Director's Corner by Ronald J. Sokol, MD

As 2013 comes to a close and we look ahead to 2014, I wanted to take this opportunity to reflect on a few of the CCTSI accomplishments in the past 12 months.

In January 2013 we submitted our NCATS/NIH grant application and received notification of our score in June 2013. The last week of September we received our Notice of Grant Award and immediately thereafter the government shut down. We continued to move forward in planning while awaiting to hear direction from NIH. Once the government was “back to work” in mid-October, the official announcement was made by NIH that the CCTSI at the University of Colorado Denver was one of 15 institutions to receive a new CTSA grant award.

We were awarded $52.4 million for a 4 year 7 month grant cycle, absorbing only a 3.5% sequestration reduction over what was requested. NIH has changed some of the requirements for the national CTSA program and we are in the process of instituting many of these changes, which will be communicated to you over the next several months. Please also note that our UL1, TL1 and KL2 grant numbers have changed (yet again) for this grant cycle (see CCTSI website for details).

We are undergoing CCTSI organizational re-engineering and process improvement to make us as efficient as possible and to continue to be able to provide the same high quality resources, services, training and education, regulatory support and pilot grant funding that our investigators have come to expect. Our new organizational structure and policies and procedures will be the focus of the next Newsletter. In the meantime, keep an eye on our website (cctsi.ucdenver.edu) for updates.

Colorado State University is the newest CTSA partner institution, which will strengthen our bandwidth for translational research and collaboration. We will continue to work towards achieving a single statewide academic home for clinical and translational research, along with our partners at UC Denver, CU Boulder, University of Colorado Hospital, Children’s Hospital Colorado, National Jewish Health, Denver Health, the Denver Veteran Affairs Medical Center, and Kaiser Permanente of Colorado, as well as over 20 community based organizations throughout the state. The CCTSI continues to support researchers at all levels of the translational spectrum. As you read this newsletter, you will gain insight into some of the very exciting work taking place.

My office door is always open. Feel free to contact me or anyone in the administrative staff if you have questions or suggestions regarding programs and procedures within the CCTSI.

We look forward to an eventful 2014!

Sincerely,
Ronald J. Sokol, MD
Director of CCTSI
ronald.sokol@childrenscolorado.org

Upcoming Events & Important Dates

Request for Applications: “Improving Research Through Community-Academic Partnerships”

The Colorado Clinical and Translational Sciences Institute (CCTSI) Community Engagement & Research (CE&R) and the Partnership of Academicians and Communities for Translation (PACT) are currently accepting applications for Pilot Grant Award funding. This RFA is intended to support community-academic partnerships to perform pilot studies that will strengthen relationships and produce preliminary data for future competitive grant applications. Funded projects may encompass partnership development, project planning, capacity building (i.e., data collection and management, recruitment and outreach, etc.) as well as implementation of research projects within specified areas of emphasis (cardiovascular disease, childhood chronic conditions, social emotional health). $200,000 of funds are available for this round of CE&R Pilot Grant Awards.
Research Features

Health Benefits of Vitamin C – It’s All in the Delivery

During the late 90s and early 2000s, many scientific studies demonstrated the health benefits of intra-venous and intra-arterial administration of Vitamin C (ascorbic acid). These benefits included superior vascular function (better ability to dilate and constrict), improved regulation of blood pressure, increased resistance to damage from unhealthy behaviors (such as smoking a cigarette or eating a fatty cheeseburger), and enhanced ability to burn calories (thus helping to prevent unwanted weight gain). The implication of these studies was, if short-term infusion of Vitamin C provided health benefits, so too might long-term oral supplementation. Unfortunately subsequent research did not support this idea. Many large population studies failed to demonstrate decreased disease risk and/or greater health benefits in people who regularly supplemented their diet with Vitamin C. In order to explain these disappointing observations, a variety of theories were presented; one of these theories pertained to delivery.

When Vitamin C is delivered directly into the circulation, such as with a needle inserted into a vein or artery, the amount of Vitamin C starting in the syringe is the same amount of Vitamin C that eventually appears in the blood. Not so when Vitamin C is taken orally, such as in the form of a pill. During the journey from the mouth to the blood, Vitamin C undergoes volatile interactions with biological juices, including saliva, oral bacteria, stomach acids, digestive juices, and then, when it finally makes it out of the gut, it faces additional challenges from the juices in the liver. In summary, the 500 mg of Vitamin C swallowed in a pill might be less than 200 mg by the time it arrives in the blood. For Vitamin C supplementation to be effective, it may need an alternative mode of delivery…

Enter the liposome! Liposomes are tiny (microscopic) bubbles. They have an outer shell comprised of healthy fatty acids (phospholipids) and a hollow center that can be filled with a variety of substances, including Vitamin C. When liposomes filled with Vitamin C are swallowed, the outer layer of the liposome protects the Vitamin C from gastric juices and liver enzymes. Once in the blood, the outer layer dissolves, liberating the Vitamin C. This allows the Vitamin C to travel from the mouth to the blood without being degraded by normal digestive processes – at least that’s the theory.

A team led by Christopher Bell, Ph.D., an Associate Professor in the Department of Health and Exercise Science at Colorado State University, and supported by Empirical Labs, a nutraceutical manufacturing facility located in Fort Collins, is comparing Vitamin C concentrations in the blood after swallowing a “normal” Vitamin C pill, and after ingestion of Liposomal Vitamin C in liposomes. Figure 1 shows that, compared with “normal” Vitamin C ingestion (single dose of 4 g), ingestion of Liposomal Vitamin C (also 4 g) leads to appreciably greater circulating Vitamin C concentrations, supporting the idea that liposomes facilitate Vitamin C delivery.

So what? The next step in the study is to determine if this increased circulating Vitamin C concentration is meaningful. One way to test this is to provide a physiological challenge that may cause temporary damage to tissues. In this regard, Bell and colleagues have been studying forearm ischemia reperfusion injuries. Ischemia describes any tissue that has been deprived of blood and oxygen. Reperfusion occurs when the blood and oxygen supply is returned. Unfortunately depending on the duration of ischemia, reperfusion can actually cause damage to tissues, as the oxygen interacts with metabolites produced by the oxygen-deprived tissues to generate oxidative stress. A medical example of this is a heart attack (or myocardial infarction). When a blood vessel in the heart becomes blocked, a portion of the heart is deprived of oxygen. When the heart’s natural defenses eventually overcome the blockage and re-perfuse the area, an injury can occur, resulting in permanent damage. Vitamin C may be able to help prevent or reduce this damage.

For obvious reasons, it is not possible to induce heart attacks to test the theory, so instead Bell and colleagues are focusing on the forearm to mimic an ischemia reperfusion injury. Abdominal pressure cuff is inflated above the elbow such that blood is unable to enter (or leave) the forearm for 20 minutes. When the pressure in the cuff is released (much to the relief of the study volunteers) blood is sampled from the re-perfused forearm and tested for circulating factors that are indicative of damage (or oxidative stress). In preliminary studies, Bell and colleagues are showing that when a person consumes Liposomal Vitamin C prior to the ischemia reperfusion, the damage is prevented.
The take-home hypothesis of this research is: when Vitamin C is ingested in liposomes, the resulting circulating concentration of Vitamin C is high, and this concentration might be sufficient to decrease the damage associated with ischemia reperfusion injuries, such as heart attacks. Essentially, liposomes may represent Vitamin C care packages for your heart.

Bell’s lab group in the Department of Health and Exercise Science at Colorado State University in Fort Collins is looking for volunteers to participate in these ongoing research studies. To learn more about participating in this Vitamin C study and others like it, please contact the lab via email: physiology@cahs.colostate.edu

FIGURES

Figure 1. Circulating Vitamin C concentrations are greater when Vitamin C is ingested in liposomes.

Figure 2. Ingestion of liposomal Vitamin C protects against the damage inflicted by an ischemia-reperfusion injury caused using a blood pressure cuff around the upper arm and inflated to very high pressures for 20-minutes.

Exercise Timing Study Receives CCTSI Micro Grant

Despite the short-term effectiveness of lifestyle interventions for weight loss, many individuals regain significant weight within a 1 year period. Regular physical activity is one of the best predictors of sustained weight loss and current activity guidelines recommend high levels of activity to prevent weight regain after weight loss. However, most individuals are not able to achieve and sustain high levels of exercise during typical weight loss programs when diet and exercise interventions are initiated concurrently.

For this reason, it is important to evaluate new strategies to help people achieve the high levels of exercise known to prevent weight regain. The optimal time to begin exercise during a lifestyle weight loss program is an area that has not previously been studied. Dr. Victoria Catenacci MD, Assistant Professor of Medicine in the Division of Endocrinology, Metabolism, and Diabetes and her collaborators (Drs. Edward Melanson, Daniel Bessesen, Holly Wyatt and Pan Zhaoxing) have recently been awarded a 5 year NIH R01 grant to study this question. The new CCTSI Micro Grants program will provide additional support for some of the assessments performed in this study at through the outpatient CTRC at UCH.

The aim of the Exercise Timing Study is to evaluate whether an exercise intervention timed after diet-induced weight loss (rather than initiated at the same time) improves exercise adherence and long-term weight loss. The study researchers believe that exercise initiation after weight loss may improve exercise adoption and adherence and promote long-term weight loss because: 1) exercise may be easier to perform at a lower bodyweight, 2) injury rates (and exercise attrition) may be reduced after weight loss and 3) it may be more effective to focus on a single behavior change at a time (rather than attempting to change diet and exercise behaviors at the same time). The study design involves an 18 month randomized controlled trial in which healthy overweight subjects receive either standard behavioral therapy (a traditional behavioral weight loss program where diet and exercise changes are initiated at the same time) or sequential behavioral therapy (a program that focuses solely on dietary changes in the initial 6 months, and then incorporates exercise in the ensuing 6 months). The study will compare the effect of the interventions on body weight, body composition, physical activity, fitness, dietary energy and fat intake, adherence to weight control eating behaviors, exercise-related injuries, exercise enjoyment, and behavioral variables related to the hypothesized benefits of sequential intervention delivery.

The study is currently recruiting healthy adults age 18-55, body mass index (BMI) 28-40 kg/m2, non-smokers who are currently exercising less than 100 minutes per week, and have no history of diabetes, heart disease, or medical conditions that limit physical activity. Subjects must be willing to participate in a group-based weight loss program and attend regular group meetings. Subjects must also be willing to start an aerobic exercise program either as soon as they start the study or after a delay of 6 months. Interested subjects can contact Kristen Bing at Kristen.Bing@ucdenver.edu.

Bulletin News

The Perinatal CTRC research nursing staff have been busy this past year! The staff have supported over 20 different protocols in Labor & Delivery and the NICU at the University of Colorado Hospital, the NICU at Children’s Colorado Hospital and the NICU at Exempla St. Joseph’s. From January to October 2013 they collected cord blood on 364 deliveries, performed 246 PeaPod body
composition studies, approached 436 families about participating in various studies in the NICU and Labor & Delivery, enrolled 191 volunteers into studies and completed 1,456 patient study visits.

The Perinatal CTRC’s most senior nurse, Lucy Fashaw, BSN, RNC-NICU obtained her certification as a Certified Clinical Research Professional (CCRP) from the Society of Clinical Research Associates (SOCRA) this year. SOCRA’s international certificate program was developed to evaluate a CCRP’s knowledge, understanding, and application of the conduct of clinical investigations involving humans in accordance with the International Conference on Harmonisation Guideline for Good Clinical Practice (ICH/GCP), the United States Code of Federal Regulations (CFR) and the ethical principles that guide clinical research consistent with the principles of the Nuremberg Code, the Belmont Report and the Declaration of Helsinki.” Congratulations Lucy on accomplishing this milestone!

Jennifer Nash, BA joined the Perinatal CTRC in November as a newest Professional Research Assistant. She previously worked with Dr. Anne Lynch on the Colorado Baby Blanket Program and on the National Children’s Study. Please welcome Jennifer to the team!

It has been a full year and we thank the Perinatal CTRC staff, which consists of Patricia Adkins, BSN, RNC-NICU, Lucy Fashaw, BSN, RNC-NICU, CCRP, Amy Lamprecht, BSN, RNC-NICU, Jennifer Nash, BA, Megan Vestal, BS, and Christine Reed, ND, MSN, CCRP for all their hard work. Our Perinatal CTRC is a unique resource among CTSAs programs nationally and continues to facilitate research into a most vulnerable and critically ill population, providing the highest quality of investigation and safety for participants.

CCTSI Program Spotlight

The CCTSI would like to congratulate Fernando Pineda-Reyes on his recent appointment to the National Center for Advancing Translational Sciences (NCATS)/Advisory Council Working Group on the Institute of Medicine’s (IOM) Clinical & Translational Science Award Program Report. He is the only community representative on this esteemed NIH advisory council. CEO & Founder of CREA Results (Community Research Education & Awareness), Fernando has served on the planning committee for all three National Community Partner Forums on Community-Engaged Research and has served on the PACT council for the Community Engagement Core of the CCTSI since its inception. We are truly honored to have Fernando represent the CCTSI and all 62 CTSAs nationally.

To learn more about the Working Group visit: http://www.ncats.nih.gov/about/ncats-council/wgs/ctsa-iom/ctsa-iom.html

For more information on Fernando Pineda-Reyes’ community based organization visit http://crearesults.org/

National Consortium Update

Please check out the full December 2013 newsletter from the National Center for Advancing Translational Sciences (NCATS) to get the latest updates from NCATS.

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