

Harold Hamm Diabetes Center Quarterly Newsletter



Jed Friedman, Ph.D.
Director, Harold Hamm Diabetes Center
Chickasaw Nation Endowed Chair

Director's Corner. Thus far, despite the COVID-19 setback, 2020 has been a successful year with our new faculty recruits getting laboratories up and running, new grants awarded and clinical faculty working via telehealth or Zoom meetings. In this issue, we spotlight two very different outstanding researchers who are long-term members of the HHDC research base. Ashley Weedn, M.D. is a dedicated Pediatrician focusing on interventions and treatment for childhood obesity and Hui-Ying Lim, Ph.D. uses the power of drosophila (flies) genetics to uncover novel pathways for signals released from the heart with different diets and their role in disease.

We also congratulate the recipients of the HHDC-PHF pilot grants, equipment grants and team science awards. Looking ahead, HHDC has been developing three research foci, which will lead to the formation of research teams to focus on three research themes from the basic science level, to clinical investigation and finally to the population in a translational way. In each of these themes, research will focus on the mechanisms involved in health and disease, the study of treatment intervention and the implementation of preventive strategies. Look for details and call for proposals from HHDC in the second half of the year.

COVID-19 Update: HHDC Takes the Lead on Awareness Campaign

In an age where culture and economies are information-driven, constant change is the norm. We have learned to anticipate and accept it. The entry of COVID-19 into the arena of public health has demanded an unprecedented response to quickly revise policies, protocols, procedures and techniques that keep patient safety as the imperative value. Because patients with diabetes are part of a population at greater risk related to the new coronavirus, Harold Hamm Diabetes Center is at the forefront of intensified public education efforts as we launch an aggressive patient-centered campaign.

Incorporating a full range of media platforms, campaign messaging is three-pronged. Awareness – increase understanding about how COVID-19 elevates risk for people with diabetes or prediabetes, emphasizing ways to stay healthy and manage diabetes more effectively.

Education – facilitate communication between Oklahomans and their healthcare providers, which promotes improved management of diabetes.

Amplification – reinforce the message and mission of the Harold Hamm Foundation and Harold Hamm Diabetes Center across multiple communications channels and leverage the advocacy of influencers in the community.

Our message will span a region that encompasses the state and extends into Texas via Altus (Sherman and Wichita Falls) and Arkansas in a broad swath from Fort Smith to Rogers.

We have survived and thrived, now into the second quarter of a calendar year where COVID-19 is present in every form of communication, from scientific research and healthcare concerns to commercial ads for every kind of consumer product. Our work to diminish and contain the adverse consequences of diabetes is unrelenting and we continue to develop partnerships for better patient programs to serve a broad scope of patient populations. Our clinicians continue to deliver first-rate care to every patient, even as we pursue enhanced treatment and ultimately, a cure.

The most difficult challenges often give rise to the most innovative solutions. We are grateful for the support of everyone associated with the Harold Hamm Diabetes Center that makes it possible to remain focused on our mission to care.

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Ashley Weedn, M.D., MPH, FAAP
Assistant Professor
Medical Director, Healthy Futures

Dr. Ashley Weedn, a board-certified pediatrician, serves as the Medical Director for the Healthy Futures Clinic and the Director for the Pediatric Obesity Program within Pediatrics. Dr. Weedn attended the University of Oklahoma Health Sciences Center for both her medical degree and Masters of Public Health. Dr. Weedn has served on various local, state, and national committees to assist with advancing clinical care, community programs, and policies to address pediatric obesity and improve child health outcomes.

The Healthy Futures Clinic is the only pediatric weight management clinic in OKC. It was developed in 2012 after a year of planning and funding from Chesapeake. The clinic expanded last year to seeing patients one day a week, previously only seeing patients a half-day per week. They have seen over 250 patients since the clinic opened in August of 2012 and currently follow over 60 active patients.

Research Spotlight:

Dr. Ashley Weedn Directs the Childhood Obesity Clinic at HHDC: From 2 to 18-Year Olds

Childhood obesity remains a top public health concern with 17% of Oklahoma youth who have obesity. To help address this epidemic, the Department of Pediatrics supports a comprehensive pediatric obesity program, which includes clinical services, research, community outreach, and education.

The Healthy Futures Clinic, located at the Harold Hamm Diabetes Center, is a multidisciplinary pediatric weight management program for children and adolescents, ages 2-18 years, who have severe obesity (BMI \geq 120th percentile) or obesity (BMI \geq 95th percentile) with comorbidities. The team consists of a pediatric dietitian, psychologist, physical therapist and Dr. Ashley Weedn, a pediatrician trained in weight management. The clinic is a family-centered and evidence-based program designed to help the entire family implement and maintain healthy behaviors to improve overall health. The clinic participates in a national clinical research registry, the Pediatric Obesity and Weight Evaluation Registry, to identify best practices for the treatment of children in multidisciplinary weight management programs. Additionally, the Healthy Futures team has partnered with the Chickasaw Nation to develop and implement a pediatric weight management clinic within the Chickasaw Nation to provide comprehensive clinical services for children and families with obesity and a research registry to assess intervention outcomes specific to their population. Community-based participatory research with Chickasaw Nation focusing on prevention initiatives in early childhood is also underway.

Recently, we have analyzed data from our Healthy Futures Clinic that have shown improvements in cardiometabolic health in addition to BMI reduction among our patients. We are excited to partner with our Chickasaw Nation colleagues to examine similar outcomes for AI children participating in their Empowered Living Clinic, the only tribal multidisciplinary pediatric weight management clinic in Oklahoma. Previous research has focused on the epidemiology of obesity among preschool-aged children participating in tribal and Oklahoma WIC programs as well as school-aged children through Schools for Healthier Lifestyles Program.

Community outreach endeavors include partnerships with Blue Cross and Blue Shield Caring Van Foundation to provide body mass index screening for children in community settings and collaboration with TSET to provide evidence-based and consistent messaging on healthy behaviors for families. Education includes a partnership with the Oklahoma State Medical Association to provide training to primary care providers on weight management in their practices and through webinars, as well as development and dissemination of toolkits on the assessment and management of pediatric obesity for primary care providers through the Oklahoma Chapter of the American Academy of Pediatrics. Additional education initiatives are the inclusion of trainees from various disciplines in the Healthy Futures Clinic to provide them with an opportunity to better understand behavioral treatments for children and adolescents with obesity.



Hui-Ying Lim, Ph.D.
Assistant Professor

Dr. Hui-Ying Lim is an investigator at Harold Hamm Diabetes Center and an assistant professor at the University of Oklahoma College of Medicine teaching Renal Physiology. Dr. Lim attended Columbia University for her Ph.D. and Sanford-Burnham Medical Research Institute for her postdoctoral training.

*The goal of her research is to understand the molecular genetic mechanisms that govern cardiac physiology and energy metabolism, by utilizing an integrated approach of cell biology, biochemistry, sophisticated optical imaging and the power of *Drosophila* genetics.*

HHDC Investigator Earns Second NIH Grant

Maintaining systemic energy homeostasis is vital for the physiology of all living organisms. The heart has emerged as an important tissue in the regulation of normal systemic lipid homeostasis; however, the underlying mechanisms remain incompletely understood, mainly due to the paucity of cardiac-derived factors being identified that direct systemic lipid metabolism. On the other hand, obesity and its complications, such as lipotoxic cardiomyopathy, constitute a medical emergency in the United States and much of the Western world. The current dogma is that a high-fat diet (HFD) induces cardiac gene expression changes that evoke maladaptive and intrinsic effects within the heart. Very little is known about whether and how HFD elicits cardiac gene expression changes that mediate protective and systemic effects on lipid metabolism. Gaining a better understanding of this process will open a new paradigm and helps guide the development of new and more effective therapeutic approaches aimed at augmenting the natural adaptive responses of the heart to combat human obesity and its comorbidities.

Dr. Lim's study will interrogate the role of Snail family transcription factors (Sna TFs) in the heart in maintaining systemic lipid homeostasis, by controlling the cardiac production of an innate immune effector, thioester-containing protein 2 (Tep2). Upon secretion from the heart and into the circulation, Tep2 then acts on the fat body to negatively regulate transforming growth factor- β (TGF- β) signaling which in turn modulates systemic lipid homeostasis. Lim's lab will further determine whether HFD induces the Sna TF–Tep2 axis in the heart which serves as an adaptive response to counter diet-mediated systemic obesity and lipotoxic cardiomyopathy. This work is a collaborative effort with Dr. Weidong Wang's lab at OUHSC and is funded by a recently awarded, 5-year R01 grant from the National Heart Lung Blood Institute.

Three HHDC Members were awarded patents this year:

Jian-Xing Ma, M.D., Ph.D. George Lynn Cross Research Professor of Physiology
Patent title(s): High Isomerohydrolase Activity Mutants of Human Rpe65

Jody A. Summers-Wiechmann, Ph.D. Professor of Cell Biology
Patent title(s): Inhibitors of Retinaldehyde Dehydrogenases and Methods of Use

Yusuke Takahashi, Ph.D. Associate Professor of Research in Physiology
Patent title(s): High Isomerohydrolase Activity Mutants of Human Rpe65

Congratulations to Drs. Ma, Summers-Wiechmann and Takahashi!



New Grants Manager Joins the Harold Hamm Diabetes Center

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Alexandra LeGrant
Grants Manager
Harold Hamm Diabetes Center



HHDC Researcher Paper Featured in Science Translational Medicine

[\[READ MORE\]](#)

Michael Rudolph, Ph.D.
Assistant Professor,
Department of Physiology
Choctaw Nation Chair in
Adult Endocrinology



HHDC Researcher Commentary Featured in Science Magazine and on NPR

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Bill Freeman, Ph.D.
Member, HHDC
Genes & Human Disease Research Program
Oklahoma Medical Research Foundation

Helmsley Trust Donates \$25,000 to the Pediatric Endocrinology Clinic to Assist with COVID Operations

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Three HHDC Faculty Members Present at the American Diabetes Association Scientific Sessions

[\[READ MORE\]](#)

New Grants to HHDC Members:

EQUIPMENT GRANTS

PI: Martin-Paul Agbaga, Ph.D.

Funding Organization: HHDC and PHF

Type of Grant: Equipment Grant

Title of Grant: Headspace Sampler for Short Chain Fatty Acids Analyses

Amount Awarded: \$34,778

Dates: 7/1/2020 to 6/30/2021

PI: Carole Dionne, P.T., DPT, Ph.D., M.S., OCS, Cert MDT

Funding Organization: HHDC and PHF

Grant Type: Equipment Grant

Title of Grant: Expanding Investigation Capabilities at the Center for Human Performance Measurement

Amount Awarded: \$54,553.11

Dates: 7/1/2020 to 6/30/2021

PI: Sowmya Krishnan, M.D.

Funding Organization: HHDC and PHF

Grant Type: Equipment Grant

Title of Grant: Bone microarchitecture in adolescents and young adults with diabetes

Amount Awarded: \$10,208.50

Dates: 7/1/2020 to 6/30/2021

PI: Michael Rudolph, Ph.D.

Funding Organization: HHDC and PHF

Grant Type: Equipment Grant

Title of Grant: A Comprehensive and Dedicated Rodent Metabolic Phenotyping Resource

Amount Awarded: \$500,000

Dates: 7/1/2020 to 6/30/2021

PI: Susan Sisson, Ph.D., RDN, CHES, FACSM

Funding Organization: HHDC and PHF

Grant Type: Equipment Grant

Title of Grant: Veggies Meter Equipment Grant

Amount Awarded: \$27,555

Dates: 7/1/2020 to 6/30/2021

New Grants to HHDC Members:

TEAM SCIENCE GRANTS

PI: Jed Friedman, Ph.D.

Funding Organization: HHDC and PHF

Grant Type: Team Science – Year One

Title of Grant: Infant Gut Microbial Species and
Programming Innate Immunity

Amount Awarded: \$99,969

Dates: 7/1/2020 to 6/30/2021

PI: Karen Jonscher, Ph.D.

Funding Organization: HHDC and PHF

Grant Type: Team Science – Year One

Title of Grant: Role of maternal fiber in development of
diabetes-promoting invariant T cells

Amount Awarded: \$100,000

Dates: 7/1/2020 to 6/30/2021

PI: Dean Myers, Ph.D.

Funding Organization: HHDC and PHF

Grant Type: Team Science – Year Two

Title of Grant: Development of a Baboon (*Papio anubis*)
Model of Western Diet and Maternal
Obesity-Mechanisms for Fetal Epigenetic
Programming of Behavior and Metabolism

Amount Awarded: \$100,000

Dates: 7/1/2020 to 6/30/2021

PI: Stephanie Pierce, M.D., M.S.

Funding Organization: HHDC and PHF

Grant Type: Team Science – Year One

Title of Grant: Pilot RCT Intervention Targeting Elevated
Triglycerides with a Point-of-Care Meter and
Omega-3 Fatty Acids to Normalize Tr
glycerides and Fetal Growth

Amount Awarded: \$99,322

Dates: 7/1/2020 to 6/30/2021

PI: David Sparling, M.D., Ph.D.

Funding Organization: HHDC and PHF

Grant Type: Team Science – Year Two

Title of Grant: The Role of CRISPLD2 in adipose function

Amount Awarded: \$100,000

Dates: 7/1/2020- 6/30/2021

SEED GRANTS

PI: William Hildebrand, Ph.D.

Funding Organization: HHDC and PHF

Grant Type: Seed Grant

Title of Grant: Type I Diabetes Autoimmune Targets

Amount Awarded: \$50,000

Dates: 7/1/2020 to 6/30/2021

As a reminder, when submitting grants in SoonerTrack, please select the box, “This Project is a Diabetes Related Project.” We would love to highlight your work in diabetes and by selecting this box, it helps us easily pull this information via monthly reporting. Thank you!



Mary Zoe Baker, M.D.
David Ross Boyd
Professor of Medicine



David Sparling, M.D., Ph.D.
Assistant Professor
CHF Paul and Ann Milburn Chair
in Pediatric Diabetes

Clinic Updates: Adult Diabetes & Endocrinology Clinic

As we have progressed in the Covid-19 pandemic, we are transitioning to more face-to-face visits. Patients are contacted prior to their visit and are asked their preference - a face-to-face visit or a virtual visit and they are accommodated. Upon arrival, all patients are screened for symptoms and their temperatures are checked. All patients must wear masks.

We are probably seeing almost 90% of our patients face-to-face for now. However, recently as the Covid-19 numbers have increased in Oklahoma we are ready at a moment's notice to return to almost all virtual visits. Our staff led by April Brawdy, our clinic manager and Christy Olson, our diabetes educator make sure the patients are informed and the caregivers get the needed blood sugar records for review during the visit.

Pediatric Diabetes & Endocrinology Clinic:

The Pediatric clinic is slowly continuing to ramp back up to prior "normal" operations, but with the added ability to use telemedicine now part of our work going forward. We are slightly limiting in-person visits to accommodate social distancing concerns.

The wet lab has re-opened under the current OUHSC guidelines; we're still somewhat limited in staff available "in person" in the lab each day, but the team regularly meets to work out a schedule, and we adapt as needed.

The clinical studies have also resumed. TrialNet never fully "closed" but we suspended in-person recruitment and screening as per OUHSC guidelines. However, the first part of TrialNet (the natural history study, or TN01) can now actually be achieved with in-home screening. It is a little labor-intensive and not optimal for all our patients, but it was able to be offered (with online consenting as per the TrialNet protocol).

In the interim we have also had a new study go through final approval; Dr. Joni Beck and Dr. Kathryn Jeter are helping head up a study looking into CGM use with close CDE supervision, to improve outcomes. This Dexcom-funded study is currently open.

We also have an upcoming Dexcom-initiated post-market analysis study, which has been going through final contracts/oversight approvals in the past month; we hope to begin enrollment in this soon.



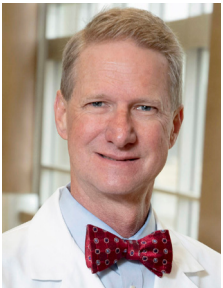
SPOTLIGHT MEMBER PUBLICATIONS:



Ann Louise Olson, Ph.D.

Weight Loss Results in Increased Expression of Anti-Inflammatory Protein CRISPLD2 in Mouse Adipose Tissue.

Jackson, R. M., Griesel, B. A., Short, K. R., Sparling, D. P., Freeman, W. M., Olson, A. L. (2019). Weight Loss Results in Increased Expression of Anti-Inflammatory Protein CRISPLD2 in Mouse Adipose Tissue. *Obesity* (Silver Spring, Md.), 27(12), 2025-2036. PMID: 31746554. DOI: 10.1002/oby.22652



David Jelley, M.D.

Identical and Nonidentical Twins: Risk and Factors Involved in Development of Islet Autoimmunity and Type 1 Diabetes.

Diabetes Care. Triolo, T. M., Fouts, A., Pyle, L., Yu, L., Gottlieb, P. A., Steck, A. K., Jelley, D. H. (2018). PMID: 30061316. DOI: 10.2337/dc18-0288



Susan Sission, Ph.D., RDN, CHES, FACSM

Interventions to promote healthy environments in family child care homes in Oklahoma-Happy Healthy Homes: study protocol for a randomized controlled trial.

Sission SB, Salvatore AL, Hildebrand D, Poe T, Merchant C, Slawinski M, Kracht CL, Stoner JA, Alcalá Lazarte N, Schneider LAF, Weber J, Jones F, Ward D. *Trials*. 2019 Aug 30;20(1):541. doi: 10.1186/s13063-019-3616-9. PMID: 31470886 Free PMC article. Clinical Trial.



Michael Stout, Ph.D.

Targeting Senescent Cells Alleviates Obesity-Induced Metabolic Dysfunction.

Palmer AK, Xu M, Zhu Y, Pirtskhalava T, Weivoda MM, Hachfeld CM, Prata LG, van Dijk TH, Verkade E, Casacang-Verzosa G, Johnson KO, Cubro H, Doornebal EJ, Ogradnik M, Jurk D, Jensen MD, Chini EN, Miller JD, Matveyenko A, Stout MB, Schafer MJ, White TA, Hickson LJ, Demaria M, Garovic V, Grande J, Arriaga E, Kuipers F, von Zglinicki T, LeBrasseur NK, Campisi J, Tchkonja T, Kirkland JL. Targeting senescent cells alleviates obesity-induced metabolic dysfunction. *Aging Cell*. 18(3):e12950, 2019



Jeanie Tryggestad, M.D.

Longitudinal Changes in Cardiac Structure and Function From Adolescence to Young Adulthood in Participants With Type 2 Diabetes Mellitus: The TODAY Follow-Up Study.

Circ Heart Fail. 2020 Jun;13(6):e006685. doi: 10.1161/CIRCHEARTFAILURE.119.006685. Epub 2020 Jun 5. PubMed PMID: 32498621.