OU Health Harold Hamm Diabetes Center Quarterly Newsletter

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

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Director's Corner

Spring has arrived. So has optimism. We are excited to announce the new vice-chair for the division of Pediatric Endocrinology, Dr. David Sparling. Dr. Sparling has an active research portfolio and is a recognized national leader in Type 1 diabetes care. We also highlight our new Native American Diabetes Research Program Coordinator, Jennifer Chadwick, who will facilitate our planned partnerships for research. In addition, we highlight Dr. Marisol Castillo-Casterjon who recently joined HHDC from the University of Colorado School of Medicine.

The spring HHDC pilot grants are under review with external reviewers for the first time. These grants recognize the high-quality research possible as a result of interdisciplinary teamwork from both established and new investigators. Launching pilot proposals with OU Health Stephenson Cancer Center is a new collaboration that we hope will bear fruit. HHDC aims to enhance the quality of diabetes research and ensure that it continues to grow our federal funding in the fight against diabetes.

This spring, the HHDC Board of Directors announced that this year's Connect+Cure Gala will be postponed until 2023, because of the pandemic. However, the Harold Hamm International Diabetes Prize will be awarded in April. Don't miss our symposium and roundtable discussion (Topic: Recent & Anticipated Advances Leading to a Cure), featuring special presentations by the 5 jury experts in diabetes - Dr. Phil Scherer, Dr. David Nathan, Dr. David D'Alessio, Dr. Al Powers, and Dr. Juleen Zierath on Friday, April 30.

As the OU Health Sciences Center announces its consolidation across the medical school, hospitals, and physicians group, it highlights the important changes to campus infrastructure that are happening as we speak. Please keep updated by visiting our **website** and social media channels to learn more about upcoming seminars, networking, educational, and grant activities.

All the best,

Jed Friedman, Ph.D.
Director, HHDC

The HHDC Newsletter is a quarterly newsletter that offers articles on HHDC events, funding opportunities, publications, research news, and training opportunities. Sign up below to receive our quarterly newsletter as well as periodic updates on the HHDC.

*To submit an item for the newsletter, please send your announcement to **katie-hoefling@ouhsc.edu***

OU Health | Harold Hamm Diabetes Center

David Sparling, M.D., Ph.D.
Assistant Professor
Associate Section Chief of Pediatric Endocrinology
CHF Paul and Ann Milburn Chair in Pediatric Diabetes

Sparling Named Associate Section Chief

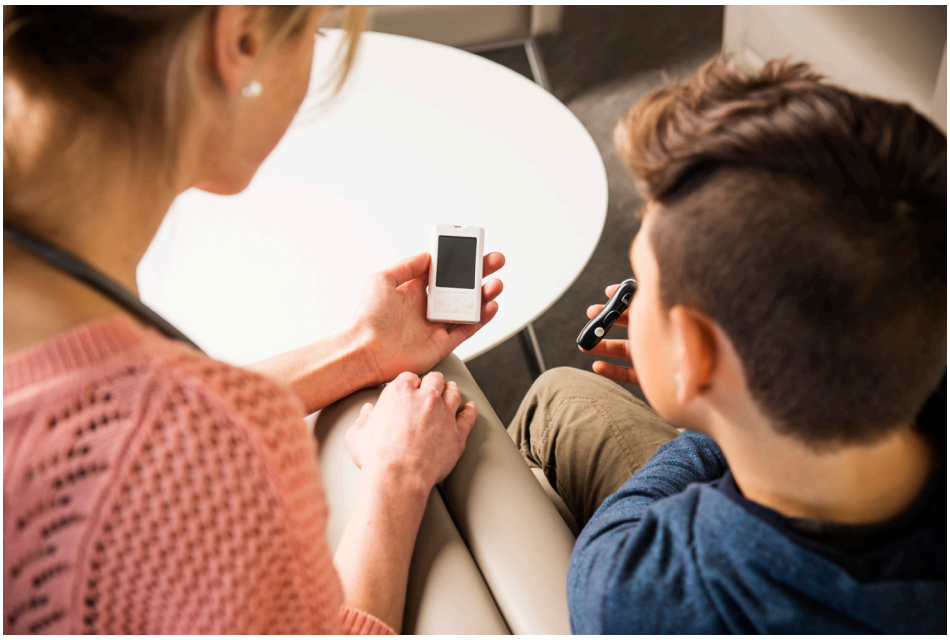
David P. Sparling, M.D., PhD, has been named associate section chief of Pediatric Endocrinology at OU Health Harold Hamm Diabetes Center. Sparling has a special clinical interest in the diagnosis and treatment of diseases affecting the endocrine system, including the care of children with Type 1 diabetes, as well as disorders involving the thyroid, growth and puberty.

In addition to his clinical expertise, Sparling is also an active researcher focusing on the causes, current treatment, and possible preventive strategies of Type 1 diabetes. As part of his research on prevention, his team is actively screening family members of patients diagnosed with Type 1 diabetes to track the potential development of maturity onset diabetes of the young (MODY) in a single family. Sparling also has his own NIH-sponsored K mentored training award examining the role of adipocytes in inflammation.

"...an active researcher focusing on the causes, current treatment, and possible preventive strategies of Type 1 diabetes."

Sparling graduated summa cum laude from the University of Oklahoma and went on to pursue his MD/PhD at the OU College of Medicine. He completed his pediatrics residency and a fellowship in pediatric endocrinology at the New York-Presbyterian Morgan Stanley Children's Hospital through the Columbia University College of Physicians and Surgeons.

Sparling serves as a member of both the Harold Hamm Diabetes Center Research Symposium Committee and the Harold Hamm Diabetes Center Research Grants Committee.



Marisol Castillo-Castrejon M.S., Ph.D.
Assistant Professor
Department of Pathology

Research Spotlight: HHDC Researcher Awarded CoBRE Grant

OU Health Harold Hamm Diabetes Center is pleased to welcome **Marisol Castillo-Castrejon, M.S., Ph.D.** Dr. Castillo-Castrejon came to the University of Oklahoma Health Sciences Center to establish a research program focused on the role of the immune system in the development of obesity and dysregulated metabolism across the lifespan. Her multidisciplinary training supports opportunities to develop and conduct more comprehensive research.

Dr. Castillo-Castrejon completed a fellowship in reproductive sciences at the University of Colorado School of Medicine, Aurora, as well as a fellowship in epidemiology and reproductive toxicology at the University of Michigan School of Public Health, Ann Arbor. She earned her doctorate in biological sciences at Universidad Nacional Autonoma de Mexico, Mexico City, where she also completed a Master of Science degree in biological sciences. Dr. Castillo-Castrejon led a clinical research effort to establish a prospective cohort of pregnant women known as the Pregnancy Research on Inflammation, Nutrition and City Environment: Systematic Analysis Cohort (PRINCESA). Her primary interest was the study of the nutritional status of pregnant women living in highly developed urban areas and the ways in which a built-environment may influence weight gain and obesity-associated risks during pregnancy. This resource has been utilized by investigators in the United States and Mexico for ongoing research studies aimed at providing interventions to promote maternal health and environmental policies. In basic and epidemiological studies, Dr. Castillo-Castrejon has investigated the inflammatory response in normal, and in adverse perinatal outcomes, such as preterm birth and intrauterine growth restriction in this cohort.

Arriving recently from the University of Colorado School of Medicine, Dr. Castillo Castrejon has been awarded a grant to pursue her work, “Estrogen Receptor Signaling in B-Cells: A Potential Role in Diabetes Risk after Menopause.” The National Institutes of Health Centers of Biomedical Research Excellence (CoBRE) grant in diabetes research will provide $50,000 in the current funding cycle. Pending demonstrated progress, the work may receive funding for up to four, two-year pilot projects at $50,000 in direct costs per year. The generation of preliminary data is expected to lead to competitive applications for external funding. Co-investigators are Michael Stout, Ph.D., assistant professor, OU College of Allied Health, and Elizabeth Wellberg, Ph.D., assistant professor, OU College of Medicine, Department of Pathology. Jian-xing Ma, M.D., Ph.D., OU College of Medicine, Department of Physiology, is the program director.

Expanding on her expertise in weight gain, inflammation, and women’s health, Dr. Castillo-Castrejon is focusing on estrogen loss during menopause, which causes changes in the distribution of body fat, alters metabolism, influences inflammation, and promotes the development of obesity and diabetes. The CoBRE study will explore the role of estrogen signaling in B-cell maturation, an area of research that remains understudied in females. Because B-cells influence whole-body inflammation and metabolism as they interact with other immune cell types, the study has the potential to discover novel, immune regulators of adipose tissue expansion, and the subsequent risk of developing menopause-associated diseases, such as Type 2 diabetes and breast cancer.

Jennifer Chadwick, B.S. (Choctaw)
Native American Diabetes Research Program Coordinator
Department of Pediatrics

Introducing HHDC Native American Diabetes Research Program Coordinator

With more than two decades of experience working with Oklahoma's Native tribes and communities, Jennifer Chadwick is ideally suited for her new role as coordinator of the Native American Diabetes Research Program with Harold Hamm Diabetes Center. Chadwick brings a keen understanding of tribal sovereignty and its influence on community-based research. She is a native Oklahoman and life-long resident, as well as an enrolled member of the Choctaw Nation of Oklahoma.

Chadwick became an affiliate member of Harold Hamm Diabetes Center in 2015. She previously worked as a research coordinator for 15 years in Pediatric Endocrinology at OUHSC. In this role, Chadwick cultivated various tribal research partnerships and was involved in significant research initiatives, including Treatment Options for Type 2 Diabetes in Adolescents (TODAY) and MOVE.

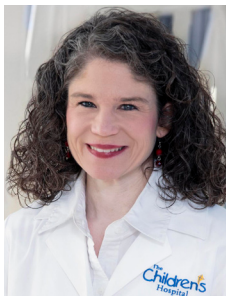
Both studies provided experience in project development, grant and IRB submissions, study execution, analysis, and publication of study results. As the first author of three publications, Chadwick and tribal co-authors highlighted their research partnerships so other tribal communities might benefit from their experiences.

Working as the Native American Coordinator for the TODAY Study and other projects, Chadwick found opportunities to improve relationships and rebuild trust by mentoring researchers in the understanding of tribal sovereignty and the importance of fostering meaningful partnerships with tribal officials, while ensuring that political and cultural sensitivities were appropriately addressed. She is co-author of several publications focused on the far-reaching, adverse health impacts of sedentary lifestyles and diabetes, primarily within Native American populations

As coordinator of the Native American Diabetes Research Program with a broad scope of responsibilities and objectives, Chadwick will facilitate research partnerships, serving as a liaison between HHDC investigators and tribal nations, communities and health boards. Her efforts will ensure collaborations are mutually agreeable and culturally appropriate.

"Harold Hamm Diabetes Center is truly a driving force nationally, in its scientific quest to understand diabetes, the impact of complications, and ways to improve health for future generations."

"Harold Hamm Diabetes Center is truly a driving force nationally, in its scientific quest to understand diabetes, the impact of complications, and ways to improve health for future generations. I look forward to the array of promising opportunities to partner with tribal communities, many of whom are afflicted, often disproportionately, with numerous public health disparities," said Chadwick. "I believe, through open, honest and respectful partnerships, American Indian communities and Harold Hamm Diabetes Center will succeed in eliminating long-term diabetes complications and improving health outcomes today and for years to come."



Jeanie Tryggestad, M.D.
Associate Professor
Department of Pediatrics

Follow Up for TODAY Study Awarded to HHDC Researcher

In response to the request for proposals to utilize stored samples from the TODAY study, Dr. Jeanie Tryggestad and colleagues submitted their proposal, "Circulating miRNAs as predictors of β cell failure and diabetes complications in youth with T2D." They hypothesize that specific circulating miRNAs will be early biomarkers of disease progression and complications in youth-onset T2D. The aims that will address this hypothesis include identifying novel miRNA biomarkers of β cell function and complications (retinopathy, nephropathy, neuropathy) in youth-onset T2D and to examine suspected and novel miRNAs abundance in youth with β cell dysfunction and microvascular disease. The newly identified biomarkers will potentially allow for early identification of subjects that would progress to β-cell failure needing more aggressive treatment. Also, the miRNAs could identify potential risk for microvascular complications prior to overt microvascular disease such that early intervention could prevent more severe sequelae such as blindness, amputation, and kidney failure.

The TODAY study started in 2004 with 699 youth with new-onset T2D at an average age of 14 years. In 2011, 572 (82%) TODAY participants enrolled in the TODAY follow-up study (TODAY2), which was conducted in two phases. Between 2011-2014, participants received diabetes-related care from the TODAY study team receiving metformin and insulin if needed to maintain glycemic control. From 2014-2020, 518 TODAY participants transitioned to a fully observational study with annual study visits, but medical management provided entirely by their healthcare providers. Dr. Tryggestad's study is for $425,00 for one year and will focus on a sub-set of about 400 of the subjects since the samples are coming from the repositories.

David Sparling, M.D., Ph.D.
Assistant Professor
Associate Section Chief of Pediatric Endocrinology
CHF Paul and Ann Milburn Chair in Pediatric Diabetes

Clinic Updates

Pediatric Diabetes & Endocrinology Clinic

The pediatric clinic continues to work hard in the face of the ongoing pandemic. In a recent review of our numbers, it appears that the suggested national trend of a recent increase in diagnoses of new-onset Type 1 diabetes may be occurring in Oklahoma as well; we are part of a national quality improvement initiative that is looking at this and its possible connection to COVID-19. Our whole team has really stepped up over the past year, adapting to new needs and technologies, from telemedicine visits and technology teaching to patients so they can upload data from their devices at home, to teaching families and patients that are admitted with COVID-19 and new-onset Type 1 diabetes via Zoom while they are in their hospital rooms! We have further plans in store to expand our electronic "footprint" as well; stay tuned! Our Type 2 diabetes-focused clinic, T2CC, also continues to expand. Drs. George and Tryggestad continue to serve this unique population with up-to-date best practices and therapies, as we meet this growing need in kids as well. We also continue to work with state shareholders in promoting best practices and advocating for our patients and all the kids with diabetes in the state.

For more of this story, go here: ▶

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

Clinic Updates

Adult Diabetes & Endocrinology Clinic

As we approach Spring, we are slowly emerging from the pandemic. All of our faculty and staff have received their COVID-19 vaccines. Some of us are volunteering for the OU Health COVID vaccine clinics, which have started offering vaccines to our patients in the past few weeks. It is so rewarding to see the joy in our patients' eyes (as we are masked) as they get the "jab".

Kacy Aderhold, APRN, joined the faculty of the OU College of Nursing as a Clinical Assistant Professor in January. Prior to joining OU, she was working in an endocrine practice and will be joining our practice with a focus on diabetes. She will begin seeing patients in the HHDC adult endocrinology clinic soon. We are excited to welcome her to OU Health.

HHDC Researcher Paper Featured in Science Translational Medicine

Despite nourishing babies for millennia, the alchemy of human breast milk remains mysterious. One unknown is how ingredients in the milk, which vary based on a mother's diet and environment, can affect a baby's health. [READ MORE]

David Fields, Ph.D.
Assistant Professor
CHF Chickasaw Nation Endowed Chair
Pediatric Diabetes

New Grants to HHDC Members:

Marisol Castillo-Castrejon, M.S., Ph.D.
Funding Organization: Diabetes CoBRE Pilot Project Core
Title of Grant: ***Estrogen Receptor Signaling in B-Cells: A Potential Role in Diabetes Risk after Menopause***
Dates: Feb. 9, 2021 – June 30, 2021, *with renewal option*
Amount Awarded: $50,000

PI: Jeanie Tryggestad, M.D.
Funding Organization: Diabetes CoBRE Pilot Project Core
Title of Grant: ***Impact of in Utero Diabetes Exposure on Mesenchymal Stem Cell Lineage Determination***
Dates: Feb. 9, 2021 – June 30, 2021, *with renewal option*
Amount Awarded: $50,000

PI: Michael Rudolph, Ph.D.
Funding Organization: Oklahoma Center for Adult Stem Cell Research
Title of Grant: ***Programming Adipose Stem Cells to Protect Against Diet-Induced Obesity***
Dates: 01/01/2021 – 12/31/2021
Amount Awarded: $167,679

PI: Jeanie Tryggestad, M.D.
Funding Organization: NIH, Type 2 Diabetes and Youth (TODAY)2 follow-up Study
Title of Grant: **Circulating miRNAs as predictors of β cell failure and diabetes complications in youth with T2D**
Dates: 3/1/2021-4/30/2022
Amount Awarded: $425,000

PI: Jeanie Tryggestad, M.D.
Funding Organization: NIH, NIDDK
Title of Grant: **Impact of in utero diabetes exposure on miRNA: effects on cellular metabolism**
Dates: 3/31/2021-3/31/2023
Amount Awarded: $150,000 (direct)

HHDC Members New Publications:

Keleher MR, Erickson K, Smith HA, Kechris KJ, Yang IV, Dabelea D, **Friedman JE**, Boyle KE, and Janssen T. Placental insulin/IGF-1 signaling and inflammation are associated with metabolic outcomes at 4-6 years of age: The ECHO Healthy Start Cohort. Diabetes, 2020 Mar;70(3):745-751.

Martin Carli JF, Trahan GD, **Jones KL**, Hirsch N, Rolloff KP, Dunn EZ, **Friedman JE**, Barbour LA, Hernandez TL, MacLean PS, Monks J, McManaman JL, **Rudolph MC**. Single Cell RNA Sequencing of Human Milk-Derived Cells Reveals Sub-Populations of Mammary Epithelial Cells with Molecular Signatures of Progenitor and Mature States: a Novel, Non-invasive Framework for Investigating Human Lactation Physiology. J Mammary Gland Biol Neoplasia. 2020 Nov 20;. doi: 10.1007/s10911-020-09466-z. [Epub ahead of print] Review. PubMed PMID: 33216249.

Ibrahim Al-Sumaih, Nga Nguyen, Michael Donnelly, Brian Johnston, **Zhamak Khorgami**, Ciaran O'Neill. Ethnic Disparities in Use of Bariatric Surgery in the USA: the Experience of Native Americans. Obesity Surgery. The Journal of Metabolic Surgery and Allied Care. OBES SURG (2020) 30:2612-2619 DOI 10.1007/s11695-020-04529-w. March 2020

Benedict Y. Hui, M.D.a, **Zhamak Khorgami, M.D.b,c,***, Justin S. Puthoff, M.D.b, Timothy S. Kuwada, M.D.a, Robert B. Lim, M.D.b, Geoffrey S. Chow, M.D.b. Postoperative sepsis after primary bariatric surgery: an analysis of MBSAQIP. Surgery for Obesity and Related Diseases - (2021) 1–6. Online ahead of the print (in-press).

Krishnan S, Rughani A, Tsai A, Palle S. Novel compound heterozygous variants in the NBAS gene in a child with osteogenesis imperfecta and recurrent acute liver failure. BMJ Case Rep. 2021 Feb 4;14(2). doi: 10.1136/bcr-2020-234993. PubMed PMID: 33542026; PubMed Central PMCID: PMC7868262.

Regelmann MO, Conroy R, Gourgari E, Gupta A, Guttmann-Bauman I, Heksch R, Kamboj MK, **Krishnan S**, Lahoti A, Matlock K. Pediatric Endocrinology in the Time of COVID-19: Considerations for the Rapid Implementation of Telemedicine and Management of Pediatric Endocrine Conditions. Horm Res Paediatr. 2020;93(6):343-350. doi: 10.1159/000513060. Epub 2021 Jan 22. Review. PubMed PMID: 33486483.

Li H, Zhang G, Guo Y, Deng J, Fischer H, Craig LB, Kem DC, Yu X. Autoimmune activation of the GnRH receptor induces insulin resistance independent of obesity in a female rat model. Physiol Rep. 2021 Jan;8(24):e14672. doi: 10.14814/phy2.14672. PMID: 33356018; PMCID: PMC7757370.

Deng J, Guo Y, Zhang G, Zhang L, Kem D, Yu X, Jiang H, **Li H.** M2 muscarinic autoantibodies and thyroid hormone promote susceptibility to atrial fibrillation and sinus tachycardia in an autoimmune rabbit model. Exp Physiol. 2021 Feb 7. doi: 10.1113/EP089284. Epub ahead of print. PMID: 33550676.

Li H, Guo Y, Zhang G, Deng J, Fischer H, Craig LB, Yu X, Kem DC. GnRH receptor autoantibodies induce polycystic ovary syndrome-like features in a rat model. Exp Physiol. 2021 Feb 12. doi: 10.1113/EP089109. Epub ahead of print. PMID: 33576068.

Nadeau H, Maxted M, Madhavan D, **Pierce S**, Feghali M, and Scifres C. Insulin dosing, glycemic control, and perinatal outcomes in pregnancies complicated by type-2 diabetes. Am J Perinatol. 2020 Oct. PMID: 33065743

Wolfs D, Lynes M, Tseng Y, **Pierce S**, Bussberg V, Darkwah A, Tolstikov V, Narain N, Kiebish M, **Rudolph MC**, Demerath E, **Fields D**, and Isganaitis E. Brown fat-activating lipokine 12,13-diHOME in human milk is associated with infant adiposity. The Journal of Clinical Endocrinology & Metabolism. 2021 Jan 23;106(2):e943-e956. doi: 10.1210/clinem/dgaa799. PubMed PMID: 33135728; PubMed Central PMCID: PMC7823229.

Presby DM, **Rudolph MC**, Sherk VD, Jackman MR, Foright RM, **Jones KL**, Houck JA, Johnson GC, Higgins JA, Neufer PD, Eckel RH, MacLean PS. Lipoprotein Lipase Overexpression in Skeletal Muscle Attenuates Weight Regain by Potentiating Energy Expenditure. Diabetes. 2021 Feb 3;. doi: 10.2337/db20-0763. [Epub ahead of print] PubMed PMID: 33536195.

Kurup, K., Matyi, S., Giles CB., Wren, JD., Jones, K., Ericsson, A., Raftery, D., Wang, L., Promislow, D., Richardson, A., and **Unnikrishnan, A**. (2021). Calorie Restriction Prevents Age-Related Changes in the Intestinal Microbiota. Aging.

Kruti B. Shah, Steven D. Chernausek, Lori D. Garman, Nathan P. Pezant, Jasmine F. Plows, Harmeet K. Kharoud, Ellen W. Demerath, **David A. Fields.** Human Milk Exosomal MicroRNA: Associations with Maternal Overweight/Obesity and Infant Body Composition at 1 Month of Life. Nutrients 2021, 13(4), 1091; **https://doi.org/10.3390/nu13041091**

S. Ribo, D. Sánchez-Infantes, L. Martinez-Guino, I. García-Mantrana, M. Ramon-Krauel, M. Tondo, E. Arning, M. Nofrarías, &. Osorio-Conles, A. Fernández-Pérez, P. González-Torres, J. Cebrià, A. Gavaldà-Navarro, E. Chenoll, E. Isganaitis, F. Villarroya, M. Vallejo, J. Segalés, J. C. Jiménez-Chillarón, T. Bottiglieri, E. W. Demerath, **David A. Fields**, M. C. Collado, C. Lerin, Increasing breast milk betaine modulates Akkermansia abundance in mammalian neonates and improves long-term metabolic health. Sci. Transl. Med. 13, eabb0322 (2021).

Upcoming Metabolic Research Conference Speakers

Monday, April 5 – Sohail Khan, MBBS, MPH, CIP
Director of Health Research/Co-Chair CNIRB
Cherokee Nation
What Every Researcher Needs to Know About Interacting with Sovereign Tribal Nation IRB's

Monday, April 19 – Norman Hord, Ph.D., MPH, RD
Professor and Chair
Department of Nutritional Sciences
College of Allied Health
University of Oklahoma Health Sciences Center
Nitrate Promotes Enhanced Exercise Performance in Zebrafish (Danio rerio): Metabolomic and Signaling Determinants in Whole Fish, Skeletal Muscle and Liver

Monday, May 3 – Katie Page, M.D.
Associate Professor of Medicine
Co-Director, Diabetes and Obesity Research Institute
Department of Internal Medicine
Division of Endocrinology, USC Keck School of Medicine
Shaping Future Health: Early-Life Determinants of Brain and Metabolic Disease Risk

Monday, May 17 – Xia "Shelley" Lei, M.D., Ph.D.
Assistant Professor
Department of Biochemistry & Molecular Biology
Oklahoma State University
CTRPs and Metabolic Disease

New HHDC Lab Staff:

Mohammad Hasan, Ph.D.
Postdoctoral Fellow
Li Lab

April Teague, M.S.
Research Associate
Friedman/Jonscher Lab

OU Health | Harold Hamm Diabetes Center

Hamm Prize Jury Symposium 2021

With the 2021 Selection Jury for the HAROLD HAMM INTERNATIONAL PRIZE for BIOMEDICAL RESEARCH in DIABETES

Friday, April 30
Virtual Symposium

To register, visit: https://bit.ly/3fyOKcs

8:00 am

Adipose Tissue as the Central Hub for Metabolic Disease

Philipp E. Scherer, Ph.D.

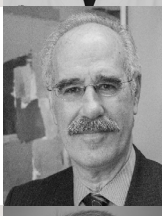
Professor, Department of Internal Medicine Gifford O. Touchstone Jr. and Randolph G. Touchstone, Distinguished Chair in Diabetes Research, Director, Touchstone Diabetes Center, Interim Chair, Department of Cell Biology, The University of Texas Southwestern Medical Center

8:55 am

Advancing Diabetes Prevention and Treatment through Multi-center Studies: A Team Sport

David M. Nathan, M.D.

Director, MGH Diabetes Center and Clinical Research Center Professor of Medicine, Harvard Medical School



9:35 am

The Incretin Effect in Physiology, Pathophysiology and Pharmacology

David A. D'Alessio, M.D.

Professor of Medicine and Director Division of Endocrinology and Metabolism, Duke University Medical Center

10:30 am

How do we understand islet abnormalities in diabetes?

Alvin C. Powers, M.D.

Joe C. Davis Chair in Biomedical Science, Professor of Medicine, Molecular Physiology and Biophysics, Director, Vanderbilt Diabetes Center Chief, Division of Diabetes, Endocrinology, and Metabolism, Vanderbilt University Medical Centeri

11:10 am

Metabolic Consequences of Type 2 Diabetes: Balancing Genes and Environment for Personalized Care

Juleen R. Zierath, Ph.D.

Professor, Department of Physiology and Pharmacology, Karolinska Institute, Sweden, University of Copenhagen, Denmark

Noon

The Road to a Cure

Recent and Anticipated Advances Leading to a Cure in Diabetes

ROUNDTABLE DISCUSSION

OU Health | Harold Hamm Diabetes Center