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TRANSLATIONAL PROFILE

Neonatal vascular expert Robin Steinhorn makes time for translational research

WHEN NEONATOLOGIST Robin Steinhorn began her career as a pediatrician, she had no intention of becoming a research scientist. But her encounters with persistent pulmonary hypertension in newborns (PPHN), a potentially deadly condition that exacerbates newborn respiratory failure, and her frustration with the ineffectiveness of existing treatments, deeply troubled her. After completing her residency and a fellowship in neonatal/perinatal medicine at the University of Minnesota, she underwent additional fellowship training in the use of extracorporeal membrane oxygenation (ECMO), a system that provides heart-lung bypass support. That was 26 years ago.

Now chair of the UC Davis Department of Pediatrics and medical director of UC Davis Children's Hospital, Steinhorn is an internationally recognized expert on fetal pulmonary vascular development and neonatal pulmonary hypertension. Her research findings during the past two decades have contributed substantially to an understanding of and treatment for PPHN.

"The majority of babies with PPHN are in every other way perfectly healthy. They fail, though, to make the transition in the delivery room from blue to pink. As a clinician during the early years of my career, I knew that if I could just get that little baby through a couple of days, the recovery process



Robin Steinhorn, M.D.

would begin," Steinhorn said. "This condition haunted me enough that I became involved with ECMO therapy, the first life-saving treatment available for the condition."

But that wasn't sufficiently satisfying for her. She wanted to understand the nature of the underlying abnormalities in vascular signaling in order to reverse the condition sooner and eventually to prevent it altogether. She first gained that opportunity at the State University of New York in Buffalo in 1991, where she joined colleagues studying pulmonary vascular biology and entered the realm of translational medicine.

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DIRECTOR'S MESSAGE

Lars Berglund, M.D., Ph.D.

I AM PLEASED TO SHARE two new research opportunities that will advance the development of biomedical researchers. It is no small feat when programs of this nature come to fruition. These opportunities have become available through the efforts of dedicated teams of faculty, administrators, grant writers, researchers and program managers who construct and administer these novel programs.

First is the "Frontiers of University Training to Unlock the Research Enterprise" (FUTURE)

program at UC Davis, which is focused on expanding professional growth opportunities for graduate students and postdoctoral fellows. FUTURE is funded by the NIH Director's Broadening Experiences in Scientific Training (BEST) initiative, which recognizes that the traditional academic path that serves as the current model for biomedical research training does not fully prepare scientists for the broad array of career opportunities available in industry, business,

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New clinical research facility opens at UCDCMC

CLINICAL RESEARCH became easier for health-care investigators at UC Davis Medical Center in March. That is when the Clinical and Translational Science Center's new clinical research facility opened in the Cypress Building, a location convenient for investigators as well as the participants in studies. The new facility is generating excitement not only because of its prime location, state-of-the-art equipment, and comprehensive resources and services, but also for the specialized nursing staff who can be deployed for "just-in-time" research protocols at the patient bedside in the hospital.

The new facility has 3,500 square feet of clinic space with equipment and an experienced 16-member staff who focus on conducting protocol-specific clinical research. With four infusion chairs, a procedure room, two phlebotomy stations, two examination rooms, two interview rooms, and a



room with a hospital bed, this clinic is designed to meet a variety of outpatient research needs. Additionally, there is a laboratory processing room with

a centrifuge and -80°C freezer, and an exercise laboratory with a DEXA machine, EKG stress treadmill and bike system, and metabolic cart. Plenty of workspace is available for investigators and coordinators to use during their patients' appointments. The new clinic space consolidates the CTSC Clinical Research Center (CCRC) presence at the Sacramento Veterans Affairs Medical Center and Ticon building locations.

"The convenient location in the Cypress facility will strengthen integration of clinical and translational research with the institution's teaching and clinical missions, as it will allow all research team members to directly interact with patients and study subjects," observed CCRC director Ted Wun, associate dean for research and chief of the Division of Hematology and Oncology. Nicole Hansen, CCRC associate director, noted that the location adjacent to the hospital enables CCRC staff to immediately

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CCRC Research Action Services

Staff members are trained and qualified to obtain informed consent and collect specimens and data without compromising inpatient clinical care and operations. Available services include:

- Clinical Research Nurses: Protocol-specific procedures and direct nursing care for subjects enrolled in Institutional Review Board-approved studies; certified in chemotherapy administration, moderate sedation, and Advanced Cardiac Life Support (ACLS)/Pediatric Advanced Life Support (PALS).
- Research Dietitian: Nutritional status assessments; food record processing and analysis; nutritional counseling to optimize research protocol adherence; metabolic and calorie-controlled meal planning and preparation.
- Clinical Research Coordinators: Regulatory support; subject recruitment and visits; budget development.
- Exercise Physiologist: Measure body composition, bone density, total body water, energy metabolism and expenditure, and resting metabolic rate; administer cardio-respiratory fitness and exercise stress tests; analyze data.
- Laboratory Staff: Sample collection and processing; DNA/RNA isolation; prepare samples for proteomics and flow cytometry; multiplex cytokine, chemokine and metabolic analyses.
- Research Subject Advocate: Available for consultation with medical or nursing staff members, patients and family members.

respond to requests for clinical trials support when opportunities present themselves.

“The new location serves as the hub for the Research Action Nurses, who are available to respond to ‘just-in-time’ protocols that are typically initiated in the emergency room, with research activity continuing during a patient’s inpatient stay. The program gives investigators immediate access to qualified clinical research personnel to implement research protocols without affecting hospital operations and clinical care,” Hansen said. “Our

expanded services, staff and space allow us to assist more investigators across disciplines and at all levels of their careers, from M.D.s, Ph.D.s and R.N.s, to medical and nursing students and scholars.”

Flexibility to meet the various needs of investigators and accommodate the many requirements for research subjects remains a hallmark of the CCRC, since all CCRC staff members are trained in human subjects’ protection, good clinical practices, protocol implementation, and compliance. CCRC staff members also

are available to see subjects at locations outside of the CCRC, including all UC Davis Health System clinics, other local community sites and research participants’ homes.

“We offer off-site and home visits to help encourage subject recruitment and retention,” Hansen explained. “When investigators contact me, we determine the feasibility and the budget for services to fulfill the clinical requirements of their protocols,” she added. “We are an investigator- and patient-centered resource that will enhance research within UC Davis Health System.” §

DIRECTOR’S MESSAGE *continued from page 1*

government and other non-academic settings. The program is designed to enrich current training experiences and enhance less commonly nurtured skills and competencies, including communication across disciplines, entrepreneurial thinking and knowledge transfer. Through partnerships with institutional leaders, industry and other organizations, the program will enable trainees to cultivate critical specialized skill sets needed to thrive in a broad range of biomedical careers. One of only 10 in the nation, this new NIH grant was awarded to UC Davis in October 2013 and is led by a team of three principal



Lars Berglund, M.D., Ph.D.

investigators, Drs. Fred Meyers, Andy Hargadon and myself (www.ucdmc.ucdavis.edu/publish/news/newsroom/8400).

Second, a team of representatives from UC BRAID (Biomedical Research Acceleration, Integration and Development) established the UC Center for Accelerated Innovation (UC CAI), one of only three centers funded by NHLBI (<http://uccai.ctsi.ucla.edu/>). This program leverages the expertise and resources of the five UC medical campuses. Using industrial product-development practices to incubate technologies with high commercial potential, a rich research base supports a diverse pipeline of diagnostics, devices, therapeutics and tools for heart, lung and blood diseases.

The UC CAI program, administered by UCLA, has four goals: 1) Engage University of California heart, lung and blood disease innovators in entrepreneurship through a comprehensive education, training and mentorship program; 2) Solicit and select technologies with high commercial potential that align with the National Heart,

Lung and Blood Institute’s mission and respond to unmet medical needs or significant scientific opportunity; 3) Incubate our most promising technologies in accordance with industry requirements to facilitate their transition to commercial products that improve patient care and enhance health; and 4) Create a high-performing sustainable infrastructure that will serve as a model for academic research centers.

I encourage investigators and scholars/trainees to explore new ground and take advantage of these resources as they seek to advance their research and career development. For more information about the FUTURE program, contact Dr. Jennifer Greenier (jennifer.greenier@ucdmc.ucdavis.edu), director of program development, and for more information on UC CAI, contact Dr. Laura Marcu, College of Engineering (lmarcu@ucdavis.edu). The UC Davis CTSC website offers additional details about the UC CAI (<http://www.ucdmc.ucdavis.edu/ctsc/area/translationalresearch/UCCAI.html>).

Multi-campus inquiries determine clinical trial feasibility

NOTHING WILL BRING AN IDEA for a clinical study to a screeching halt faster than a shortage of potential research subjects. What options does an investigator have? A new multi-campus patient inquiry tool can help resolve such a stalemate.



UC Research eXchange (UC ReX) Data Explorer is a tool that allows researchers to query the aggregate databases of the five medical campuses at UC Davis, Irvine, Los Angeles, San Diego and San Francisco. Using a secure, web-based drag-and-drop interface, Data Explorer identifies the number of patients who meet the inclusion and exclusion criteria specified in the query.

UC ReX is a component of the University of California Biomedical Research Acceleration, Integration and Development (UC BRAID) program that links research activities

across the five UC medical campuses – all recipients of a Clinical and Translational Science Award.

According to Nick Anderson, director of informatics research for the UC Davis School of Medicine, UC ReX enables researchers to search de-

identified records for more than 12 million patients on the UC medical campuses.

Search criteria include demographics, diagnosis and procedure codes

(ICD-9 and CPT), top 150+ lab orders, and an evolving set of prescribed medications.

“UC ReX Data Explorer generates an aggregate numeric count of patients matching query criteria at each local integrated data warehouse. Using those data, researchers can take steps to establish research permission for identifying individual potential research participants,” Anderson explained. “The strength of Data Explorer is its capacity to explore a very large and heterogeneous patient population directly from the desktop, and through

this process, develop preliminary data for clinical research design.”

Without Data Explorer, researchers would have to define, gain approval, and run individual queries at each of the five data warehouses separately, a time-consuming and cumbersome process. Using Data Explorer, investigators can isolate cohorts by medical characteristics and estimate the incidence of rare diseases across California. The result is an ability to expand a study from a single to

“Researchers can use Data Explorer to structure queries that identify, for example, all African American females 55 to 75 years of age who have been diagnosed with diabetes and cardiovascular disease and have been discharged to a hospice-care setting.”

– Nick Anderson

Five steps from query to recruitment

1. Obtain patient counts from all five UC sites using UC ReX.
2. Recruit co-investigators at each site from where you want to access data using research networking tools, such as DIRECT2Experts, if needed.
3. Obtain UC Davis IRB approval if requested research data includes identified datasets.
4. If applicable, the other UC sites can use Trust and Rely to expedite their IRB approval process.
5. Work with your co-investigator(s) to obtain the list of patients you want to recruit at each of the UC medical centers.

multi-site proposal and to assess the feasibility of creating targeted enrollments, such as the number of potentially eligible patients by gender, race and ethnicity.

“Researchers can use Data Explorer to structure queries that identify, for example, all African American females 55 to 75 years of age who have been diagnosed with diabetes and cardiovascular disease and have been discharged to a hospice-care setting,”

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FEATURED SCHOLAR

Melissa Loja, M.D., M.A.S.

At a glance

- Integrated Vascular Surgery resident at UC Davis, inaugural class
- Completed the CTSC T32 program in 2011 with a research interest in head and neck cancer
- Current research interests: outcomes in vascular surgery
- Research mentors: Nasim Hedayati and Misty Humphries, Department of Surgery, Division of Vascular and Endovascular Surgery

Who or what inspired you to seek a career in medicine and research?

In the fourth grade I had an inspiring teacher who encouraged me to think about being a physician. From an early age my interest in research led me to attend science fairs. This interest was rekindled as an undergraduate when I worked in the UC Davis Department of Entomology under Edwin Lewis, studying the behavior of entomopathogenic



Melissa Loja, M.D., M.A.S.

nematodes. His mentorship helped spark a new passion for science and discovery.

How has the T32 program enhanced your life and career thus far?

The T32 program helped expand my vision of what research can encompass, allowing me to find my own research interests. I worked with a variety of mentors and fellow researchers across disciplines, and gained a network of colleagues to collaborate with and help guide my career. I gained fundamental knowledge

in the conduct of research from the ground up, with invaluable lessons in ethics, biostatistics, grant writing and more.

My experience in the T32 program continues to influence the type of projects I choose during my residency, and gave me the background needed to undertake these projects. Because there is not a lot of time to complete research projects during a surgical residency, having a solid foundation certainly helps.

Are you working on any research projects?

I'm currently working on a few projects with the Division of Vascular Surgery, one investigating differences in treatment of peripheral arterial disease between races. Also, I am still continuing work on optical imaging of oral cancer with D. Gregory Farwell in the Department of Otolaryngology, which I started during my T32 year.

UC Rex *Continued from page 4*

Anderson said. "Data Explorer is a dynamic hypothesis-generation tool that can perform a broad range of analytics that researchers would never before have been able to accomplish so economically and efficiently."

Because the output is simply the de-identified number of potential subjects who match query criteria, the process does not constitute actual research, and no prior Institutional Review Board (IRB) review or patient consent procedure is necessary to perform such queries. Researchers then can use the results to determine which of the other UC medical centers may be in a position to participate in a collaborative study.

Clinical and teaching faculty members, research fellows, medical residents and students are eligible to use Data Explorer, and training sessions are readily available.

"Data Explorer has unparalleled capabilities for population-level data discovery across an enormous aggregate of data, while also creating a path for development of closer collaborations among clinical and translational research throughout the UC system. It is a highly

unique system that can assist in moving an investigator quickly from a discovery process to the design and conduct of actual clinical research," Anderson said. "Any investigator who wants access to Data Explorer can begin by contacting us through the CTSC." §

Visit <http://ucrex.org> on the web to learn more. Some of the information for this article was adapted from the Data Explorer pages of other UC campuses.

UC Rex Data Explorer: Access and training

For more information or to register for training, visit the UC Davis Data Explorer web page: <https://www.ucdmc.ucdavis.edu/ctsc/area/informatics/UCREX.html>
To request help or submit questions, send an e-mail to ucrexdex@ucdmc.ucdavis.edu

So much data – but what does it all mean?

BEFORE “TEAM SCIENCE” and “multidisciplinary investigation” became hot topics in the field of clinical and translational research, there was one consistent multidisciplinary member of the research team – the biostatistician. While medical scientists have expertise in their field of study, the biostatistician is the data evaluation expert. The importance of this relationship has become increasingly crucial over the years as the complexity and immensity of research data has grown. Recognizing investigators’ needs for readily accessible statistical assistance and consultation, the CTSC has assembled a team

of expert biostatisticians who are ready to tackle researchers’ study design and data analysis needs.

“We have a breadth of analytical techniques with which many researchers may be unfamiliar. These methods allow us to examine data in a variety of ways, and identify and extract unique patterns and dynamics from the analysis. Sometimes through the analysis we make discoveries that researchers had not anticipated,” said Sandra Taylor, the Biostatistics Program’s senior statistician. Along with four other biostatisticians, she works under the direction of Dr. David Rocke,

director of the CTSC Research Design and Biostatistics Program.

Medical residents, graduate students and faculty members can seek assistance from the staff of the Biostatistics Program, which includes three faculty statisticians and three doctoral-level staff statisticians. The program’s facilities at the CTSC and on the Davis campus are available to any investigator from the Schools of Medicine, Nursing, or Veterinary Medicine, as well as the Colleges of Engineering and Biological Sciences.

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NEW APPOINTMENT

Nick Anderson appointed CTSC Biomedical Informatics director

THE CLINICAL AND TRANSLATIONAL SCIENCE

Center is delighted to welcome Nick Anderson, the new director of the CTSC Biomedical Informatics program. Anderson, an accomplished researcher with private industry and academic experience, joined the UC Davis faculty in September as the Robert D. Cardiff Professor of Informatics in the Department of Pathology and Laboratory Medicine, and director of



Nick Anderson, Ph.D.

research informatics for UC Davis School of Medicine. His research and academic expertise encompass clinical-translational data sharing, patient-centered health research and bioethics policy issues. His recent work has focused on development of institutional-scale biospecimen and data repository resources for research, and he is actively engaged in advancing these areas across the UC Davis and University of California campuses.

Anderson also brings along considerable experience as an academic mentor, with a primary goal of supporting students who seek to improve the quality of health and health information in society. He expects his mentees to become skilled writers, critical thinkers and socially active academic citizens who take personal responsibility and seek perspective by cultivating balance in their lives.

Originally from Auckland, New Zealand, Anderson has lived in the United States since 1979 and became a U.S. citizen in 2002. He received a bachelor’s degree in computer science from

Evergreen State College in Olympia, Washington, a master’s degree in biomedical informatics from Oregon Health & Science University in Portland, and a doctoral degree in biomedical informatics from the University of Washington in Seattle as a National Library of Medicine predoctoral research fellow. An adventurer at heart, he journeyed into informatics 33 years ago with a drive to master a variety of software platforms. Anderson’s extracurricular interests lie in vintage cars, brewing beer, the culinary arts and outdoor activities, including backcountry skiing, snowboarding and mountaineering.

With broad and relevant research experience in biomedical informatics and his unique perspective on life, Anderson is well-equipped to guide the UC Davis CTSC program in a direction that embodies his academic foci, with the *joie de vivre* that he brings to all aspects of his life.

“We assist with all phases of research,” said Taylor, who manages the program’s daily operations and performs data analyses. “We can help investigators design their studies,

and determine if they have sufficient samples and are collecting data in a manner that will answer their questions. We also help researchers write sections of grant proposals that describe how the data analysis will address the specific aims of the study. We analyze the data they collect, and prepare figures and written reports to aid in the interpretation of the findings.”



Biostatistician Sandra Taylor (center) discuss a project with investigator Tina Palmieri (left) and research coordinator Terese Curri.

Although the Biostatistics

Program accepts raw data submitted in plain text comma-delimited files, data collected in REDCap (Research Electronic Data Capture) or the Velos clinical trials data management system is preferred because those applications prevent contamination of numerical fields with text and ensure consistency among entered data. The CTSC Biomedical Informatics program also can help researchers design a database (see “Is there an app for that?” in CTSC Connections, Fall/Winter 2012–2013).

“One thing we cannot do is fix a poorly designed study that is already under way,” Taylor said. “That is why we encourage investigators to talk

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Robin Steinhorn *Continued from page 1*

“I didn’t even pick up a pipette until I was three years out of my training. That’s when I discovered that research was a surprisingly good fit for me,” said Steinhorn. “I was a translational scientist to my core before we even had coined that term. I’ve always been in that zone between the bench and the bedside. My interest in the laboratory is rooted in wanting to learn more about clinical problems and how to solve them.”

Born and raised in Akron, Ohio, Steinhorn spent the first 24 years of her medical career east of the Mississippi before joining the UC Davis faculty in the autumn of 2012.

“I was attracted to come here because I saw UC Davis as a place of amazing opportunity,” said Steinhorn, whose decision was heavily influenced by the cadre of “phenomenal scientists” who were working in her area of interest and the presence of a well-established CTSC. “I recognized UC Davis as a place where you have a chance to write history, to be a part of shaping the evolution of medicine

and translational science at a very interesting time in our country as we wrestle with some of the thorniest problems we’ve ever faced in science and in clinical care.

“My decision has turned out to be even better than I expected, as I’ve realized that as a new faculty member, you don’t just join UC Davis. You’re joining all of the University of California,” she said, adding that UC BRAID (www.uc-braid.org) tightens her connection with fellow pediatric scientists at other UC medical schools. Steinhorn serves as a member of the UC BRAID Child Health working group.

“Involvement of patient populations and the tremendous intellectual expertise at all five UCs vastly increases the potential impact of a research project,” Steinhorn said. “BRAID will progress into a very powerful model.”

Steinhorn was also impressed by the longevity of the UC Davis CTSC and the breadth of its resources.

“UC Davis was among the first sites that received funding through

the Clinical and Translational Science Award to establish the CTSC, and it provides crucial training to my younger faculty members. Thanks to the CTSC, I inherited several talented investigators who have rapidly progressed through those early years and are now successfully competing for external funding. As chair of a department with more than 100 pediatricians, I have a deep passion about developing their careers,” Steinhorn said. “The CTSC’s experience with clinical trials is a huge asset here, and the CTSC is invaluable for my own research portfolio as well.”

There is one challenge that the move to UC Davis has not changed for Steinhorn. As a clinician-investigator, medical director and department chair with many duties and passions competing for her time, Steinhorn has not found a way to extract more than 24 hours out of any given day.

“Time won’t stop for me, but I keep doing what I love, and it’s just never led me wrong,” Steinhorn mused. §

Biostatistics *Continued from page 7*

with us when they first plan their study. We will discuss their specific aims, hypotheses, data sources, the comparisons that they want to make, and the relationships they may want to establish. That information then forms the basis for the sample size calculations. We will also try to discern any confounding factors that may inhibit their ability to make their intended inferences.” Taylor and her colleagues use applications such as SAS and R to process data and conduct statistical analyses.

Taylor brings a scientific background to her position. She had worked over a decade as a wildlife biologist, engaged in habitat conservation and restoration, before she developed a captivating interest in biostatistics. She sidelined that career and enrolled at UC Davis in the biostatistics program through which she obtained a master’s degree in 2006 and a Ph.D. in 2009.

“I love this job,” enthused Taylor, who enjoys helping researchers solve problems. “When investigators come

in bewildered and overwhelmed by their data, I am happy when I can say, ‘OK, we can handle this.’ Analyzing their data and presenting the results in a manner that they understand and is accessible to them is really rewarding.” §

Two ways to obtain statistical support

- Click the “Request Services” link on the CTSC home page.
<https://ctscassist.ucdmc.ucdavis.edu/redcap/surveys/?s=vsjHnX>
- Reserve a spot at the Biostatistics Office Hours, held most Tuesdays at noon at the CTSC. <https://ctscbiostatisticsworkshop.acuityscheduling.com/schedule.php>

Office Hours sessions offer an opportunity for investigators to consult with a statistician about the design, analysis or presentation of medical research studies in a friendly, informal setting.



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