Nothing lost in translation

AS A CHILD, he was always fascinated by bugs and toads, and watched *Wild Kingdom*, a popular television show that aired from 1963 to 1985. Wondering “How does this work?” served Michael Lairmore well on his path to becoming dean of the UC Davis School of Veterinary Medicine, a prolific author and an internationally recognized translational scientist.

Lairmore’s introduction to translational science began when, as a veterinary pathology resident, he learned that a virus initially associated with immunodeficient patients in San Francisco was classified in the same retrovirus family as a sheep retrovirus that he had been studying in the laboratory where he was completing his doctoral thesis.

“The human virus, which we now know as the AIDS virus, had the same characteristics as the sheep virus,” Lairmore said. “For decades retroviruses had been established as causes of disease in sheep, horses and cats. When infected with this virus, sheep exhibited lymphoid interstitial pneumonia, a common outcome of pediatric patients who develop AIDS.”

Lairmore’s experience and expertise grew to bridge multiple disciplines to address basic questions related to viral causes of disease, such as cancer, and the biology of retroviruses. He developed one of the first models of AIDS-associated pediatric pneumonia and discovered the first human T-cell leukemia/lymphotropic virus type 2 infection in native Indian populations in Central America – work that subsequently was recognized as an endemic infection among indigenous populations throughout North and South America.

DIRECTOR’S MESSAGE

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

Asmuth leads VA research enterprise

Since the inception of the General Clinical Research Center in 2004, David Asmuth has played a key leadership role in our program. His contributions to our center have been focused primarily on clinical and regulatory affairs. Specifically, he has been our director of the Clinical Research Center, a research unit focused on the delivery of patient care in clinical trials, and also led the Regulatory Knowledge and Support Program, which provides guidance and resources in support of clinical trials. In addition to those very important roles at the UC Davis CTSC, Dr. Asmuth is a professor of infectious diseases who specializes in HIV research in the Department of Internal Medicine at the UC Davis School of Medicine. He was a Peace Corp volunteer in the U.S. Agency for International Development’s Rural Health project, which took him to Mali, West Africa, in 1977. He also served as an Institutional Review Board (IRB) member for seven years and was a UC Davis IRB committee chair for eight years. With 62 publications, Dr. Asmuth has established himself as an investigator with much to offer in the research realm.

This expertise was noted by the U.S. Department of Veterans Affairs (VA). In April 2012, Dr. Asmuth was
prominence as concurrent associate director for Basic Sciences and Shared Resources in the Comprehensive Cancer Center and the associate dean for Research and Graduate Studies in the College of Veterinary Medicine at The Ohio State University, where he gained insights into university-wide resources that support translational sciences across disciplines.

When The Ohio State University joined the NIH clinical and translational science award consortium in 2006, Lairmore noticed a significant improvement in communications and programmatic activities across the schools of health science – medicine, veterinary medicine and pharmacy.

“Sitting down at the same table with representatives from all of the health science groups was a stimulus for many innovative developments, from new mentoring programs to original plans for shared resources,” he said.

Based on his translational research, Lairmore was elected as a member of the Institutes of Medicine of the National Academies of Science in 2010 and a fellow of the American Academy of Microbiology in 2011. In the fall of 2011, he became dean of the UC Davis School of Veterinary Medicine.

Under Lairmore’s direction, translational science has become a significant component of the new strategic plan in the School of Veterinary Medicine.

“We are seeking ways to pair our basic sciences and field-based sciences in pursuit of problems related to human medicine,” he said. “Expanding on the ‘one health’ concept that was embedded within the vet school many decades ago, we conduct veterinary medicine clinical trials very much in parallel and synergy with studies at the School of Medicine to improve animal, human and environmental health and to address complex health problems.”

Incorporating multidisciplinary expertise across a wide range of research areas, from dysphasia and gastrointestinal issues to toxicology, improves health for all by increasing preclinical knowledge.

No longer actively engaged in scientific research, Lairmore is now focused on promoting the entire school’s efforts. “I’m still doing research, but it’s on people and programs.”

**DIRECTOR’S MESSAGE continued from page 1**

~Lars Berglund

“Dr. Asmuth leads the VANCHCS Research and Development (R&D) Program, which oversees protocols in human, animal and basic laboratory research.”

named associate chief of staff for research and development for the VA Northern California Health Care System (VANCHCS). Now deployed to the Sacramento VA Medical Center in Mather, Dr. Asmuth leads the VANCHCS Research and Development (R&D) Program, which oversees protocols in human, animal and basic laboratory research. Research areas encompass health systems, including health outcomes, quality, access, utilization and cost; geriatrics; cancer; neuroscience, including audiology, Alzheimer’s disease, cognitive neuropsychology and visual motor protocols; liver disease; heart disease; and endocrine disorders, including diabetes mellitus, bone metabolism, and those associated with cholesterol.

The R&D Program also oversees research protocols at the Martinez Outpatient Clinic and Center for Rehabilitation and Extended Care, and the Sacramento VA Medical Center, in addition to collaboration with UC Berkeley and UC Davis at the Alzheimer’s Disease Center at the Martinez campus. In addition, VANCHCS houses a nine-bed clinical research center, operated by the CTSC and developed through a partnership with UC Davis. This unit, located at the Sacramento VA Medical Center, offers a setting to conduct state-of-the-art, safe and controlled inpatient and outpatient studies. Active clinical projects range from Alzheimer’s disease and AIDS to cancer and bariatric weight reduction.

We congratulate Dr. Asmuth on his transition, and look forward to ongoing productive research collaborations with the VA in the years to come.
SPOTLIGHT ON COLLABORATION

NeuroNEXT: Research acceleration through collaboration

A LACK OF COLLABORATORS, equipment or study participants can mean the end of a study before it even gets started. But a new initiative – the National Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT) – gives investigators working on proposals and studies for the National Institute of Neurological Disorders and Stroke (NINDS) access to a collaborative research network to facilitate the process.

Established by NINDS, NeuroNEXT fosters partnerships with academia, private foundations and industry to assess promising new therapies, increase the efficiency of clinical trials before embarking on larger studies and respond quickly as new research opportunities arise. The network includes 25 institutions with major neurology, physical medicine and rehabilitation clinical trials under way. Earlier this year, UC Davis became one of only four institutions on the West Coast to participate in the network.

Loosely based on the cooperative oncology group model supported by the National Cancer Institute and the National Institutes of Health (NIH), NeuroNEXT created a group of like-minded investigators with similar patient populations who are interested in clinical research. Because not every individual investigator may have access to the full range of expertise, or to all of the logistical or patient resources necessary to conduct a clinical trial, the consortium helps fill in the gaps.

NeuroNEXT enables investigators to vet their study protocol design with knowledgeable colleagues, gather information to help them advance the more promising projects, develop data collection and data capture tools for use across multiple sites, and conduct scientific reviews in preparation for NIH grant submission.

According to Erik Henricson, UC Davis NeuroNEXT operations director and an associate director of clinical research in the UC Davis Department of Physical Medicine and Rehabilitation, NeuroNEXT enables researchers to conduct or participate in early-phase clinical trials that would be difficult or impossible to conduct on their own. Resource sharing also helps streamline efforts and reduce redundancies.

“Suppose a researcher needs 50 patients to conduct a safety trial of an investigational drug but has only five patients who might be candidates. The network can link the researcher with investigators at other institutions who are willing to collaborate on the study using the same protocol,” he said. “The ability to leverage patient populations and expertise across the country to conduct studies that individual investigators might find too daunting or that might be logistically impossible to conduct at a single site is a tremendous advantage to investigators and to the scientific community nationwide.”

NeuroNEXT is available for researchers from all disciplines who are focused on a neurological disease or condition and who plan to submit grant proposals to NINDS. “If you have an idea for a biomarker or an early-phase clinical trial in any of the diseases that NINDS covers, they are willing to hear it, regardless of your medical specialty. It could be a trauma project for individuals with head injury or a neonatal intensivist’s study of stroke in newborns. If it is related to the brain or the neurological or neuromuscular systems, it is fair game,” Henricson said.

UC Davis participates in NeuroNEXT through a cooperative agreement with the Department of Physical Medicine and Rehabilitation, Center for Neuroscience, MIND Institute, and Departments of Neurology and Neurological Surgery. Randev Sandhu, UC Davis NeuroNEXT coordinator, encourages investigators to take advantage of the services offered by the CTSC to support their research efforts.

“The CTSC enables investigators to leverage support in research design, implementation and clinical trials assistance,” said Sandhu. “NeuroNEXT can play an important role in the translation of research into clinical practice by providing investigators an avenue to conduct larger Phase II, safety-oriented studies. It can also help investigators participate in the acceleration of trials and involve participation of junior faculty scholars, which has the potential for leading to more advanced grant opportunities.”

Contact Randev Sandhu at randev.sandhu@ucdmc.ucdavis.edu or visit www.ucdmc.ucdavis.edu/pmr/research/neuronext.html for more information about NeuroNEXT and proposal submissions.
Is there an app for that?

WHAT IF THERE WERE A TOOL that could determine the number of patients with a specific set of conditions to support a proposed study, even before it was submitted as an Institutional Review Board (IRB) application? Or, if a researcher could find collaborators with interests and expertise that complement a particular area of study? How about an easy-to-use, web-based application that would enable investigators to build and manage their own online research database? Can computer technology truly be a user-friendly, indispensable asset in the conduct of biomedical research?

Kent Anderson, associate director of the UC Davis CTSC Biomedical Informatics program and manager of research information technology (IT) for the UC Davis Health System, says “yes” – and he should know. Anderson was the original database architect for the UC Davis General Clinical Research Center, a National Institutes of Health (NIH)-funded program that was a precursor to the CTSC.

At that time there was more of a distinction between IT and the interdisciplinary focus of biomedical informatics, which explores the most effective uses of biomedical data, information and knowledge for scientific inquiry. Anderson recalls that back then his work, building and managing databases, was very IT-focused. “Since the CTSA consortium began in 2006, we evolved to become a strong technology partner in numerous informatics and clinical research grants, leading to the implementation of innovative, cutting-edge tools specifically aimed at helping investigators conduct research.”

The UC Davis Health System chief information officer, Mike Minear, also serves as the director of the CTSC Biomedical Informatics program. Minear’s position overseeing Health System IT and Research IT establishes a platform to integrate biomedical informatics with other health system technology services, enabling enterprise-level assistance for all researchers.

The work of Tina Palmieri, professor of surgery and director of the UC Davis Regional Burn Center, exemplifies how this integrated effort helps researchers. Palmieri turned to the CTSC Biomedical Informatics team when she was funded by the Department of Defense, through the American Burn Association, to conduct a series of multicenter clinical trials that required extensive informatics and IT support.

“Since the CTSA consortium began in 2006, we evolved to become a strong technology partner in numerous informatics and clinical research grants, leading to the implementation of innovative, cutting-edge tools specifically aimed at helping investigators conduct research.”

~ Kent Anderson, associate director, CTSC Biomedical Informatics program

Biomedical informatics: A core strength at UC Davis

This interdisciplinary field aims to effectively use biomedical data, clinical information and knowledge for scientific inquiry, problem solving and decision making to improve health.

Recent work has earned UC Davis numerous recognitions, including two Larry L. Sautter Golden Awards for Innovation in Information Technology from the University of California Office of the President:

Volunteer Registry (2012)
Cohort Discovery (2010)
The CTSC Biomedical Informatics unit helped her utilize a tool called Cohort Discovery, along with the latest data collection and management technology. Cohort Discovery provides investigators with the ability to search patient data for study cohorts without compromising the Health Insurance Portability and Accountability Act and other privacy requirements. This allows researchers to access large, intricate de-identified datasets, making the process of designing studies and generating hypotheses more efficient and comprehensive.

“The CTSC Biomedical Informatics team assisted in matching informatics technology with our research projects,” Palmieri said. “These projects ranged from international multicenter trials to analysis of registries and individual research projects. Proper matching of informatics with research is essential to the success of meaningful projects.”

Sam Morley, manager of the CTSC Biomedical Informatics group, emphasizes that his unit helps researchers identify the appropriate technologies to attain desired results. Researchers often arrive at the CTSC with just a vague idea of what data they need, how to identify a cohort of patients with specific characteristics, or how to gather data during a study. Consultation helps investigators gain understanding about the complexity of building a useful and compliant database.

“Proper matching of informatics with research is essential to the success of meaningful projects.”

~ Tina Palmieri, professor of surgery and director of the UC Davis Regional Burn Center

“We show researchers why they should use a tool like REDCap, rather than Access or Excel,” Morley said. “Our data-retrieval team helps researchers hone in on exactly what they need to access patients from the electronic medical record (EMR) who meet study criteria. We can also point investigators to tools or resources to help them recruit volunteers for studies, collaborate with other researchers doing similar work, or determine ontology standards.” These biomedical informatics technologies and services exemplify the CTSC’s goal to support research across the clinical and translational spectrum.
FEATURED SCHOLAR

Cardiologist Ehrin Armstrong

Heartache is not new to cardiologist Ehrin Armstrong. In fact, it’s his life’s work. As an interventional cardiology fellow and researcher in the UC Davis Division of Cardiovascular Medicine, Armstrong is using flow cytometry, microfluidic adhesion assays and other sophisticated techniques to better understand the immune system’s response to a heart attack. His research is focused on the biology of specific immune system cells (subtypes of monocytes, the pro-inflammatory CD14++ and CD16++ cells) and their role in mounting an inflammatory response that forms plaque in coronary arteries.

“We have excellent immediate treatments for a heart attack, but we still don’t understand the biology of what happens afterward to prevent secondary coronary events,” he said. “My research on monocytes and inflammation aims to identify biomarkers that can be used as a tool to identify subgroups of patients who are at increased risk for subsequent cardiovascular events.”

A recent graduate of the Mentored Clinical Research Training Program (MCRTP) at the UC Davis CTSC, Armstrong is conducting research with two primary mentors – Jason Rogers, director of interventional cardiology at the UC Davis Vascular Center, and Scott Simon, a UC Davis professor of biomedical engineering who specializes in monocyte integrin biology and microfluidics. Armstrong credits this synergistic combination of mentors for making his interdisciplinary research even possible.

Frederick Meyers, executive associate dean at the UC Davis School of Medicine, underscores the benefit of multidisciplinary mentoring. “By interweaving clinical cardiovascular medicine, clinical translational science methods and bioengineering, Armstrong and his mentors demonstrate the synergy of team science.”

Armstrong has received numerous honors and awards for his leading-edge work. In 2012, the Society for Cardiovascular Angiography and Interventions recognized his oral abstract among the best at its annual meeting, and he received the American College of Cardiology’s Young Author Achievement Award for the best manuscript published in the Journal of the American College of Cardiology: Cardiovascular Interventions.

Of his experience, Armstrong said, “The MCRTP encourages young investigators to pursue innovative approaches to answer a research question. Interacting with physicians and scientists from across the UC Davis campus who have different levels of research experience opened up a number of opportunities for collaboration.”

Curiosity for pursuing innovative approaches to patient care, in combination with careful research and analysis, provides insights to identify novel ways to help patients. This is the essence of biomedical research that Armstrong exemplifies in his quest to find answers.

Congratulations to CTSC pilot project awardees

The UC Davis CTSC Pilot Award Program sparks innovative and collaborative scientific investigations by supporting robust new research paradigms, technologies and tools, and by establishing partnerships that enhance team science. The CTSC is pleased to announce the recipients of new pilot projects funded in partnership with Rosa B. Sherman Pediatric Research Awards, as well as the four research teams receiving the CTSC’s Highly Innovative Awards for 2012:

“Transition of Health Care for Youth With Special Health Care Needs Using EMR for Training Pediatric Residents,” Robin Hansen, professor of pediatrics

Transition of health care from pediatric to adult-oriented health care systems for youth with special health-care needs is an important area that is usually not part of the pediatric residency curriculum. As more health systems move towards using electronic medical records (EMR), developing a simple, easy-to-use EMR template to address some of the key transition issues in a systematic way could save time, and improve efficiency, patient satisfaction and quality of care. The overall hypothesis is that resident training in transition planning and use of an EMR template will increase knowledge for both residents and families regarding this process and result in systematic improvements in quality of care provision as patients transitioning to adult-care services.

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PILOT PROJECT Awardees continued from page 6

“Improving Speech Outcomes Through the Use of a Novel Game-Based Speech Therapy,” Travis Tollefson, associate professor of otolaryngology

Orofacial clefts, including cleft lip and cleft palate, are among the most common congenital anomalies. Children with orofacial clefts require multiple surgical procedures and long-term speech therapy. Although early intervention is associated with higher likelihood of success at attaining proper speech production, younger children have difficulty sustaining interaction with the therapist, comprehending tasks, and staying motivated to comply with therapy. This project aims to develop a novel method of speech-therapy delivery that is engaging, portable and applicable beyond the speech therapist’s office.

“Mechanisms by Which Human Milk Peptides and N-Glycans Shape the Infant Intestinal Microbiota,” Mark Underwood, associate professor of pediatrics

Sepsis and necrotizing enterocolitis are the most common causes of mortality after the first two weeks of life in premature infants. Both of these complications are associated with the composition of the intestinal microbiota and are less common in premature infants who receive their mother’s milk. Previous studies at UC Davis have demonstrated that human milk oligosaccharides play an important prebiotic role in shaping the composition of the intestinal microbiota. In this study, similar methodologies are proposed to evaluate two minimally studied, bioactive human milk components: glycoprotein-associated N-glycans and peptides.

“Acylcarnitines and Inherited Disorders of Fatty Acid Oxidation: From Clinical Diagnostics to Active Players in Driving Inflammation and Myopathy,” Sean Adams, associate adjunct professor of nutrition at UC Davis and researcher at the USDA Western Human Nutrition Research Center

Inborn errors of metabolism include disorders of fat combustion such as enzyme deficiencies that are associated with fatty acid utilization by mitochondria. In many of these diseases, patients do not display symptoms until the body experiences an additional stress such as an infection or illness, intense exercise or fasting. Under these conditions, the fatty acids increase in the bloodstream and overwhelm the body’s ability to utilize them. This proposal will test if metabolites associated with the perturbation of fat metabolism do not just mark disease, but actually participate in pathways of cell stress that are involved in deteriorating metabolic health in muscle.

“Inflammation, Genetic Risk Factor, and Cardiovascular Disease – New Insights from Studies in Nonhuman Primates,” Enkhmaa Byambaa, assistant adjunct professor of endocrinology

Cardiovascular disease (CVD) is the number one cause of mortality worldwide and, in the U.S. alone, more than 2,200 people die of CVD each day – an average of one death every 39 seconds. A high CVD risk remains despite appropriate therapeutic management of established risk factors, including LDL cholesterol, emphasizing the need to identify other contributing factors. Over the years, there has been increasing evidence for the causative role of lipoprotein(a), or Lp(a), in CVD development, and screening for elevated Lp(a) has been recommended. Yet the underlying mechanisms for the atherogenic role of Lp(a) remains poorly understood. The goal of this project is to validate the suitability of the rhesus monkey as a model system for Lp(a) studies and to investigate the associations of inflammatory burden with Lp(a) and allele-specific apolipoprotein(a) levels.

“The Development of a Novel Drug Delivery System that Targets the Blood-Brain Barrier,” Angie Gelli, associate professor of pharmacology

One hundred million Americans suffer from some type of devastating brain disorder. These disorders include cancer, infection (meningitis, encephalitis), neurological conditions (epilepsy, migraines) and neurodegenerative diseases (Parkinson’s, Alzheimer’s, ALS and Huntington’s disease). Treating any type of brain disease is extremely challenging because the blood-brain barrier (BBB) prevents most clinically relevant drugs from reaching the brain.

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PILOT PROJECT Awardees  continued from page 7

The goal of this study is to develop an enabling technology that increases the permeability of the BBB to a new type of silicon nanoparticle that can carry a therapeutic payload and is biodegradable.

“Microglial Cells Regulate Development of the Prenatal Cortex Under Normal and Pathological Conditions,” Stephen Noctor, assistant professor of psychiatry and behavioral sciences

This study aims to understand the mechanisms that regulate prenatal development of the cerebral cortex under normal and pathological conditions. Specifically, studies will demonstrate that the immune system regulates cell genesis in the developing brain, which will develop new lines of investigation on pathological conditions such as schizophrenia and autism, in which immune system activation during gestation has been implicated.

Visit http://www.ucdmc.ucdavis.edu/ctsc/area/pilot/index.html for more information on the CTSC Pilot Award program.

The projects described above were supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through grant number UL1 TR 000002.

ANNOUNCEMENTS AND EVENTS

CTSC Career Development Seminar: “Using the iPad for Productivity”
Dec. 3, Medical Education Building, Room 2222
Chris Brandt, D.V.M., M.S., UC Davis School of Veterinary Medicine
11:30 a.m.-12:00 p.m. iPad Basics for Beginners
12:10 p.m.-1:00 p.m. Productivity Tools
1:10 p.m.-2:00 pm Advanced Productivity Tools

Description and registration information on the CTSC Event Calendar at http://ctscapps.ucdmc.ucdavis.edu/eventcalendar/calendar.aspx

Find us on Facebook https://www.facebook.com/UcDavisClinicalAndTranslationalScienceCenter

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