

CTSCconnections

Building research teams of the future to improve human health • SPRING 2012

Kimber Stanhope researches dietary sugars

Consequences of fructose consumption not so sweet

PIONEERING STUDIES by nutritional biologist Kimber Stanhope conducted with the Clinical and Translational Science Center (CTSC) are revealing new information about the metabolic effects of sugar consumption, and point to a possible cause-and-effect relationship between fructose intake and cardiovascular disease. Stanhope anticipates that findings from a study she conducted in 2005, and an ongoing investigation that will continue through 2015, may provide important new information for revised nutritional guidelines for safe upper limits of sugar consumption.

Research studies that Stanhope and her colleagues have published in scientific journals attracted the attention of CBS television's *60 Minutes* program. Producers at *60 Minutes* dispatched a news crew to the CTSC Clinical Research Center (CCRC) at the Sacramento VA Medical Center to observe research subjects participating in Stanhope's current study.

The earlier research, also conducted at the CCRC, compared the effects of consuming high levels of glucose or fructose, constituting 25 percent of each participant's energy intake. In that closely controlled study, 32 overweight subjects between 40 and 72 years of

age lived during a two-week baseline period at the CCRC and participated in numerous experimental procedures while they consumed weight-maintaining diets high in complex carbohydrate. They subsequently returned to their homes for eight weeks and drank either a glucose- or fructose-sweetened beverage with each meal. They then returned for another carefully administered two-week period at the CCRC, during which all the same experimental procedures were repeated and they consumed weight-maintaining diets that included the glucose- or fructose-sweetened beverages.

"Study participants who drank fructose had increased lipid levels, decreased insulin sensitivity and increased levels of the fat that surrounds visceral organs, and they exhibited increased *de novo* lipogenesis – the process by which the liver turns sugar into fat," said Stanhope, a registered dietitian and associate project scientist in the School of Veterinary Medicine's Department of Molecular Biosciences.

"None of these changes were seen in the group that drank the glucose-sweetened beverages. The study is

(Continued on page 2)

60 Minutes crew covers CCRC research

A CBS TELEVISION 60 MINUTES

news crew spent three days at the CTSC's Clinical Research Center (CCRC) in October gathering information about the sugar consumption studies that nutritional biologist Kimber Stanhope and colleagues have been conducting.

CNN's chief medical correspondent, Sanjay Gupta, is a neurosurgeon who periodically serves as a *60 Minutes* guest correspondent for medical science stories. Stanhope said the *60 Minutes* crew shot more than 20 hours of video.

"They filmed the subjects through almost every experimental procedure, including biopsies. They filmed the staff preparing meals and sugar-sweetened beverages, and interviewed me and the subjects.

(Continued on page 5)



Kimber Stanhope, Ph.D., M.S., and CBS 60 Minutes correspondent Sanjay Gupta, M.D.

Photo by Jon-Nolan Paresa, Department of Veterans Affairs, Northern California Health Care System

Fructose

Continued from page 1

important because it shows very clear metabolic differences between glucose and fructose. That difference had not been well documented in humans until this study,” Stanhope added.

The current study, even more ambitious, encompasses 200 subjects aged 18 to 40, who range from normal weight to overweight. Participants are organized into eight research study groups to compare the effects of commonly consumed sugars – high-fructose corn syrup (HFCS) and sucrose – with those of glucose and fructose.

more than glucose does. That is important because these results – even more directly than our first study – suggest that the association between high-sugar diets and cardiovascular disease may specifically be due to cause and effect,” Stanhope said. “Two weeks after giving the subjects high-fructose corn syrup, we saw an increase in the risk factors for cardiovascular disease, specifically LDL cholesterol and apolipoprotein-B.”

Stanhope’s collaborators on these studies include principal investigator Peter Havel, a UC Davis professor of molecular biosciences and nutrition; Nancy Keim at the USDA Western

samples, dispensed study beverages as outlined in the protocol, and ensured safety and protocol adherence,” said registered nurse and CCRC Associate Director Nicole Mullen. The CCRC’s nurse practitioner prepared drafts of physician orders and nursing flow sheets that mirrored the IRB-approved protocol; gathered medical histories from subjects and conducted physical exams; conveyed information to study physicians; and performed the gluteal adipose tissue biopsies.

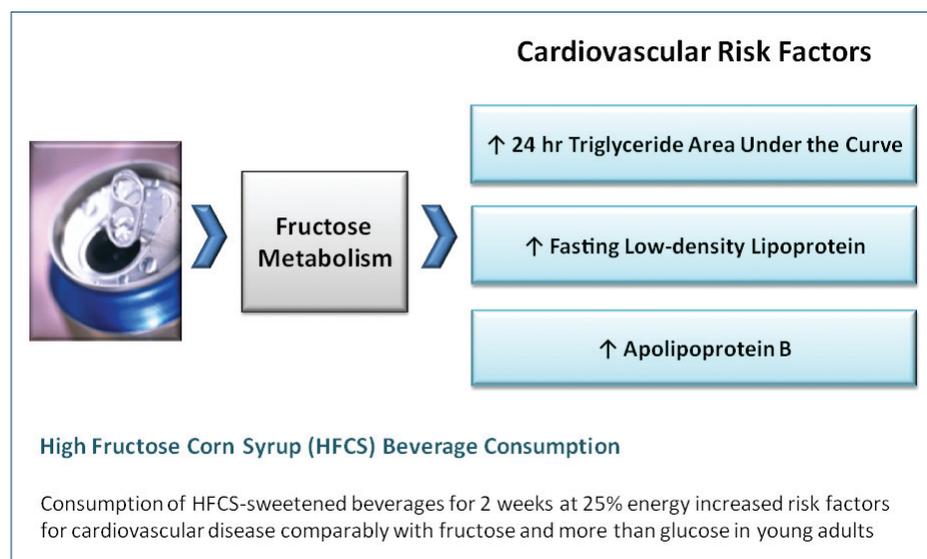
“Our exercise physiologist conducted DEXA scans, measured total body water using a bioimpedance spectroscopy device, conducted metabolic testing, and compiled data for the principal investigator monthly,” Mullen added. Further, the CCRC’s dietitian supervised meal preparation and trained the study staff in food-handling safety and labeling regulations.

Stanhope credits the CTSC staff and the CCRC facilities for contributing to the success of her studies.

“The reasons we were able to show the differences so clearly are partly related to how carefully the study was controlled using the CCRC facilities,” Stanhope said. She is preparing grant proposals for two more studies that she plans to also conduct at the CCRC.

The project described is supported by the National Center for Research Resources through grant #UL1RRO24146 and the National Center for Advancing Translational Sciences, National Institutes of Health.

Kimber Stanhope is scheduled to present a seminar titled “Are fructose-containing sugars (HFCS and sucrose) contributing to the epidemic of metabolic syndrome?” at the CTSC on April 26 at noon.



Participants each begin with three days of baseline study at the CCRC, followed by a 12-day outpatient period and conclude with a return visit to the CCRC. Even though the study is still under way, initial results were published in the *Journal of Clinical Endocrinology and Metabolism* in October 2011.

“Early results from the first 48 subjects showed very clearly that beverages sweetened with high-fructose corn syrup increased lipids – risk factors for cardiovascular disease – comparably to fructose and significantly

Human Nutrition Research Center; and Lars Berglund, John McGahan and Valentina Medici of the UC Davis School of Medicine.

Throughout the studies, CCRC’s research nursing team managed all subject care activity and implemented the protocol.

“Our nurses assessed eligibility, collected and processed more than 200 blood specimens for serial blood sampling, conducted oral glucose tolerance tests and heparin trials, collected and processed urine



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

“By sharing experiences and ideas, leaders from the medical centers are seeking UC-wide solutions to advance the potential beyond what any single center can accomplish alone.”

UC BRAID program fuels research

THE UC OFFICE OF THE PRESIDENT and Clinical and Translational Science Awards programs have launched a new initiative to fuel collaborative research. Known as UC Biomedical Research Acceleration, Integration and Development (UC BRAID), the program aims to harness and focus research in California, accelerating academic partnerships to benefit human health.

UC BRAID also aims to stimulate ideas that challenge the status quo and overcome the phalanx of barriers that limit biomedical research. For example, investigators face ever-changing regulatory requirements and obstacles in their ability to advance research that improves health while maintaining the highest level of

patient safety and privacy. Our aim is to help investigators overcome these difficulties through an improved organizational infrastructure that is supportive while respecting the need for compliance.

By sharing experiences and ideas, leaders from the medical centers are seeking UC-wide solutions to advance the potential beyond what any single center can accomplish alone. To date, UC BRAID has established working groups to address methods to streamline contracting practices, IRB review, informatics, drug discovery and development, and metrics to define processes and outcomes of the program. Visit www.ucbraid.org/ for more information.

FEATURED SCHOLAR

Nephrologist Lorien Dalrymple

INFECTIONS THAT COMMONLY AFFLICT DIALYSIS PATIENTS may also substantially increase their risk of cardiovascular problems, according to research conducted by nephrologist Lorien Dalrymple. Funded with a K12 grant from the CTSC, Dalrymple is investigating the types, rates and risk factors for infection and the associated cardiovascular consequences of infection in patients with chronic kidney disease (CKD) on dialysis.

“I became interested in understanding the epidemiology and consequences of infections in patients with CKD because infection and cardiovascular disease are leading causes of hospitalizations and death in

this population,” said Dalrymple, who attributes her research career trajectory to CTSC support.

“Numerous CTSC resources have been fundamental to my success as a researcher,” Dalrymple said. “CTSC offers career development awards, mentorship, grant-writing support, and opportunities to present research and obtain directed feedback from peers at a critically important time, early in career development.”

Dalrymple’s work has impressed Richard L. Kravitz, associate director of the K12 Training Program in the CTSC.

“Dr. Dalrymple is a terrific exemplar of a young, translational clinician-investigator. Her work on inflammation, infection and heart



Lorien Dalrymple, M.D., M.P.H.

disease in patients with CKD addresses critical problems at the margins of nephrology, cardiology, infectious disease and implementation science,” said Kravitz, who is also co-vice chair of research, and professor in the Department of Internal Medicine. “She recently received a very good score from NIH for an extramurally supported K-award. We hope this award will propel her to further success.”

Clinical Trials Resource Group guides researchers

EVEN THE MOST EXPERIENCED

researcher can find the myriad of regulations and requirements that govern clinical trials confusing. All clinical trials go through three major stages of activity (pre-study, study conduct and post-study), and each phase has distinct requirements, depending upon the nature of the project. Fortunately, UC Davis clinical researchers have access to a CTSC resource to assist them. The Clinical Trials Resource Group (CTRG) helps clinical research teams navigate the labyrinth of regulations and requirements encountered in planning and conducting clinical trials.

Kate Marusina, manager of the Regulatory Knowledge and Support Program, including the CTRG team, assists with each phase of the study process. For example, team members can help with the documentation required to gain regulatory approval of human-subject protocols and compliance with Institutional Review Board (IRB), FDA and Medicare regulations through the duration of a study. Marusina and her staff accommodate a variety of requests from investigational teams in every phase of the project. The group can develop consent forms, prepare IRB submissions, file IND, IDE and other regulatory

documentation, monitor clinical trials, and determine which charges are payable by insurance or study funds.

“Recently we assisted a MIND Institute researcher in completion of the entire IRB submission packet for a study involving children with genetic disorders. We prepared the parental consent form for this study,” Marusina said. “Since the study enrolled patients of various ages, we also composed the forms required for minors to participate, such as an assent form for ages 12 to 17 and a letter of information for ages 8 to 11. We also helped prepare a telephone screening script to describe eligibility requirements for parents of potential subjects. Because screening is part of the informed-consent process, the document had to include specific information required by the IRB,” Marusina explained. With assistance from the CTRG, the project was approved in a timely fashion so the study could proceed on schedule.

Monitoring study activity is another service that the CTRG offers to help investigators comply with applicable regulatory requirements.

“Once a study protocol is approved by the IRB, we can create regulatory binders and offer guidance on required documentation, including

study personnel responsibility logs, training logs and study-product accountability documentation,” Marusina said. “A monitoring plan is typically protocol-specific to reflect the variables of the study, such as number of subjects, study visits and study-related procedures, and reflects the overall complexity of the trial. We also go to the study site to review study documents for completeness and accuracy.”

“On an institutional level, Dr. Marusina is fostering an organizational structure to integrate and refine clinical research process flow, operations and compliance throughout UC Davis.”

~ **Kitty Lombardo**
administrative director, CTSC

In addition, the Clinical Trials Resource Group hosts a robust education program that includes training for clinical research budgeting and billing, the informed-consent process, coverage analysis, navigating the clinical trials process, and other relevant topics. The CTRG team includes certified clinical research professionals Denise Owensby and Virina De Jesus, who oversee clinical trial monitoring services and help investigators prepare IRB paperwork; Suzan Bruce, a certified professional coder who specializes in coverage analysis and billing; and Debie Schilling, an analyst who performs data extraction and analysis.

Visit www.ucdmc.ucdavis.edu/clinicaltrials/forinvestigators/forinvestigators.html for more information about the Clinical Trials Resource Group.

Clinical Trials Resource Group services

- IRB, FDA and Medicare regulations
- IRB application forms, ICFs, annual reports, AEs and Deviations
- Filing of INDs and IDEs
- Coverage analysis (determining what is payable by insurance, and what is payable by the study account)
- Study monitoring
- Preparing for regulatory audits (FDA or industry sponsors)
- Coordination of study subject visits
- Preparing case report forms
- clinicaltrials.gov

Cooperative radiochemistry facility emerges

CONSTRUCTION BEGAN in early January for a new research, training and production facility that will vastly improve logistics for bench-to-bedside radiopharmaceutical conveyance. The facility is being built within the Institute for Regenerative Cures on Stockton Boulevard, adjoining the CTSC.

The project is being developed cooperatively by UC Davis Health System, PETNET Solutions Inc. (a wholly owned subsidiary of Siemens Medical Solutions USA Inc.) and Northern California PET Imaging Center (NCPIC). The PETNET commercialization and distribution components are scheduled to begin operation by this summer. Julie L. Sutcliffe, a UC Davis associate professor of biomedical engineering and hematology and oncology, anticipates end-of-year completion of the training and research facilities, which she will direct.

“This project constitutes a perfect

synergy between academia and industry,” Sutcliffe said.

“The unique partnership with PETNET will function as a pipeline for commercialization of the concepts and compounds that UC Davis researchers develop. The CTSC will help expedite translations of those diagnostic and therapeutic radiopharmaceutical agents,” said Sutcliffe, who also is director of the cyclotron and radiochemistry facility at the UC Davis Center for Molecular and Genomic Imaging. “When I came to UC Davis nine years ago, I went from clinical to totally preclinical work, but my vision for the field then and always will be translation.”

The research component is aimed at developing specialized molecular agents for use not only in oncology, but also in neurology and cardiology. Sutcliffe emphasizes the importance of the training component to build a diverse, highly qualified nuclear science work force.



Photo by Dennis McCoy, Sacramento Business Journal

Julie Sutcliffe, Ph.D.

The new facility has not been officially named; project architects have informally labeled it the biomedical cyclotron research facility, while Sutcliffe and her colleagues have dubbed it R2@UC Davis (radiochemistry research and training at UC Davis). The facility's location on the Sacramento campus is strategic because of the short radioactive half-life of PET radioisotopes, many of which are usable for only a few minutes to a few hours.

Julie Sutcliffe will present a talk titled “New opportunities for molecular imaging at UC Davis, bench to bedside” at the CTSC on May 24 at noon.

60 Minutes *continued from page 1*

They also made some comparative graphics showing the large amount of fruit that contained the same amount of sugar that our subjects consumed in their sugar-sweetened beverages,” Stanhope said.

CCRC Associate Director Nicole Mullen helped coordinate approvals and accommodations for the *60 Minutes* crew to observe and interview the research subjects. She worked with public information representatives at the UC Davis campus, UC Davis Health System and Veterans Affairs.

“I helped bring the right people to the table to make sure we had all the necessary approvals in place, said Mullen. “I checked in with the Compliance Office, with Public Affairs, and the Institutional Review Board at UC Davis to make sure that inviting participants to be a part of this media coverage was acceptable. This was necessary because it had not been anticipated as a part of the protocol,” she explained. She and her team made certain that all research subjects were willing to be part of the news coverage. “As it turned out, all of them were very enthusiastic.”

The broadcast date for the segment has not been announced.

Partnership in action to improve community health

THE AFRICAN AMERICAN LEADERSHIP COALITION (AALC), which was formed in 2008 as a coalition of community organizations, leaders and agencies concerned with the plight of African Americans in the Sacramento area, is taking part in a new UC Davis community involvement initiative. Several members of AALC's Health Committee – including Tina Roberts of the Roberts Family Development Center and Edward Lewis of the Sacramento chapters of Black Greek Letters organizations – participated in the June 2011 Community Engagement and Health Partnerships Workshop sponsored by the CTSC and the Center for Reducing Health Disparities.

The purpose of this workshop, facilitated by nationally known community-based participatory research expert Nina Wallerstein, was twofold: to discuss how community-academic research partnerships can bring together the interests and health practices of communities and cutting-edge research from academic medical centers; and to announce the availability of pilot funding for innovative partnerships between communities and UC Davis.

Roberts, Lewis and a third AALC member, Joyce Askia from Sacramento County's Black Infant Health Program, were aware of UC Davis pediatrics professor Dennis Styne's work to help thwart diabetes and obesity among

Native-American populations. With the help of the CTSC Community Engagement program, they made contact with Styne, and together developed a proposal to work with African-American families in Sacramento. The new project will begin with a survey of participants to ascertain knowledge of diabetes and obesity in their families and the community. Using the study results, the project organizers will work with these same families on development of family action plans to change behaviors that lead to diabetes and obesity, and to maintain constructive behaviors that protect against these diseases.

Funding from the CTSC will enable key community members to assume pivotal roles in the design, data collection and analysis of a pilot study of 24 African-American families. Meetings with participating families are expected to start in March.

Styne, who holds the Yocha Dehe Chair for Pediatric Endocrinology, said the study's goal is to "empower the community to play an active role in identifying those factors that deter people from developing the healthy habits that reduce their likelihood of obesity and Type 2 diabetes. This approach differs from classic study models in which studies are directed toward a community in a unidirectional manner," he said.

"This grant is unique because it's the first step in creating a process in which members of the community are more involved in research and are active partners in reducing health disparities," said Roberts, whose organization conducts education and recreation programs for children in North Sacramento.



Shown in the kitchen of the Roberts Family Development Center are Dennis Styne, M.D. (left), Tina Roberts (center) and Linda Ziegahn, Ph.D. (right), representing the CTSC Community Engagement and Research Program. (Photo by Karin Higgins, University Communications.)

Linda Ziegahn, community engagement manager at the CTSC, helps identify the communities interested in partnering with UC Davis researchers and introduces them to the researchers who want to collaborate with those communities as equal partners focused on improving health. She hopes that the results of this pilot study will lead to larger studies and eventually to community interventions that will improve the overall health of African-American families.

“In the future we would like to see better access to fresh fruit and vegetables, schools assigning more time

“By engaging those groups underserved by health services, we believe we are starting in the right place.”

~ **Linda Ziegahn, Community Engagement Manager**

to physical education, and food banks revising the type of food provided for low-income families,” said Ziegahn.

“By engaging those groups underserved by health services, we believe we are starting in the right place.”

In addition to this project, CTSC-funded community-engaged research studies also will investigate premature births and low birth weights in African Americans, and physical- and mental-health conditions among Iraqi refugees.

The project described is supported by the National Center for Research Resources through grant #UL1RRO24146 and the National Center for Advancing Translational Sciences, National Institutes of Health.

NEW APPOINTMENT

Ted Wun named associate dean for research

Ted Wun, chief of the Division of Hematology and Oncology, has been named associate dean for research at the UC Davis School of Medicine. In his new role, he will be responsible for working with Lars Berglund, senior associate dean for research, in expanding the breadth and depth of research at the health system, as well as implementing the health system’s 2011–2016 Strategic Plan to increase high-impact, interdisciplinary research. His duties also will include coordinating efforts in implementation science throughout the health system and serving as the health system representative to the Association of Academic Health Centers.

“I’ve had the privilege of working with Ted over the years, and he has

certainly proven his drive and dedication to research,” said Berglund, who also is program director of the Clinical and Translational Science Center (CTSC). “He is an excellent collaborator and will bring his broad experience and perspective in shaping the future landscape of research at the health system.”

With this new appointment, Wun will add to his roles as director of the CTSC Clinical Research Resources and Facilities program, chief of the Division of Hematology and Oncology at UC Davis, and chief of hematology oncology at VA Northern California Health Care System. Wun joined UC Davis Medical Center in 1992 and is currently a professor of medicine in the Division of Hematology and Oncology, as well as professor of pathology and laboratory medicine.



Ted Wun, M.D.

He graduated magna cum laude from Union College in Schenectady, N.Y., and from Albany Medical College. He is board-certified in internal medicine, hematology and medical oncology.

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RESOURCES AND COURSES

Comparative Effectiveness Research Methods course:

<http://ctsa-cermethodscourse.org/>

Mentoring Academy Web site:

www.ucdmc.ucdavis.edu/mentoring

Medical Research for Residents:

http://ctschiostatistics.ucdavis.edu/index.php?option=com_content&view=article&id=6&Itemid=7

“Presentation Tips” video by Estella Geraghty, M.D., M.S., M.P.H./C.P.H.

<https://chtapps.ucdmc.ucdavis.edu/VideoConf/Events/meta/1119-500k.asx>

Informed Consent Bootcamp Webinar – available April 2012

For the most current information about this webinar, please visit
www.ucdmc.ucdavis.edu/clinicaltrials/Training/training.html

Upcoming Special Events: Visit the CTSC Event Calendar at
<http://ctscapps.ucdmc.ucdavis.edu/eventcalendar/calendar.aspx>

March 21 “Some Assembly Required: Organizing in the 21st Century” – Noshir Contractor, Ph.D. (CTSC Translational Science Seminar)

April 26 “Are Fructose-Containing Sugars (HFCS and sucrose) Contributing to the Epidemic of Metabolic Syndrome?” – Kimber Stanhope, Ph.D., R.D. (CTSC Translational Science Seminar)

May 2 Qualitative Health Symposium

May 24 “New Opportunities for Molecular Imaging at UC Davis, Bench to Bedside” – Julie Sutcliffe, Ph.D. (CTSC Translational Science Seminar)

June 15 CTSC Clinical Research Training Program:

& 22 www.ucdmc.ucdavis.edu/clinicaltrials/Training/training.html

Recurring workshops

CTSC Biostatistics Workshop, Tuesdays, 12 noon – 1 p.m., CTSC

- An opportunity to present biostatistics questions in an informal setting
- E-mail Sandy Taylor (sltaylor@ucdavis.edu) to register for one of the workshops

REDCap Workshops, by appointment, CTSC

- An opportunity to consult a database design expert regarding your REDCap questions
- E-mail Ayan Patel (ayan.patel@ucdmc.ucdavis.edu) for more information.

Please send a message to CTSCMail@ucdmc.ucdavis.edu if you wish to be added to the CTSC announcements mailing list.



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