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The Rockefeller University 1901
SCIENCE FOR THE BENEFIT OF HUMANITY

Center for Clinical and Translational Science
e-NEWSLETTER

Center News

New Certificate Program in Clinical and Translational Science Graduates First Class

By Angela Slattery

In September 2008, a new Certificate Program in Clinical and Translational Science began at Rockefeller University. Eighteen students from across campus participated in the inaugural class. In June 2009, all of the program's students graduated and received a Certificate in Clinical and Translational Science from the university. The Certificate Program, which is sponsored by the Center for Clinical and Translational Science (CCTS), was developed in collaboration with students and postdoctoral fellows to provide trainees with an introduction to the principles and practices of clinical and translational research.

2009 Inaugural Certificate in Clinical and Translational Science Class

The Certificate Program is a one year program that consists of two courses. Each student was required to create her or his own hypothetical human subjects protocol, including an informed consent form. To further familiarize the students with the protocol review process, the students then functioned as a mock IRB, reviewing each of the protocols and offering suggestions to insure the optimal design and the greatest protection of the human subjects that would participate. The protocols that were submitted in fulfillment of the requirement of the course were of exceptionally high caliber and offered insights into the clinical research interests of the talented group of investigators who enrolled in the program. Dr. Barry Coller, director of the Certificate Program stated,

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CCTS and Clinical Directors Network Successfully Complete First Collaborative Project

By Angela Slattery

In the fall of 2008, through the Advisory Committee on Community Engagement and Recruitment (ACCER), Clinical Scholar Dr. Andreas Mauer was introduced to Dr. Jonathan Tobin, President and CEO of the Clinical Directors Network (CDN). CDN is a not-for-profit network that supports community-based health centers, including their patients, practitioners, and other affiliated organizations. Community health centers work with CDN to assist with projects and facilitate community engagement.

Dr. Mauer and his mentor, Dr. Barry Coller, were interested in developing and validating a Web-based bleeding history phenotyping system. The goal of this initial project was to validate the instrument. The eventual goal is to provide the system to all authorized investigators with Internet access so that they can have the opportunity to collect bleeding history data in a standardized way and store the information in a single, uniform database. This database would aggregate deindentified data obtained by many different investigators and would be freely accessible to investigators worldwide. Potential applications of the system include: 1) improving diagnosis of bleeding disorders, 2) identifing the fewest number of questions needed to exclude the presence of a significant bleeding disorder with high probability, 3) identifing patients whose laboratory data and bleeding symptoms are discordant for future gene-gene and gene environment studies, and 4) assessing the medically optimal and most cost-effective way of deciding whether to order an extensive laboratory evaluation.

Dr. Mauer obtained approval to enroll 500 normal healthy participants in this study from the Institutional Review Board (IRB) and Advisory Committee for Clinical and Translational Science (ACCTS). CDN was an ideal partner for this project because it could assist in recruiting participants from community settings and their participation would broaden the diversity of the population

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New Certificate Program in Clinical and Translational Science Graduates First Class

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"I am extremely impressed with the scientific and medical sophistication of the projects and the techniques proposed; we are continuing to assess whether some of these protocols might be performed in our hospital. This is an exciting possibility for us."

The first course, Introduction to Clinical and Translational Science, was offered in fall 2008. It was twelve weeks long and consisted of two 90-minute lectures per week. The first lecture of each week described an important element in clinical and translational science (e.g., biostatistical considerations, human subjects protection, study design, etc.). The second lecture of each week was a scientific presentation by a Rockefeller University investigator explaining her or his research, emphasizing the element taught at the beginning of the week.

The second course in the program, Introduction to Scientific Techniques in Clinical and Translational Science, began in March 2009. Led by Drs. Sarah Schlesinger and James Krueger, the goal of this course was to introduce students to core resources available at Rockefeller University and to demonstrate scientific/technical methods that are currently employed to address critical problems in human biology. Another purpose for the course was to familiarize the students with the Rockefeller University personnel available to aid them in applying these cutting edge technologies. The final project for the course had the students return to the protocols they had developed in the Introduction to Clinical and Translational Science course and enhance the protocols by adding new techniques such as bioimaging, high throughput screening, or gene targeting that would augment the research design and facilitate their ability to test their hypotheses.

Both courses received high evaluation marks by the students, with 100% of the students reporting that they would recommend the courses to others, nearly 75% of the students stating the course changed their views about clinical and translational research, and approximately 67% of the students stating that the course made them more likely to conduct clinical or translational research. In terms of the evaluation scores for the Certificate in Clinical and Translational Science program as a whole, 100% of the responders stated they would recommend the program to their peers and felt that the program should continue to be offered to the Rockefeller community. One interesting indication of the impact of the program is that two of the students decided to alter their career paths and apply for admission to medical school.

In August of this year, Dr. Coller reviewed the course materials, student projects, and evaluations for the Certificate in Clinical and Translational Science Program with Dean Sid Strickland and Assistant Dean Emily Harms. Based on the rigor of the courses, the quality of instruction, and the level of participation required, the Dean's Office decided that both courses will now be offered for credit. CCTS is planning to offer the Certificate Program in alternate academic years based on the assessment of likely enrollment and faculty availability. The next Certificate Program is scheduled to begin in the fall of 2010.

CCTS and Clinical Directors Network Successfully Complete First Collaborative Project

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studied. Drs. Coller and Mauer visited the Jersey City site together, met with the staff, and learned from them about the bleeding (hemostasis) problems they face in their practice. Dr. Coller provided a lecture on hemostasis for primary care physicians and described the goals of the project. Ultimately, from the 500 total participants in the study, 365 were seen at Rockefeller University Hospital, 75 were seen at Metropolitan Health Center in Jersey City, NJ and 60 were seen at Newark Community Health Center in Newark, NJ. Dr. Mauer oversaw the project and Dr. Chamanara Khalida from CDN played an important role in recruiting and interviewing patients, as well as educating the staff at the sites about the project. The time from study approval to study completion was approximately 10 months; the Clinical Research Support Office (CRSO) recruitment program, with the outstanding assistance of the CDN staff, made this accomplishment possible.

In addition to CDN's role in assisting with participant recruitment, the project benefited enormously from Dr. Tobin's expertise in study design and statistical approaches. Data from the study were presented by Dr. Mauer in July 2009 at the International Society on Thrombosis and Hemostasis meeting in Boston. Dr. Tobin, Dr. Mauer, and Dr. Coller are working together on future collaborations. Dr. Mauer stated that, "Dr. Tobin has been extremely helpful with so many aspects of this project. I look forward to future collaborations with Dr. Tobin and CDN."

If you would like to contact Dr. Tobin to discuss whether your project may benefit from collaborating with CDN, you can contact him at JNTobin@CDNetwork.org or call 212-382-0699 ext. 234.

Clinical Scholars Program Graduates First Class of Master's Degree in Clinical and Translational Research

By Angela Slattery and Jennifer Spada

In June of this year, the Clinical Scholars program had four graduates who were the first to receive the new Master's Degree in Clinical and Translational Research. The KL2 Clinical Scholars program, which is supported in part by the Rockefeller University Clinical and Translational Science Award (CTSA), is a training experience designed to prepare physician-scientists and select doctoral level PhD investigators for independent careers in clinical and patient-oriented translational research.

Left to right: Dr. Barry Coller, Dr. Edgar Charles, Dr. Marina Caskey, Dr. Lisa Neff, and Dr. Allegra Grossman

Dr. Marina Caskey, Dr. Edgar Charles, Dr. Allegra Grossman, and Dr. Lisa Neff were honored at a graduation dinner celebration, surrounded by other Clinical Scholars, mentors, and administrative staff. Each graduating scholar was acknowledged by her or his mentor and presented with her or his degree. Dr. Coller, the director of the Center for Clinical and Translational Science (CCTS), congratulated the first class of scholars on their achievements and their commitment to use the full power of the scientific method to improve human health and alleviate suffering from disease. Dr. Sarah Schlesinger, co-director of the Clinical Scholars Program within the CCTS stated, "It has been inspiring to watch our ideas for the Clinical Scholars program grow into reality. I am most impressed by the talent and commitment of our graduates. Each of them is a remarkable young physician/scientist with an important contribution to make. I believe that the Clinical Scholars Program has given them the tools they need to move forward and make a difference."

Dr. Marina Caskey trained in Infectious Diseases at Weill Cornell Medical Center, and after completing her fellowship, joined the laboratory of Dr. Ralph Steinman. As a Clinical Scholar, Dr. Caskey studied the immune responses elicited by a novel HIV-1 vaccine in which a monoclonal antibody delivered the antigen to the dendritic cells for processing and immune stimulation. She has also worked to bring this novel candidate HIV vaccine into Phase I clinical development at the CCTS. Upon completing the Clinical Scholars program, Dr. Caskey will continue her work on the HIV-1 vaccine in Dr. Steinman's laboratory.

Former Chief Clinical Scholar Dr. Edgar Charles' interest in Hepatitis C virus (HCV) began during his NYU fellowship where he was responsible for the care of many patients suffering from HIV/HCV co-infection. His interests in viral pathogenesis and immunology led him to the Laboratory of Virology and Infectious Disease under the direction of Dr. Charles Rice and Dr. Lynn Dustin. Dr. Charles' research is focused on the mechanisms by which HCV infection leads to B cell dysregulation. Dr. Charles received a prestigious NIH K08 award from the National Institute of Allergy and Infectious Disease (NIAID) to support his research under the mentorship of Drs. Rice and Dustin. He will continue his research on HCV with a view toward the development of novel therapies.

Shortly after she began her Endocrinology Fellowship at Weill Cornell Medical College, Dr. Allegra Grossman developed a strong interest in diabetes and metabolism. As a result, she was eager to join Dr. Markus Stoffel's Laboratory of Metabolic Diseases to study fundamental aspects of diabetes. As a Clinical Scholar, Dr. Grossman conducted studies on the relation of obesity with frequency of meals and expression of the important transcription factor FOXA2 in adipose tissue of human subjects with obesity/insulin resistance. Additionally, she developed her own study to investigate whether vitamin D repletion improves insulin resistance. Dr. Grossman is currently a Senior Medical Scientist at Amgen, where she is working on Phase I studies in the areas of osteoporosis and diabetes.

Before joining the Clinical Scholars Program, Dr. Lisa Neff completed fellowships in Endocrinology and Clinical Nutrition at Tufts-New England Medical Center and the USDA Human Nutrition Research Center on Aging at Tufts University. In Dr. Jan Breslow's Laboratory of Biochemical Genetics and Metabolism, Dr. Neff's research focused on identifying effective nutritional interventions for obesity and the metabolic syndrome. She successfully completed both a randomized metabolic diet study and a longitudinal weight management intervention study during her time in the program. The preliminary data from her metabolic diet study suggests that clinically significant improvements in insulin resistance, inflammation, and other obesity-related derangements can be achieved through dietary changes, even in the absence of weight loss. Plans are being made to launch a new fully-powered clinical trial building on these results. In the fall of 2009, Dr. Neff will join the Comprehensive Center on Obesity at Northwestern University and will serve as an Assistant Professor in the Division of Endocrinology. She will continue to study and treat individuals with obesity and related metabolic derangements.

Integrated Research Information System (iRIS) Update

By Donna Brassil

The Center for Clinical and Translational Science (CCTS) utilizes the electronic Integrated Research Information System (iRIS), which offers many components that are advantageous to the investigators, coordinators, other research staff, Institutional Review Board (IRB) members, and the members of Advisory Committee for Clinical and Translational Science (ACCTS). This issue will highlight the advantages of being designated one of the Key Study Personnel (KSP) in iRIS.

What are KSP?

For research studies, Key Study Personnel (KSP) are Rockefeller University faculty and staff named on a clinical research study. They may be a Principal Investigator, co-Investigator, Nurse Practitioner, Coordinator, Bionutritionist, Lab Technician, etc.

Protocol Submission Sign-Off Request

Before a study is officially accepted by iRIS, Key Study Personnel will receive an email from ruhstudies@mail.rockefeller.edu with a subject line stating: Protocol Submission Sign-Off Request. Completing the sign-off is an important step in the process and needs to be completed before the study enters the review process. This ensures that all study personnel have seen and support the pending protocol. Personnel should log onto the iRIS Submission System at https://clinfo10.rockefeller.edu/. The user ID and password are identical to those used for the Rockefeller University email system. After logging into iRIS, KSP can view all submitted documents related to the study. At the same time while in iRIS, KSP are asked to complete the now paperless Conflict of Interest (COI) form. Both of these are essential components of the IRB submission process. If any member of the study team does not sign-off on the study, the study will not be submitted to the respective review boards.

One great advantage of the electronic submission system is that each KSP can view all study submission documents and sign off on the study regardless of where they are located as long as they have internet access and have logged into the University's Virtual Private Network (VPN).

If you have any questions about iRIS, feel free to contact Ross Gillman (212) 327-8930; Ummey Johra at (212) 327-7877; or Donna Brassil at (212) 327-7886.

Center Achieves Community Engagement Milestones

By Rhonda Kost, MD

In April 2009, Dr. Kenneth Olden, Founding and Acting Dean of the new City University of New York (CUNY) School of Public Health, sited at Hunter College, joined the Advisory Committee on Community Engagement and Recruitment (ACCER) as an advisor to, and collaborator with, the Rockefeller University Center for Clinical and Translational Science (CCTS). ACCER, a subcommittee of the Advisory Committee for Clinical and Translational Science (ACCTS), is responsible for the implementation of the Community Engagement Key Function at Rockefeller. Dr. Olden brings a wide breadth and depth of experience in science, public policy, and community engagement to his leadership of the new School of Public Health and to Rockefeller. Dr. Olden served as Director of the National Institute of Environmental Health Sciences and the National Toxicology Program from 1991-2005, where he was recognized internationally for his leadership. More recently, he was a Yerby Visiting Professor at the Harvard School of Public Health. Dr. Olden has defined the goal of CUNY's School of Public Health as "to train interdisciplinary urban public health researchers and practitioners capable of working across all levels of analysis, disciplines, and social sectors -- such as health, education, the environment, and criminal justice -- to address complex urban public health problems."

Dr. Olden and the ACCER Board, (consisting of Mr. Joseph Bonner, Dr. Barry Coller, Dr. Peter Holt, Dr. Bonnie Kaiser, Dr. Rhonda Kost, Ms. Maija Neville, and Dr. Jonathan Tobin), have begun developing plans to foster interdisciplinary collaborations that partner traditional population-focused public health concerns, including health disparities, with biological and mechanistically focused research on the molecular basis of stress and its impact on health risk. Coupling these disciplines holds great potential for synergy in addressing public health challenges and accelerating the dissemination of research findings into practice.

Dr. Daniel Blumenthal, Professor and Chair of the Department of Community Health and Preventive Medicine at Morehouse School of Medicine served as a consultant to CCTS under the auspices of a Duke University CTSA consortium-wide project termed the Community Engagement Consultative Service (CECS). Dr. Blumenthal has served as a consultant to the World Health Organization in Geneva; a VISTA Volunteer physician in Lee County, Arkansas; as an Epidemic Intelligence Service Officer with the Centers for Disease Control in Atlanta; and as a medical epidemiologist with the World Health Organization Smallpox Eradication Program in India and Somalia. Dr. Blumenthal visited the Rockefeller campus on May 20, 2009 and, in addition to providing his consultation, delivered a Clinical Research Seminar, entitled: "Community Partnerships for Translational Research." The Rockefeller team described the current program to Dr. Blumenthal

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Center Successfully Applies for Four American Recovery and Reinvestment Act of 2009 (ARRA) Administrative Supplements

By Maija Neville

On March 19, 2009 the National Center for Research Resources (NCCR) issued a request for Administrative Supplements to institutions and organizations with active NIH Research Grants. This request was based on the American Recovery and Reinvestment Act of 2009 (ARRA), which was signed into law on February 17, 2009 with the goal of promoting job creation and economic development, along with accelerating the pace and achievement of scientific research. Supplements could be submitted under an NIH CTSA parent award. The goal of each supplement was to advance either the NCRR Pilot Project Mechanism, the CTSA Consortium Strategic Goals, Collaborative Community Engagement Research, Science Education and Dissemination, Collaborative and Basic and Translational Research, or Research Workforce Development and Dissemination. Of the Supplements submitted by the Rockefeller University Center for Clinical and Translational Science (CCTS), four were recommended for funding on July 15, 2009. If awarded at the requested budgets, they will result in $2,234,770 in additional total funding over two years. Five new staff members will be hired to conduct the studies. A brief description of the supplements recommended for funding are provided below.

1. Administrative Supplement for Enhancing NCRR Pilot Project Mechanism, Knut Wittkowski, secondary PI. This Pilot Project aims at using the NCBI CASP database of Genotypes and Phenotypes (dbGAP): (1) to empirically validate a methodology by comparing its results to those from traditional approaches; (2) to conduct a proof of principle analysis to explore a recent finding from ongoing research under the parent CTSA award which suggests that genetic factors may determine why psoriasis affects primarily the skin in some patients, while others develop psoriatic arthritis; and (3) to accelerate sharing of technology through rapid dissemination of the results, Web-based documentation of the analyses as case studies for the use of the novel technology and development of training material in collaboration with neighboring CTSA institutions in the New York City area.

2. Administrative Supplement to Advance Translational (T1 & T2) Research, Agata Smogorzewksa, secondary PI. Using the Bleeding History Phenotyping System as a prototype of a comprehensive patient phenotyping instrument, this submission proposed the creation of a comprehensive, ontology-driven phenotyping system and database for Fanconi anemia (FA). Work stemming from this proposal will create a uniform phenotyping ontology based on a comprehensive Fanconi Anemia Phenotyping Questionnaire (FAPQ) that will be designed and peer-reviewed by experts in the field. Information will be used to generate a Fanconi anemia phenotyping database (FAPD), which will be accessible to physicians and researchers worldwide through a secure Web-based interface.

3. Administrative Supplement to Advance Translational (T1 & T2) Research, Knut Wittkowski, secondary PI. To Advance Translational (T1 & T2) Research by increasing accuracy and accelerating analyses and dissemination of results, two critical enhancements with long-term implications for the use of the Rockefeller-developed programs µStat and WISDOM as resources for clinical and translational research will be made. (1) CCTS will partner with industry to move WISDOM another step towards becoming a comprehensive support system for clinical and translational scientists by making the meta database already used for the REDCap link a resource shared with a graphical user interface to assist and provide help with specifying statistical analyses to be performed on the µStat Web server. (2) A full time software engineer will be hired to provide technical assistance to clinical and translational researchers while enhancing the capacity, stability, and functionality of the grid, in general, and automating the iterative resubmission of interim results as the number of factors analyzed increases. After the 2-year period, WISDOM will facilitate clinical and translational research as a coherent user interface with intelligent, knowledge-based help for both REDCap as a data entry system and µ-stat as an innovative statistics server. To accelerate further development, it will have been ported to the industry standard Java and have

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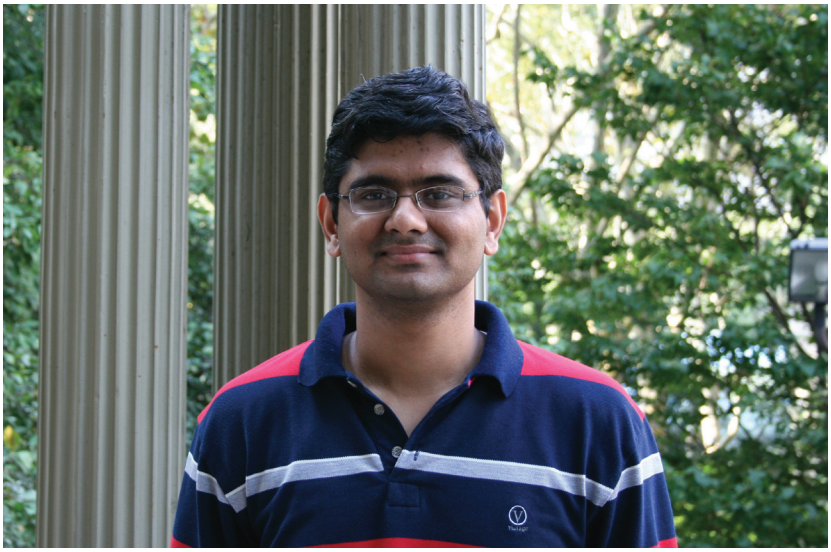
Center Achieves Community Engagement Milestones (continued from page 4)

through a series of meetings with faculty, ACCER members, Clinical Scholars, and collaborators, including Dr. Kenneth Olden and Dr. Jonathan Tobin, President and CEO of Clinical Directors Network, a community-based research network. From a list of 30 practices endorsed by the CECS workgroup, Rockefeller was asked to focus on 1-2 best practices around which to build the consultation. Rockefeller selected: 1) how to design flexible projects that incorporate the community, and 2) building long term relationships with community partners.

After reviewing all the materials and conducting his analysis, Dr. Blumenthal judged the Rockefeller program to be "highly likely" to continue to be successful in achieving our stated goals, and in executing the plan of action. He noted that the CCTS's "strategic alliances with partners that have deep connections to the community" was an extremely appropriate approach for Rockefeller.

Meet the Scholar: Swaroop Pendyala, M.D.

By Jennifer Spada



Dr. Swaroop Pendyala received his medical degree from Christian Medical College, India in 1997. After completing his degree he spent time working as an acute care physician internationally, first in England and then in Jamaica. He began his residency in Internal Medicine at the University of Texas in Galveston, which he completed at St. Luke's-Roosevelt Hospital of Columbia University, New York in 2007.

Dr. Pendyala initially became interested in medical research while working under Dr. William Mitch during his first year of residency at the University of Texas. Under the guidance of Dr. Mitch, his research involved understanding the role of phosphatidyl 3-kinase (PI3K) as the major signaling pathway in controlling muscle mass in different catabolic medical conditions. After moving to New York for his third year of residency, he worked on projects to understand the role of bone marrow-derived cells in the pathogenesis of chronic pancreatitis and pancreatic cancer with Dr. Timothy Wang at Columbia University. During his time at Columbia he met Dr. Peter Holt, a Senior Research Associate in the Laboratory of Biochemical Genetics and Metabolism at the Rockefeller University, who introduced him to the Clinical Scholars program. At that time he wanted to join a research lab to gain experience in translational research in gastroenterology.

In 2007, Dr. Pendyala was accepted into Dr. Jan Breslow's Laboratory of Biochemical Genetics and Metabolism as a Clinical Scholar under the mentorship of Drs. Breslow and Holt to investigate the mechanisms involved in increased risk of colorectal cancer in obese individuals. Dr. Pendyala stated, "Forty -two percent of all colon cancers are diagnosed in obese individuals. With a quarter of the adults in the United States being obese and nearly two thirds of the adults being overweight the incidence of these cancers in the future will undoubtedly increase. We still do not understand the mechanisms that contribute to the increased risk of colon cancer with obesity."

Dr. Pendyala is currently working on two studies at Rockefeller University Hospital. The first, which was funded by a pilot grant from the CTSA, is investigating the presence of inflammation in the colorectal epithelium of obese women and the effects of weight loss by dietary intervention on the inflammation. Thus, this study is testing whether the increased inflammation associated with obesity provides a direct link to increased risk of malignancy. Preliminary results have shown improvement in inflammatory markers in the colorectal mucosa after weight loss by dietary intervention. His second study is exploring the ways that a "Western style" diet increases the risk of colorectal carcinogenesis. "The Western style diet is a major risk factor for colorectal carcinogenesis, but there is very limited information on how it promotes carcinogenesis; this study is aimed at trying to gain insights into the earliest changes in different molecular pathways in the colorectal epithelium. We hope that by understanding these early changes we will be able to direct future studies to preventive strategies that target these specific pathways."

When asked to discuss his experience as a Clinical Scholar at Rockefeller University, Dr. Pendyala stated "The Clinical Scholars program has been amazing, especially in helping me to understand and learn the process of conducting translational research. Going through the rigor of good clinical practice and attending Institutional Review Board meetings has given me the confidence and training to conduct translational research. Dr. Barry Coller has been a great source of knowledge and support in understanding the process of becoming a successful researcher. Additionally, Drs. Holt and Breslow have been remarkable mentors, as they have experience as preeminent translational researchers."

When asked about his future, Dr. Pendyala said, "I will be starting my gastroenterology fellowship at Columbia University's St. Luke's-Roosevelt Hospital. I will be applying for further grant support for larger clinical studies based on the initial information obtained from the studies conducted here at Rockefeller University Hospital. My career plan is to focus on understanding the molecular mechanisms of sporadic colorectal cancer in normal and obese individuals by conducting translational research studies. I believe that my training in the Clinical Scholars program has provided me with the skills to achieve academic success!"

~ Rockefeller University Hospital Centennial Celebration ~ Discoveries Advancing Medicine

As part of the centennial celebration of the Rockefeller University Hospital, Dr. Elizabeth Hanson has led a project to create a permanent record of more than 100 medical advances that have come from Rockefeller faculty. To share this wealth of exciting information, we will highlight one of these Discoveries Advancing Medicine in each future e-Newsletter. We start by featuring the remarkable translational research contribution by Louise Pearce and her colleagues.

Barry Coller, MD

Louise Pearce and the First Drug for African Sleeping Sickness

By Elizabeth Hanson, PhD

In 1920 Louise Pearce (1885-1959) traveled to the Belgian Congo (now Democratic Republic of the Congo) to field test a new drug against trypanosomiasis, or African sleeping sickness. This fatal disease, caused by a blood parasite, was epidemic. Working in a clinic in the country's capital, Pearce developed a protocol for testing the drug's safety, effectiveness, and optimum dosage. Called Tryparsamide, the new treatment cured about 80 percent of patients, although high doses given for severe cases had the side effect of partial or complete loss of vision. This achievement received immediate international recognition. For decades Tryparsamide remained the standard treatment for trypanosomiasis.

Tryparsimide was derived from arsenic. In 1909 Paul Ehrlich, in Germany, had developed an arsenic-derived drug called Salvarsan, which was the first effective treatment for syphilis. Since Ehrlich had also found that related arsenic compounds could kill trypanosomes, Simon Flexner, director of the Rockefeller Institute, directed two chemists, Walter Jacobs and Michael Heidelberger, to develop new arsenic formulations for treating trypanosomiasis in humans. Flexner enlisted two members of his own laboratory, Wade Hampton Brown and Louise Pearce, to study the disease, and test the experimental drugs, in animal models. When the four scientists determined that Tryparsamide was the most promising drug, Pearce traveled to Africa to conduct human trials.

Louise Pearce received the AB from Stanford University in 1907 and the MD from the Johns Hopkins University School of Medicine in 1912. That year she took a research position at the Rockefeller Institute under Simon Flexner, the Institute's director, and she was promoted to associate member in 1923. Pearce remained at Rockefeller the rest of her career. Much of her work was devoted to developing animal models for the study of human cancers. Of the researchers involved in developing Tryparsamide, Pearce was the most celebrated: she was awarded the Belgian Order of the Crown in 1921 and the King Leopold II Prize in 1953. The recipient of many additional awards and honorary degrees, Pearce also served as president of the Women's Medical College of Pennsylvania from 1946 to 1951.

Selected Publications

Pearce L. Tryparsamide treatment of African Sleeping Sickness. Science, 1925, 61:90-92

Pearce L and Rivers TM. Effect of a filterable virus (Virus III) on the growth and malignancy of a transplantable neoplasm of the rabbit. J Exp Med, 1927, 46: 81-99 http://www.jem.org/cgi/reprint/46/1/81

Pearce L. The Treatment of Human Trypanosomiasis with Tryparsamide. A Critical Review. Monograph no. 23. New York: Rockefeller Institute for Medical Research, 1930

Casey AE, Rosahn PD, and Pearce L. The association of blood cell factors with the transplantability of the Brown-Pearce tumor. Cancer Res, 1942, 2: 284-289

Further Reading

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Corner, GW. A History of the Rockefeller Institute, 1901-1953. (New York: Rockefeller Institute Press, 1964), 144-148

Grinstein LS, Biermann CA and Rose RK, eds. Women in the Biological Sciences: A Bibliographic Sourcebook (Westport, CT: Greenwood Press), 1997, 384-390

The Clinical Research Support Office Post-Approval Audit Program

PART II: Documenting Enrollment, and a New and Improved Informed Consent Template

By Rhonda G. Kost, MD

In the past three years, no audit findings of clinical studies at Rockefeller University have identified significant risks to participant safety, or serious violations of subjects' rights. The audits did, however, identify instances of omissions of tests or visits, and incomplete documentation. These lapses can be addressed by process improvement and increased attention to detail. In this article, we will review the required documentation of participant enrollment, which includes a fully executed Informed Consent Form, completed HIPAA form, and a well-designed Enrollment Note.

Informed Consent and HIPAA forms

Among the most common audit findings around the process of enrollment are irregularities in the completion of the Informed Consent Form. A properly completed Informed Consent Form is executed with: 1) the correct, current IRB-approved version of the form as listed on-line; 2) all sections completed, including the Sample-Storage and Future-Use section (more below); 3) signatures on the correct line from the participant him/herself (not a spouse or friend, even if the spouse or friend has better handwriting), except where a legal guardian, parent, or proxy is indicated; 4) current date recorded at the time of the signing, on the correct line, by the person signing the document; 5) any corrections made by the person who made the original entry, with a single line through the original entry, dated, and with initials of the corrector next to the correction. Finally, no ad lib additions or deletions may be made to the content of an IRB-approved consent form; for example, no circling, cross-outs, underlining or write-in words for emphasis should appear on the form as they invalidate the form as IRB-approved. Among HIPAA forms, the most common lapse is omission of the contact information section.

One effective way assure correct documentation is to assign a research team member the task of thoroughly reviewing the forms for correct completion by the participant at the time of the study visit, preferably before the investigator or participant has left the clinic. This insures that the errors are identified when the signatories are still available to correct their entries in real time. The investigator's signature should be the final sign-off of the form as checked and complete.

New Informed Consent and HIPAA Templates

In response to our audit findings that participants are asked to provide duplicate contact information several times during the enrollment process, including when completing the HIPAA form, we consulted the Office of General Counsel and IRB to review whether the contact information section of the HIPAA form was in fact required. As a result of these reviews, the contact information field has been eliminated from the HIPPA form. Similarly, in response to audit findings, and in collaboration with the Office of General Counsel and IRB, we have rewritten the Sample-Storage and Future-Use section of the Informed Consent form template, making it much shorter and simpler. Both of these new forms should be available for use for November or December submissions to the IRB.

Enrollment Notes

Documentation of eligibility and informed consent, both of which are required by Good Clinical Practices (GCP) and federal regulations (46 CFR 46.117 and 21 CFR 50.27), is captured by Rockefeller University IRB Procedures (Section 6.1) in the requirement for an Enrollment Note. The Enrollment Note should document: 1) the eligibility of the participant for the protocol, 2) that the subject had a chance to ask questions and have them answered prior to signing the ICF, 3) that the ICF was signed prior to the subject undergoing any study-related procedures, and 4) that a copy of the signed Informed Consent Form (ICF) was given to the subject.

There can be subtleties to the Enrollment Note. It may not be possible to satisfy all four elements of the Enrollment documentation listed above on the same day. Regarding eligibility, for instance, if informed consent is signed at a given visit, but not all inclusion/exclusion criteria can be satisfied until test results return at a subsequent time, then the documentation of Enrollment would consist of two notes, one written to document items 2-4 above, and a subsequent note written to verify that inclusion/exclusion criteria were satisfied. In documenting that all of the participant's questions were answered, it is recommended that a summary statement of the nature of the questions the participant asked be included (e.g., "the participant requested and was given clarification about the visit schedule and schedule of compensation.") It is not, however, necessary to document every question. It is best to avoid judgments about the participant's comprehension such as "the participant now understands," unless a formal assessment of comprehension was made. Rather a statement of fact, such as "the participant stated that the explanation was clear."

The signatures on the Informed Consent must always include the date, entered by the person signing. In establishing clearly that Informed Consent was signed before any study procedures began, for instance when study procedures begin on the same day that Informed Consent is signed, the record should include notation of the time that the Informed Consent Form was signed, and precede the time that any procedures are documented to have begun. Finally, the regulations requires that a copy of the ICF be given to the participant, not just offered, even if the participant declines it. You can explain to the participant that they are required to accept it, but not keep it.

An Enrollment Note Template/Checklist can structure and facilitate the documentation of each of the required

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Center Successfully Applies for Four American Recovery and Reinvestment Act of 2009 (ARRA) Administrative Supplements (continued from page 5)

an innovative and easily expandable help system to facilitate training and dissemination.

4. Administrative Supplement for Research Workforce Development and Dissemination, Edward Barbour, secondary PI. This supplement proposes to create a comprehensive course in the area of Applied Bioinformatics for the further education of clinical researchers. The field of bioinformatics, which applies information technology to molecular biology data, is being elevated to a prominent role as newer equipment for DNA, RNA, and protein sequencing is generating vast amounts of data from scientific experiments. Therefore, it is of great value to the researchers responsible for such experiments to understand the tools and techniques that are available to analyze this vital data. As in many areas of rapidly advancing technology, many educational programs are not able to keep up with the advanced pace of this educational need. This submission will fill that gap by creating a Web-based course that will contain numerous examples and exercises, giving the researcher the full advantage of knowing what it takes to draw valid scientific conclusions from such data. This course will look at the subcategories of bioinformatics including genomics, protein structure and interaction networks, metabolomics, natural language processing, and simulation using complex systems. The course will also expose the researcher to currently available bioinformatics tools including open source and leading third party tools, as well as the low level components used to build such tools.

The Clinical Research Support Office Post-Approval Audit Program
PART II: Documenting Enrollment, and a New and Improved Informed Consent Template
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elements. During the conduct of audits of active studies, auditors routinely verify that the elements of an Enrollment Note has been properly documented for every participant. The Facilitation Office is available to help investigators construct such templates before starting the study. If deficiencies in the Enrollment Note are detected on audit, the auditor will assist the investigator in amending the record as part of a Corrective Plan of Action. As always, the Clinical Research Support Office (CRSO) (x7709) and Facilitation staff members (x7886) are available to help research teams achieve compliance, and are always available to answer any questions or help solve any problems that arise for investigators and their staff.

Workflow, Tools, and Habits

Coordinators from the Facilitation office are available to help research staff members develop tools to ensure the completion of protocol-related activities and appropriate scheduling of study visits and procedures; worksheets created through the iRIS electronic system can be a helpful resource as well. Taking advantage of the support of the Facilitation Office, iRIS workflow, and post-audit recommendations from the CRSO, research teams can develop routine practices that make regulatory compliance a straightforward and automatic part of daily study conduct.

In the next issue: Documenting, Reporting, and Avoiding Protocol Deviations and Violations

Photo Credit: Karen Smith

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