and personalized leather bookmarks.



Members of the outpatient unit staff include (standing, left to right), Cecilia Trilla-Hernandez, Dana Panepinto, Lori Tam, R.N., Maggie Guiland, Kathy Bell, R.N., and Olga Ford, N.A. Seated: Kelly McClary and Melissa Offenhartz. Not pictured: Delia Delarama, R.N., Lalitha Mantha, R.N. and Mosizert Murphy, N.A.



Kelly McClary, R.N and Melissa Offenhartz, R.N.



Left to right: Lalitha Mantha, Melissa Offenhartz, Lori Tam and Delia Delarama



Vedanta Sharma



Ellen Martin



Marian O'Rourke

Pharmacy System Upgrade

by Johanne Andersen and Jean Jenkins

The Hospital IT and Pharmacy Departments successfully completed a major upgrade of the Horizon Meds Manager Pharmacy Information System last January. The upgrade included the installation of McKesson Corporation's most advanced system (8.1), as well as infrastructure upgrades of computers, servers, and printers. An upgrade contract was negotiated in the spring by Jean Jenkins, The Rockefeller University Hospital IT project manager, with support from the legal and pharmacy departments. The upgrade project began in October 2004.

How does the upgrade improve our medication use process?

The hospital investigated the Medication Use Process in 2003. As our guiding principle, we determined that patient safety was our primary goal, and decided that any new system or a change to an existing system should:

- be as safe or safer than the system being replaced
- be as effective or more efficient than the system being replaced
- be less confusing than the system being replaced
- make it easier to "do right and harder to do wrong"

The upgrades of the Pharmacy Information System meet all these principles, as shown in the list of enhancements below.

The Upgrade Process

Jean Jenkins led the hospital project team, which included Johanne Anderson, research pharmacist, Alex Peshansky, system manager, and Eamonn O'Donnell, interface programmer. The team was responsible for procuring the new hardware and creating the test environment, developing the interfaces to existing systems, and evaluating the functional and technical aspects of the system.

Comprehensive testing was conducted throughout the process to insure that the system was working properly before implementation. Realizing that all IT systems have the potential to be out of service, the system was specifically engineered so that there would be minimal disruption of pharmacy service in the event of a hardware or software failure.

Enhancements

The enhancements to the Pharmacy Information System can be divided into three categories, patient safety, increased efficiency in workflow, and enhanced reliability of the computer system.

Enhanced patient safety features include:

- screening orders for conformity to minimum and maximum drug dosage
- customizing dosing with respect to patient's age and renal or hepatic function
- alerting the pharmacist and physician when drugs are contraindicated, based on the patient's diagnosis or the drug's side effects
- screening drugs for appropriateness in pregnant or lactating patients
- screening for specific pediatric and geriatric precautions
- screening of the patient's own medication
- setting up protocols that allow therapies to be linked together for a specific research or treatment protocol
- setting limits for dispensing of a drug to insure compliance with the protocol
- limiting prescribing to only individuals that have the proper credentials and privileges
- building of small rule-based programs to automate safety alerts



Jean Jenkins and Johanne Andersen

Efficiency enhancements include:

- automatic generation of unique system-defined national drug codes, which previously were generated manually
- task organizer that reminds the pharmacist that certain tasks need to be done.
- automation of certain tasks, e.g., generation of patient medication profiles
- new methods for communication between the pharmacist and other users of the system

Reliability features include:

- automated printing of patient medication profiles, prescription logs, and medication labels overnight, so that hardcopies will be available in the case of a system outage
- upgrades to more reliable operating systems and databases
- improved printer that produces clear, precise drug labels

These improvements have elevated Pharmacy Information System to state-of-the-art standards. Please let us know if you have suggestions for further improving this system or tailoring it to the needs of your research team.

Adding WISDOM to Clinical Studies

by Knut Wittkowski

From the conception of a clinical study to the publication of its results, a principal investigator or study coordinator needs to describe the study several times:

- for the power calculation relating the primary aims to the number of subjects put at risk
- in the documents for funding agencies, GCRC scientific advisory committee (GAC), and Institutional Review Board (IRB)
- for creation of a database, paper or online case report forms (CRF), and instructions for nurses
- when producing the graphs, tables, and analyses needed for monitoring study progress and subject safety, publishing the results, and generating hypotheses for subsequent studies.

Given the increasing amount of genetic, genomic, proteomic, and metabolic data to be handled, and the often idiosyncratic nature of the various analysis programs typically used in a research environment, this process is cumbersome and error-prone. As the complexity of experimental designs and the choice of statistical methods increases, so does the need for data management and decision support.

In my Ph.D. thesis I developed a formal representation of study design knowledge and the PArametric and NOnparametric Statistics (PANOS) system to assist investigators in choosing a statistical method, finding a program that implements this method, and then generating the appropriate program code. As with many ‘expert systems’, however, knowledge acquisition remained a bottleneck. When this approach was commercialized by SAS, Inc. in 1989 as JMP, therefore, only a small portion of the knowledge required for more comprehensive assistance was incorporated.

In January 2005, Claudia Peissert, a scientific database programmer with extensive experience in modern rapid prototyping systems, joined the hospital. Since then, she has developed a Web-based graphical interface where investigators or study coordinators can describe clinical trials interactively in sufficient detail to allow for support during various study related tasks. This knowledge acquisition module is the first step in the development of a Web-based Interactive Study Design, Operation, and Monitoring (WISDOM) system.

The version of WISDOM to be released in October 2005 will contain a knowledge base and interfaces for:

- **protocol writing:** producing a “study timeline” to be included with a protocol
- **database creation:** on a server running Oracle in a fashion that is entirely transparent to the user
- **data entry:** producing paper CRFs and online data entry forms
- **security:** presenting browser windows for uploading data from spreadsheets and downloading data for analyses, thereby adding back-up, a relational database, and Web access to the current workflow

In the next version, the PANOS system will be integrated, so that investigators will gain support for:

- **analysis:** accessing S-Plus and the multivariate u-statistics (μ STAT) tools for high-throughput non-parametric statistics developed by my group and currently made available on the hospital’s grid of PCs (managed by Alex Peshansky, Head of the Hospital’s Informatics Core) via the Web on muStat.rockefeller.edu (supported by Cameron Coffran, The Rockefeller University IT department).

Further steps will include improvements based on feedback from our investigators, but also addressing:

- **sample size calculations:** allowing to simulate power for complex designs
- **(more) protocol writing:** pre-populating protocol templates for NIH’s ProtoType system
- **study management:** providing nurses with workflow information
- **monitoring:** detecting emerging profiles of adverse events (by automatically accessing μ STAT)
- **review:** providing the Institutional Review Board with progress information.

I welcome your feedback about these new tools and suggestions for additional features that may facilitate your research.

Online Clinical Research Teaching Modules Near Debut

by Dr. Rhonda Kost, Clinical Research Officer

The Clinical Research Office initiative to develop a series of novel online teaching modules to train the research community in both basic and advanced elements of safe and ethical conduct of clinical research is almost ready for its debut. The modules are part of an educational program based on the NIH Clinical Center’s Guidelines and Six Standards for Clinical Investigative Research: 1) Clinical Informatics and Data Support; 2) Biostatistics Support; 3) Protocol Review; 4) Human Resources and Physical Plant; 5) Quality Control & Quality Assurance, and 6) Training and Education. Training and Education in human subjects protection encompasses history, standards, ethics, IRB, protocol design and writing, and informed consent.

The most familiar element of Training and Education – the core Human Subject Protection Training (HSPT), required of every researcher conducting human subjects research – is well covered elsewhere, and we chose not to redesign this. For instance, along with 1,000 other academic institutions, The Rockefeller University Hospital subscribes to the CITI website as one of the basic Human Subjects Protection training options available to all personnel conducting human subjects research at the hospital. For more information on our HSPT policy and training options, please to visit www.clinfo.rockefeller.edu.

Many elements of the Guidelines and Standards for Clinical Investigative Research are not covered elsewhere, however, and we sought to develop these at the hospital for our research community and our collaborators. For instance, most investigators know that Informed Consent is a process, that it must contain certain federally specified elements, that it must be free of coercion, etc. Fewer investigators, however, may know how to administer a simple test of human subject comprehension after providing information to prospective research subjects; or that the test only takes a few minutes; or that simple behaviors such as accepting telephone calls that interrupt an interview, exhibiting certain types of body language during the interview, or making subtle implications about potential therapeutic benefit may subvert a free and voluntary consent. The Informed Consent and Therapeutic Misconception modules address these and other important issues.



Rhonda Kost

Moreover, investigators are often told by the IRB that the language of their consent forms is too sophisticated, but they may not know how to simplify it. The “Readability and the Informed Consent Document” module addresses this issue in practical terms.

Together with Dr. Kost, Andrea Scott of the Clinical Research Office has drafted many versions of text, and she has worked with focus groups of Rockefeller coordinators, Clinical Scholars, and investigators to refine the

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New Outpatient Computerized Scheduling System Is a Big Hit

by Jean Jenkins

The Outpatient Scheduling System has streamlined the patient scheduling process for the hospital's Outpatient Clinic. Developed in 2002, the system provides an online patient appointment book, and has completely replaced the paper schedule. Daily schedules are easily visible through a Web-based interface, and include the patient's name and medical record number, the time of the appointment, the study name, and the physician or nurse practitioner in charge of the study. A comments field provides an opportunity to include other details about the patient visit, such as medical tests ordered or specific patient instructions.

The system has already undergone a series of improvements suggested by staff. E-mail notifications to the Unit Clerks, for example, are now generated when a patient changes or cancels an appointment. In addition, graphical representations of appointment status have been added. Color schemes (green if the patient attended the appointment, red with the patient's name "lined out" if the patient was a no-show) allow nurses to quickly identify last-minute scheduling changes.

The scheduling system interfaces directly with the ADT system, insuring accurate and uniform reporting. At the end of each day, the Nursing Unit Clerks review and finalize the day's appointments. They then select the "Insert Into ADT" option from the scheduling system menu, which automatically loads the day's patient information into the ADT system. Unit Clerks also generate reports from the scheduling system that are used for monthly NIH reporting. Prior to having these options, patient lists were written by hand for data entry into the ADT system, and monthly NIH statistics were tallied manually. Cecilia Trilla-Hernandez, Outpatient Unit Clerk, praised the new

scheduling system: "The system is easy to use and not only saves me time, but also reduces the chance for error."

Patient care improvements are another result of the Outpatient Scheduling System. "The scheduling system provides a clear and quick way of identifying patients who will be seen today and in the future," says Dana Panepinto, Outpatient Unit Clerk. "For investigators, as well as patients, information can be accessed in a matter of minutes, whether it concerns an upcoming appointment or procedures that may have been requested."

Earlier this year, patient scheduling was made available to the research labs. Study coordinators and nurses from the Aaron Diamond AIDS Research Center (ADARC), Kreek Lab, Krueger Lab, and other labs were trained on the system and began scheduling their own patients. The systems security architecture is designed so that lab personnel can manage only their own lab's appointments. Susan Parker, MPH and new Study Coordinator for ADARC, who has extensive experience in clinical research settings, says that by allowing the scheduling of appointments online instead of on paper, the automated patient scheduling system allows her to focus more attention on patients and protocol procedures involved in the ADARC studies.

Future enhancements to the Outpatient Scheduling System are planned for this summer. These will include enhanced search capabilities, more specific e-mail notifications of appointment changes, and additional reports.

If you are interested in knowing more about the Outpatient Scheduling System, would like to suggest new improvements, or would like to request a user ID, please contact Melissa Offenhartz at extension 8105.

Honoring Dr. Emil Gotschlich

On June 29th, 2005 more than 100 colleagues, friends, and family celebrated Dr. Emil Gotschlich's upcoming transition to Emeritus status on July 1st, 2005, at a barbecue held in his honor in the Faculty Club and Philosopher's Garden.

Brief comments were offered by several of the attendees. Dr. Vince Fischetti reviewed Dr. Gotschlich's many scientific achievements, most notably the development of a vaccine for meningitis that has saved lives throughout the world. Dr. James Krueger expressed his appreciation to Emil for his efforts in supporting clinical investigation at Rockefeller through difficult times and wished him well in his new status as an Emeritus Professor, a position he characterized as the "best job in the world". Ms. Susan Richer recounted the nearly innumerable number of meetings, grant submissions, and reports Dr. Gotschlich has attended and/or been responsible for, all performed with grace, good humor, and a commitment to excellence. Dr. John Zabriskie recounted a story of Dr. Gotschlich's inventiveness in using laboratory equipment to make a memorable, if not flavorful, vat of beer. On behalf of the staff of the office of General Counsel, Harriet Raab presented Dr. Gotschlich with a certificate awarding him a "Doctor of Law, honoris causa" and bestowing on him the title of "First and Only Honorary Member of The Office of General Counsel".

Dr. Barry Coller concluded the presentations by saying that the thread that has run through Dr. Gotschlich's career is his desire to help others by his scientific excellence, advisory roles, academic leadership, administrative leadership, collegiality, and individual mentoring. He also announced that to honor Dr. Gotschlich, his friends and colleagues have contributed to a fund to purchase a portrait of Dr. Gotschlich that will be displayed in the Rockefeller University Hospital, alongside those of other great Rockefeller University physician-scientists. Dr. Gotschlich thanked everyone for their presentations, discussed how he came to lead the Hospital and clinical research program at Rockefeller, and expressed the warm feelings he has for leading such an outstanding group of people with such an important mission.



Dr. Emil Gotschlich and Dr. Knut Wittkowski



Dr. Vincent Fischetti and Dr. Daniel Nelson



Dr. John Zabriskie



Dr. James Krueger and Dr. Jeffrey Friedman



Dr. Peter Protiva (center) shows his support for Dr. Emil Gotschlich to Alex Buenaventura (left) and Jennifer Spada (right).

Teaching Modules continued from Page 9

content, look, and feel of the modules to ultimately meet users' needs. Nationally recognized developers of other Human Subject Protections training materials have also reviewed the materials, and have applauded Andrea's modules for their content and creativity. The Rockefeller University recently invested in "Element K," a Web-based service that has a broad variety of employee training courses and offers the potential to develop customized training modules. The Clinical Research Office chose Element K to author the Clinical Research Teaching Modules, and in a surprisingly short period of time, the modules are just about ready to test and debut.

Modules that will be ready to test soon include:

- Informed Consent: An Introduction
- Readability and the Informed Consent Document
- Cross-Cultural Approaches to Informed Consent
- Therapeutic Misconception and Psychological Barriers
- Communicating Across Language Barriers: Volunteers with Limited English Proficiency
- Recruiting Minorities in Research

- IRB Policy on the Use of Translations and Interpreters
- Informed Consent for Pediatric Research
- Human Research Using Stored Samples or Data
- Quality Assurance in Data Management
- Adverse Event Reporting
- An Introduction to The Rockefeller University IRB
- Participating in Clinical Research: An Introduction for Volunteers
- An Introduction to the Scientific Advisory Committee

Each module features a series of associated questions for formal assessment. Subjects may stop at any time during a session and resume it later. Modules may be repeated until a passing score is achieved.

Look for future announcements for the debut of the first modules, and coming attractions for the modules still in development. We welcome your input in constructing and refining the modules, so let us know if you would like to volunteer for a focus group for the development of future modules. If you have suggestions for future modules or would like to comment on existing modules, please let us know by e-mailing kostr@rockefeller.edu.

Barbara O'Sullivan continued from Page 1

She has also played important roles in developing the hospital's yearly budget and negotiating our contracts with New York Presbyterian Hospital and Memorial Hospital. Ms. Richer has also made important contributions at the national level, conducting workshops for the GCRC Administrators Association. In her new role under Dr. O'Sullivan's leadership, she will be responsible for ensuring that department leaders have the administrative support they require to accomplish their goals.

Ms. Jennifer Spada, who previously provided administrative support to Ms. Richer, will also take on additional responsibilities, serving as the administrative assistant to both Dr. O'Sullivan and Ms. Richer.

This transition provides an opportunity to express the faculty's and staff's deep appreciation to Dr. Emil Gotschlich for his extraordinarily effective and devoted leadership of the hospital during the last nine years. In addition to serving as the Principal Investigator of The Rockefeller University GCRC grant, his many contributions include the design and construction of the beautiful and highly functional Robert and Harriet Heilbrunn Outpatient Research Center; rehabilitation of the third floor inpatient unit; the recruitments of Dr. Madhav Dhodapkar as a new Assistant Professor, Head of

Laboratory, Dr. Rhonda Kost as Clinical Research Officer, and Ms. Kelly McClary as Director of Nursing and Patient Care Services; two renewals of the GCRC grant; multiple outstanding reviews of the hospital by the JCAHO; significant increases in the number of human subjects protocols and hospital utilization; and providing encouraging support of new investigators, including basic scientists who previously had not conducted clinical studies.

Dr. Gotschlich has also provided exemplary leadership to our Institutional Review Board (IRB), serving as Chair for the last three years. We are especially fortunate that he has agreed to continue to serve as Chair of the IRB after his transition to Emeritus status. Dr. Gotschlich's outstanding administrative achievements complement his outstanding scientific achievements, including his pioneering work in developing a vaccine for meningitis that has saved many lives.

To mark Dr. Gotschlich's transition and to thank him for his many contributions, the faculty and staff celebrated together at a barbecue in Dr. Gotschlich's honor on June 29 in Scholars Garden and the Faculty Club. See previous page.



In Memoriam | Patricia Joy Macklin Years of Service: 1965 – 2005

by Emil C. Gotschlich, M.D.

Pat J. Macklin, a cherished member of our community for 40 years, passed away on April 14. Following high school graduation and a year of training at a medical secretarial school, Patricia Joy McDermott began her career as a secretary at The Rockefeller University in February 1965. In 1976, she joined Kathy Kleinbard, who had just been appointed Hospital Superintendent by Dr. Attallah Kappas, and the two together became the public face of the hospital.

"She was off and running," Kathy recalls. "There was the accreditation of the hospital for the first time, the grant application to take care of, operating manuals for each department, new procedures, staff restructuring, and so on and so on. Word processors replaced the IBM Selectric typewriters, setting everyone on edge – except Pat, who became an expert overnight. Recognizing her as special, all of us stopped by her desk, not to chatter – because she had no time for that – but to check in and, in some sense, recharge and re-center ourselves. This was the effect she had on all of us." She was also the one who quietly saw to it that the copying machine was properly stocked with paper and the employee refrigerator was regularly defrosted.

When Kathy Kleinbard Heinzelman left in 1988, Pat assumed responsibility for the administration of the IRB and several other functions. In time, as public awareness of the importance of protecting individuals who volunteer to participate in research studies became more prominent and the administrative burdens

escalated, she concentrated all her energies on the IRB. She was always ready to help investigators with their applications, and projected an aura that the IRB was there to serve the needs both of the study participants and the investigators. Pat adored her husband, Bill Macklin, and his family, as well as her own cherished relatives, and she had many very close friends at The Rockefeller University.

When Pat found out she had cancer two years ago, she chose to face this illness with awe-inspiring courage and optimism. She was a person with great personal style. When she needed to purchase a wig, as with everything she wore, she chose it with great care, and took real pleasure in her new curly self. Despite the travails of surgery and chemotherapy, she was always eager to come back to work as soon as possible, because she loved it and her close relations with other members of the staff so dearly.

We are terribly saddened that Pat is no longer with us, and realize how fortunate we were to have such a wonderful person as a colleague and friend for the 40 years of her life that she worked at The Rockefeller University. Fred Seitz summed it up best when he said, "God makes a few perfect people, and Pat was one of them."



GOOD NEWS



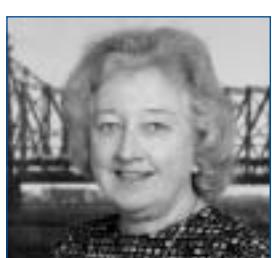
Dr. Anita Shet



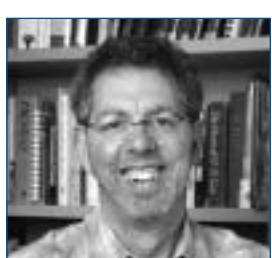
Dr. Sergey Yurasov



Dr. Christian Munz



Dr. Mary Jeanne Kreek



Dr. Jeffrey Friedman

Clinical Scholars and Fellows Honors and Awards

Dr. Kevin Heller received the "Outstanding Junior Investigator" award and a Henry Christian Award from the American Federation of Medical Research for the abstract he presented at the 2005 Clinical Research Meeting in Washington, D.C.

Dr. Anita Shet received a grant from the Richard Lounsbery Foundation, Washington, D.C., to study methicillin-resistant *Staphylococcus aureus* colonization in HIV-infected patients.

Dr. Sergey Yurasov was named a Dorothy W. Goldstein Young Scholar by the New York Chapter of the Arthritis Foundation.

Faculty Honors and Awards

Dr. Christian Munz received the Alexandrine and Alexander Sinsheimer Scholar Award and the Arnold and Mabel Beckman Young Investigator Award for his research on Epstein-Barr virus.

Dr. Mary Jeanne Kreek received the Marian Fischman Award for "outstanding scientific research career of a woman" given by the College of Problems and Drug Dependence, and the Founders Award for "outstanding scientific research and contributions to the International Narcotic Research Conference" given by the International Narcotic Research Conference.

Dr. David Ho received an honorary doctorate from Tulane University.

Dr. Jeffrey Friedman received the Gairdner Foundation International Award and the Passano Foundation Award.

Dr. Barry Coller received the 2005 Robert J. and Claire Pasarow Award in Cardiovascular Research, and was elected to the American Academy of Arts and Sciences.

THE ROCKEFELLER
UNIVERSITY HOSPITAL

UPDATE

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Editor:
Barry Coller, M.D.

Design:
John Haubrich

Contributing Editor:
Rosie Foster

Photographers:
Lubosh Stepanek, Ellen Martin,
Karen Zaremba-Soto, Jeff Smith,
Zach Veilleux

Production Manager:
Lynn Kolibaba

Hospital Façade Restoration

by Bob Nelson and Kelly McClary, RN

Restoration of the hospital's façade is more than 90 percent complete! The scaffolding has been brought down to the second floor, so most of the building's occupants will now enjoy an unobstructed view from their windows.

The remaining balcony and stone work is anticipated to be completed by September. Once it is completed, the remaining scaffolding will be removed. The upgrade for the main entrance to the A-level Outpatient Research Center will then be initiated.

We thank you for your patience during these renovations!

