July 2007

The Rockefeller University 1901
SCIENCE FOR THE BENEFIT OF HUMANITY

Center for Clinical and Translational Science
e-NEWSLETTER

Center News

Ms. Melissa Offenhartz, RN, MA, is Promoted to Director of Nursing and Patient Care Services

On May 1st, 2007 Ms. Melissa Offenhartz became Director of Nursing and Patient Care Services, succeeding Ms. Kelly McClary.

Ms. Offenhartz came to Rockefeller in January 2005 as the Nurse Manager of the Outpatient Research Unit. Based on her outstanding performance and leadership skills she was promoted to Assistant Director of Nursing the following year. She has become a role model and mentor for staff members, as well as a resource for investigators and their research teams.

Over the course of her tenure here, Ms. Offenhartz has made many contributions to the Department of Nursing as well as to the Rockefeller University Hospital and the Center for Clinical and Translational Science. She has:

- Participated in many Root Cause Analysis teams, contributing creative solutions to difficult problems.
- Revised the Nursing Department's mandatory and continuing education program meeting or exceeding all regulatory agency requirements. The success of this program is demonstrated by reports of high staff satisfaction, participation and compliance.
- Taught basic pathophysiology to undergraduate nurses during winter semester at New York University, thus promoting Rockefeller University in the field of Nursing and encouraging potential recruits to consider the specialty of Clinical Research Nursing at Rockefeller University Center for

Pilot Projects Submission Deadline is Sept. 4, 2007

Instructions for Preparing Pilot Project Grant Submissions

Grants to support pilot projects within the scope of translational or clinical studies will be supported for 1 year for amounts up to $25,000. New collaborative studies that advance clinical or translational research may also be supported by this program. A second year of funding is possible, but will be determined after a progress report for the first year is submitted and the funding will be competitive with new submissions. Approximately 4 awards will be made each year.

Applications will be reviewed by the Pilot and Collaborative Translational and Clinical Studies Subcommittee of the Advisory Committee for Clinical and Translational Science (ACCTS) and presented to the ACCTS for final determination of funding.

The key elements of a submission are

1Abstract
2. Specific Aims
3. Background and Significance
4. Preliminary Studies, if relevant
5. Research Design and Methods.
6. Literature Citations

The application should include a brief abstract. That abstract should contain an

Announcements

Brian Bennett to Lead Day-Long Good Clinical Practice Training Session

On Thursday, July 12th Mr. Brian Bennett, an acclaimed GCP trainer and frequent speaker at meetings of the Association of Clinical Research Professionals (ACRP), will give an all-day training session in GCP in Clinical Research at the Center. Investigators, coordinators, Clinical Scholars, research nurses, and all others are encouraged to attend. The session will be held in Nurse's Residence room 110B, from 9AM - 5PM. Lunch will be provided. Please click here to view the agenda for this exciting training opportunity. Please contact Ms. Donna Brassil at 212-327-7886 for further information.

Plain Language Seminar to be Presented by Wendy Mettger, M.A.

A "Plain Language" seminar will be presented by Wendy Mettger, M.A. of the Clear Language Group on Thursday, August 2nd, 2007, 12noon-4pm, hosted by the Clinical Research Support Office. The seminar is intended for investigators, Clinical Scholars, coordinators, recruiters, and others who need to communicate clearly in writing. The format of the seminar will include a 1-1/2 hour presentation of the principles and examples of the application of Plain Language principles, followed by a practical workshop in which written materials will be revised. Ms. Mettger played a critical role in the development of the National Cancer Institute's plain language informed consent template for cancer treatment clinical trials. In addition, she was awarded a 2003 NIH Plain Language Award and two Pfizer Health Literacy Visiting Lecturer Grants. Please call Dr. Rhonda Kost at 212-327-8408 (kostr@rockefeller.edu) for further information, and to confirm space in the workshop. Everyone is welcome.

New Center Core Facilities

The Metabolic Core at the Rockefeller University Center for Clinical and Translational Science offers investigators the use of several metabolic and body composition testing devices that they can incorporate into their protocols. Below is a brief description of each test. For more information, please contact Suzanne Magnotta at smagnotta@rockefeller.edu; 212-327-8397.

Estimation of Resting Energy Expenditure

The VMAX Encore Indirect Calorimeter is used to determine resting metabolic rate. This test is important to those investigators who are conducting metabolic diet studies and who need to accurately assess a subject's weight maintenance calorie needs. Respiratory Quotient (RQ) measurement is also available to determine what substrate a subject is burning for fuel at a given time-point.

Free Living Energy Expenditure

To measure free living energy expenditure, the "Intelligent Device for Energy Expenditure and Activity" (IDEEA; MiniSun, Fresno, CA) can analyze body motion, measure physical activity, monitor behavior patterns, and estimate energy expenditure in a free-living situation on 24-hour basis. The IDEEA consists of five small sensors that are attached to the body via flexible cables: one on the chest, two on the anterior part of thighs, and two on the feet. The IDEEA is a small 200-gram data collection device that can be clipped to a belt. During testing periods, subjects are connected to the device for 3 days while they perform ad lib activities. The output analyses include assessment of physical activity and energy expenditure, with high accuracy of activity type identification.

Exercise Testing

The VMAX Encore is capable of performing exercise testing when combined with a treadmill or ergonomic cycle. VO2 Max, heart rate and blood pressure are measured as a subject performs a timed, incremental exercise test to determine baseline exercise capabilities, or improvement/detraining over time.

Body Composition Measurements

The BodPod Body Composition Tracking System provides accurate, fast and safe measurements of body fat and lean body mass using air displacement technology. By measuring how much air a person's body displaces while enclosed in a known volume container, the amount of body mass, fat and fat-free mass can be calculated. The BodPod offers a more convenient method of body composition analysis than hydrostatic (underwater) weighing, without sacrificing accuracy.Total Body Water is a relatively low cost, highly accurate method of determining body fat mass. It can be determined through mass spectrometry using deuterium oxide (D2O) and Oxygen 18 stable isotope methods. The CCTS at Rockefeller University is now offering this test of body composition to its investigators. The principle is based on the theory that water is distributed in all parts of the body except body fat.

Total Body Dual energy X-ray absorptiometry (DEXA) scans measure fat and fat-free body mass. During a DEXA scan, the subjects will be positioned supine with their arms at their sides on the scanner. The software first divides pixels into bone mineral content and soft tissue compartments and then divides soft tissue compartments into fat-free mass and fat mass. Estimates of

Center Partners with Clinical Directors Network on Community Engagement

As part of its commitment to community engagement, the Rockefeller University Center for Clinical and Translational Science has developed a partnership with the Clinical Directors Network (CDN). CDN is a nonprofit organization that conducts clinical studies in community health centers throughout the United States, often in partnership with academic institutions. It is dedicated to providing and improving comprehensive and accessible community-oriented primary and preventive health care services for the poor, minority and underserved populations; its overall goal is the translation of clinical research into clinical practice. Since 1992, more than 47,000 patients in community health centers participated in studies conducted by CDN, of whom 49% were African American and 34% were Latino/a. CDN has also developed a sophisticated electronic network to support educational webcasts for physicians and other health care providers at the different community health center sites. CDN currently works with Community/Migrant Health Centers in New York, New Jersey, Maine, Connecticut, New Hampshire, Massachusetts, Pennsylvania, West Virginia, Virginia, Florida, Oklahoma, Utah, Puerto Rico, the US Virgin Islands, and Washington DC. If you would like additional information about CDN, you can visit its website www.cdnetwork.org

On March 15, 2007 the senior leadership of Rockefeller University Center for Clinical and Translational Science (CCTS) met with Dr. Jonathan Tobin, President of CDN, and his colleagues at their office in Manhattan. Based on that discussion, Dr. Tobin has joined the Advisory Committee on Clinical and Translational Science Subcommittee on Inter-institutional Collaboration, Recruitment, and Community Engagement to offer advice on community outreach and participant recruitment. The CCTS is sponsoring a series of 6 webcasts on a variety of topics of interest to primary care physicians. This will provide them with information on recent scientific and medical advances and inform them of potential opportunities for their patients to participate in studies being conducted by Rockefeller investigators. The CDN webcasts provide an opportunity to educate a wide network of primary care clinicians, patients and the general public about new scientific and medical advances and increase awareness of the University's research portfolio.

On June 20 Dr. Martin Markowitz, Clinical Director of the Aaron Diamond AIDS Research Center, presented the first webcast, Acute HIV Infection- Clinical Presentation, Diagnosis and Management. Acute HIV Infection was selected as the topic to coincide with community outreach activities scheduled at individual health centers in observance of National HIV Testing Day on June 27. Dr. Markowitz provided a case presentation and illustrated the challenges associated with accurately diagnosing new HIV infections.

Pilot Projects Submission Deadline is Sept. 4, 2007 (continued from page 1)

explanation of how the proposed project will accelerate the development of a clinical or translational project and/or benefit human health. Although this submission is based on key elements of the PHS 398 form, the entire application can be short, e.g., 3-5 pages. However, if the study involves a design where statistical methods can be used to determine the number of subjects that need to be studied, that statistical information should be included as a part of Research Design and Methods. Plans to use core resources of the Clinical and Translational Science Center should be explained in Research Design and Methods, if relevant.

Because requests to fund many projects may be received, projects will be considered for funding based principally on scientific merit and clinical or translational impact. Project proposals from K-12 Clinical Research Scholars or Rockefeller University Clinical Scholars are strongly encouraged. In the event a proposal is submitted by a trainee, the Background and Significance section should explain how the supported research will advance the career and training goals of that individual.

Once a project is evaluated for its scientific content and recommended for funding, that funding would be contingent on developing a complete protocol with sections on Human Subjects Protection and Data and Safety Monitoring acceptable to the ACCTS & IRB. Alternatively, if the project involves Vertebrate Animals, a protocol acceptable to the ACCTS & IACUC would also need to be developed.

Grants will be accepted on a rolling basis. Please e-mail an application for this grant to: jgk@rockefeller.edu.

Ms. Melissa Offenhartz, RN, MA, is Promoted to Director of Nursing and Patient Care Services (continued from page 1)

Clinical and Translational Science's Department of Nursing.

Her management style promotes broad staff participation in a wide variety of activities and initiatives. She is adept at providing constructive criticism when necessary and facilitates the development of corrective action plans with appropriate accountability and time frames. She encourages individual staff development and the development of the specialty practice of the Clinical Research Nurse.

Ms. Offenhartz received a BS in Biology from the State University of New York, a BSN from Indiana University, and an MA in Nursing Education from New York University. She worked as a staff nurse at Lenox Hill Hospital for 7 years, primarily in the Cardiac ICU. As an adjunct faculty member at NYU, Ms. Offenhartz has taught health assessment and nursing fundamentals in the undergraduate program. She has also worked at the Mount Sinai Medical Center as a Cardiac Clinical Educator.

Ms. Offenhartz's vision for the Department encompasses initiatives at the institutional, the local and the national levels. The recruitment and retention of nurses with broad clinical skills and the implementation of specialty training in the techniques, ethics, and regulatory elements of clinical research are a top priority. To that end, she has worked closely with the Human Resources Department to recruit excellent nurses to the Hospital and is developing a comprehensive orientation program to provide the necessary introductory professional training for them. In addition, she has created a comprehensive syllabus for the ongoing professional development of Nursing Department staff members. The development of a program to support an undergraduate clinical rotation in research nursing is a long term goal as well. This would bring in students from local undergraduate nursing programs and provide them with exposure to this specialized area of nursing practice and increase the visibility of the Rockefeller University Hospital throughout the nursing community. She intends for the Nursing Department at the Rockefeller University Hospital, in keeping with its history of significant contributions to research nursing, to be a key player in the development of a nationally recognized certification for Clinical Research Nursing as an area of specialty practice.

Statistical Methods and Computational Tools for Clinical Research and Personalized Medicine Services

Researchers at The Rockefeller University CTSA have developed a statistical method, termed 'µStat' (multivariate u-statistics) that improves clinical research for complex diseases and allows one to take the emerging field of personalized medicine to the next level. Under the existing paradigm, each group of diseases or category of drugs is assigned a 'signature' of genetic, genomic, and phenomic variables. This signature is then used to personalize diagnostic and therapeutic decisions for all patients. With µStat the signatures themselves can be personalized. 'µStat' program libraries are available for non-commercial use from CRAN (http://cran.r-project.org) and CSAN (http://csan.insightful.com); spreadsheets for small data sets and a Web service for whole genome and microarray scans are available from http://muStat.rockefeller.edu . Please click here to view an abstract written by Dr. Wittkowski on "Statistical Methods and Computational Tools for Clinical Research and Personalized Medicine".

On June 21, 2007, Dr. Knut M. Wittkowski, the head of the CTSA's Department of Biostatistics, Epidemiology, and Research Design, discussed the potential impact of novel statistical approaches to clinical research and personalized medicine with medical students at the New York University Medical Center.

New Center Core Facilities (continued from page 2)

bone mineral content, total body fat mass, lean mass, and percent fat are generated, along with information about regional body fat distribution.

Regional Body Composition (subcutaneous fat, visceral fat, intramuscular fat, muscle and residual tissue) is assessed by magnetic resonance imaging (MRI) using a General Electric 3.0 Tesla Magnetic Resonance Imaging System with EXCITE hardware and software. The patient is positioned supine, and between 40-60 axial images with a thickness of 7-10 mm are acquired. The field of view (FOV) will be 36-48 cm, with a resolution of 256 x 256 pixels. Interpretation of the collected data will provide estimations of regional body composition.

MRI and DEXA measurements are body composition measurements available to investigators through our collaborators at Weill Cornell Medical Center.

Assessment of Physical Activity

Self-reported leisure time and occupational activity can be determined using the MONICA Optional Study of Physical Activity (MOSPA) questionnaire, which was developed for use in the World Health Organization's Monitoring Trends and Determinants of Cardiovascular Disease (WHO-MONICA) study. Subjects are shown how to properly use a pedometer, and are be asked to complete a log of the number of steps taken every day for 7 days during four periods (the baseline testing period, the weight stability period, the weight loss period, and the weight maintenance period). This log is submitted to study staff for analysis. The number of steps the person takes per day, and their average daily physical activity are used to determine the Activity Factor used in estimating Total Energy Expenditure for metabolic diet studies.

Insulin Sensitivity Measurement

To measure insulin sensitivity, a hyperinsulinemic euglycemic clamp is used. Briefly, two intravenous catheters are placed in the subject's arms. One catheter (placed in a deep antecubital or brachial vein) is used for infusion of insulin and dextrose, and one catheter (placed in a hand or wrist vein) is used for sampling of arterialized blood. Arterialization of venous blood is achieved by placing the hand in a hand warmer. Insulin is infused at a rate of 80 mU per m2 of body surface area per minute, and 20% dextrose solution is infused to maintain the blood glucose level between 90 to 100 mg/dL. Blood glucose is monitored and recorded every five minutes throughout the procedure, and blood insulin levels are checked five times during the procedure. Once a steady-state has been reached (i.e. euglycemia is maintained with a constant rate of dextrose infusion), the insulin-mediated glucose utilization rate (M, in mg/kg/min) can be calculated. This calculation provides an estimate of peripheral insulin-mediated glucose utilization, or insulin sensitivity.

Adipose Tissue Aspiration Biopsy for fatty acid analysis, gene expression profiling, and adipose tissue inflammation

A small sample of fat tissue is removed from a subject for genechip analysis. This procedure involves sterilizing the skin with alcohol and iodine-containing soap, then temporary numbing an area of skin on the abdomen or gluteal muscle with an injection of lidocaine, followed by needle aspiration of approximately 3 grams of adipose tissue from just beneath the skin. RNA is extracted from the adipose tissue biopsy and is applied to genechip arrays to study genes that are differentially expressed in fat tissue.

The Translational Immunomonitoring Resource Center is intended to help investigators supported by the Clinical and Translational Science Award. The Immunomonitoring Resource Center will be involved in standardizing immunological assays to assist investigators and offers access to a LSR II flow cytometer and a Luminex device.

The BD LSR II flow cytometer is a powerful analyzer. It is set up with 4 lasers to allow investigators to analyze 12 multiple parameters of heterogeneous cell populations. The analyses are able to combine immunophenotyping of both surface and cytoplasmic antigens, DNA analysis and functional evaluations.

The Luminex is a recently developed flow cytometer with 2 lasers, and is a bead based system. It allows multiple analyses in a solution phase. It is capable of performing up to 100 different extracellular, intracellular, or nuclear proteins for simultaneous analysis in each sample (25 -50µ). This is achieved by the 100 unique color-coded microspheres anchored to capture antibody. The use of detection antibodies labeled with a fluorochrome allows quantification of antigen-antibody reactions that occur on the microsphere surface.

The lab is located on the second floor of the Hospital, in room 234. For more information about this new resource and to reserve access, please contact Dr. Juana Gonzalez at jgonzalez@rockefeller.edu; 212-327-7143.