

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

223rd Meeting of the
NATIONAL DIABETES and DIGESTIVE and KIDNEY DISEASES ADVISORY COUNCIL
DIVISION OF DIGESTIVE DISEASES and NUTRITION SUBCOMMITTEE
Meeting Summary

Wednesday, September 13, 2023
Hybrid Meeting

Open Session

- 1) Dr. Stephen James opened the meeting by welcoming everyone.
- 2) The minutes of the May 17, 2023, subcommittee meeting were approved.
- 3) There were no DDDN Initiative Concept Clearances to discuss.
- 4) Dr. David Saslowsky led a discussion continuing from the Full NIDDK Advisory Council Session. The discussion included the following question and response:
 - a) **Question:** One of the topics discussed from the NIDDK portfolio was women and minorities, is DDN representative of NIDDK as a whole?
 - b) **Answer:** At the program level, staff does not have access to the Principal Investigators (PI) race and ethnicity. It has been challenging to obtain data by race and ethnicity because of the privacy protection rules in place; special agreements must be obtained to receive such information. From previous presentations, it does appear that DDN is following trends.
- 5) The DDN Early Career Portfolio Planning for January 2024 was presented. The discussion included the following questions and responses:
 - a) **Question:** Regarding early K-awardee successes, outside of the NIH, can you obtain data to see if PIs have a VA award or awards with the Agency for Healthcare Research and Quality?
 - b) **Answer:** We can to a limited degree of access.
 - c) **Question:** When a grant can go into multiple subject areas, how is it divided?
 - d) **Answer:** Program Directors will review the award to help determine the best portfolio it should go into.
 - e) **Comment/Recommendation:** Reaching out to the PI asking about publications and subsequent grants may help with improving grant portfolio placement.
- 6) Dr. Saslowsky reviewed eight DDDN Funding Opportunity Announcements and reminded everyone that current NIDDK funding opportunities can be found at <https://www.niddk.nih.gov/research-funding/current-opportunities>.
 - a) RFA-DK-023-001 & RFA DK22-023 A Consortium for Gut-Brain Communication in Parkinson's Disease (U01s & U24 Clinical Trial not allowed)
 - b) RFA-DK-23-017 Continuation of the Childhood Liver Disease Research Network (ChiLDReN) Clinical Centers (U01 Clinical Trial Required)

- c) RFA-DK-23-515 Limited Competition for the Continuation of the Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Clinical Centers (U01 Clinical Trial Required)
 - d) RFA-DK-23-516 Single Source for the Continuation of the Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Data Coordinating Center (U24 Clinical Trial Required)
 - e) RFA-DK-23-014 NIDDK Catalyst Award (DP1 Clinical Trial Not Allowed)
 - f) NOT-OD-22-032 Notice of Special Interest (NOSI): Administrative Supplements for Research on Sexual and Gender Minority (SGM) Populations (Admin Supp Clinical Trial Optional)
 - g) NOT-OD-22-032-FY23 DDDN Awards SGM Administrative Supplement Program
 - h) NOT-OD-23-166 Notice of Special Interest (NOSI): Research on Family Support and Rejection in the Health and Well-Being of SGM Populations
- 7) Planned Workshop (more details can be found in the appendix):
- a) **Pharmacotherapy for Obesity in Children and Adolescents: State of the Science, Research Gaps and Opportunities** <https://www.niddk.nih.gov/news/meetings-workshops/2023/pharmacotherapy-for-obesity-in-children-and-adolescents> will be held as a hybrid meeting online and at The Bethesda Hotel in Bethesda, MD November 28-29, 2023. The overarching goal of the workshop will be to identify gaps and opportunities to guide research and speed progress in the safe, effective, and equitable use of pharmacotherapy for obesity in children and adolescents.
- 8) Completed Workshops (more details can be found in the appendix):
- a) **Neuroimmune Crosstalk in Gut: Impact on Local, Autonomic, and Gut-Brain Function** <https://www.niddk.nih.gov/news/meetings-workshops/2023/neuroimmune-crosstalk-workshop> was held at The Bethesda Hotel in Bethesda, MD on June 29, 2023. The purpose of the Neuroimmune Crosstalk Workshop was to solicit the perspectives and recommendations of experts in the fields of neurogastroenterology, immunology, and microbiology. A summary of the workshop will be in publication soon.
 - b) **Interventions for Pancreatitis: New approaches, Knowledge Gaps and Research Opportunities** <https://www.niddk.nih.gov/news/meetings-workshops/2023/interventions-for-pancreatitis> was held at the University Club in Pittsburgh, PA on July 26, 2023. This one-day workshop aimed to inform investigators of new developments in the field and identify the knowledge gaps and research opportunities that might inform possible future funding initiatives for NIDDK. A conference summary manuscript has been submitted for publication.

Closed Session

Confidentiality and conflict of interest was discussed. Council members reviewed competing applications. There were five applicants with >\$1M in NIH funding (direct costs) requiring special council review and one foreign application. There were no restorations, appeals, or skipped applications to review and vote on.

Dr. James thanked everyone for attending both in-person and via webinar. Comments and critiques regarding discussion topics and initiatives from council members are welcome and should be emailed to Drs. James and Saslowsky in advance of the next meeting.

-Appendix-

Planned Meetings and Workshops

Hybrid Meeting

Pharmacotherapy for Obesity in Children and Adolescents:
State of the Science, Research Gaps and Opportunities

November 28–29, 2023



NIH
National Institute of
Diabetes and Digestive
and Kidney Diseases



Voula Osganian, M.D., Sc.D.



NIH
National Institute of
Diabetes and Digestive
and Kidney Diseases

Leadership

Co-Chairs

Sarah C. Armstrong, M.D.

Professor of Pediatrics

Chief, Division of General Pediatrics and
Adolescent Health

Duke University School of Medicine

Ihuoma Eneli, M.D, M.S.

Visiting Professor of Pediatrics

University of Colorado

Children's Hospital Colorado

Aaron S. Kelly, Ph.D.

Professor of Pediatrics

Co-Director, Center for Pediatric Obesity
Medicine

University of Minnesota Medical School

Obesity Action Coalition

Liz Paul, Patient Advocate

NIDDK

Miranda Broadney, M.D.,

Mary Evans, Ph.D.

Barbara Linder, M.D.

Katrina Loh, M.D.

Voula Osganian, M.D., Sc.D., M.P.H.

Ken Wilkins, Ph.D.

Theresa Woo, Ph.D.

Sue Yanovski, M.D.

NICHD

Andrew Bremer, M.D.

NHLBI

Laurie Donze, Ph.D.

Charlotte Pratt, Ph.D.

OBSSR

Deborah Young-Hyman, Ph.D.

Background & Objectives

- Pediatric obesity is increasing and highly prevalent (20%) with Non-Hispanic Black and Hispanic youth and children from families experiencing poverty and/or food insecurity disproportionately affected.
- Pediatric obesity has been associated with co-morbidities including type 2 diabetes, NAFLD, dyslipidemia, elevated blood pressure, and mental health problems that can impair a child's wellbeing and quality of life and it tracks strongly into adulthood.
- Dose and duration of lifestyle modification therapy needed to meaningfully reduce adiposity is high, often limiting its feasibility in practice. Most behavioral/lifestyle interventions show only modest favorable changes in average body mass index (BMI) that are not sustained.
- Recent availability of safe and effective pharmacotherapies offers an important adjunct to behavioral therapy in a substantial number of youth. *AAP CPG: offer weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to health behavior and lifestyle treatment for 12 + years (with comorbidities, severe obesity, older age) (May consider treatment in children 8-11 years).*

Background & Objectives

- Research is needed to address important knowledge gaps to ensure appropriate, effective, safe, equitable, and successful adoption of obesity pharmacotherapy in clinical practice.
- This workshop will convene leading scientific and clinical experts with diverse expertise to discuss use of pharmacotherapy in children, systemic and individual barriers to treatment, effects on physical and mental health, quality of life and eating behaviors, and cost-effectiveness of therapy.
- Participants will identify gaps and opportunities for future research to guide 1) **best practices for use of pharmacotherapy for pediatric obesity** including prescriber training, timing of initiation, duration of therapy, combination therapies, and lifestyle supports, 2) **understanding of contextual factors** that influence equitable access and reduce barriers to care, 3) and **unique aspects of use of pharmacotherapy for obesity in children, a vulnerable population**, including bias and stigma, communication, developing autonomy, and growth and development.

Agenda

Session 1: Overview of Treatment for Pediatric Obesity

Understanding the Whole Child with Obesity and the Adverse Physical, Metabolic, and Psychological Consequences of Childhood Obesity

Ihuoma Eneli, M.D., M.S., University of Colorado

Parent and Patient Journeys with Obesity and Obesity Care

Faith Anne Heeren, B.A., University of Florida

Liz Paul, Obesity Action Coalition

The Past, Present, and Future of Pediatric Obesity Care and Overview of AAP Clinical Practice Guideline

Sarah Hampl, M.D., University of Missouri-Kansas City School of Medicine

Moderated Discussion

Aaron Kelly, Ph.D., University of Minnesota Medical School

Session 2: The Science and Rationale for Pharmacotherapy to Treat Obesity

Pathophysiology of Obesity and the Rationale for the Use of Pharmacotherapy

Ania M. Jastreboff, M.D., Ph.D., Yale University School of Medicine

Approved and Emerging Pharmacotherapies for Non-Syndromic Obesity: Clinical Trial Evidence of the Safety, Efficacy, and Tolerability of Anti-Obesity Medications

Aaron Kelly, Ph.D., University of Minnesota Medical School

Approved and Emerging Pharmacotherapies for Children with Obesity Syndromes

Jack Yanovski, M.D., Ph.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health

Moderated Discussion

Justin Ryder, Ph.D., Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern Feinberg School of Medicine

Agenda

Session 3: Use of Evidence-Based Treatments for Pediatric Obesity: When and how intensively to intervene? What factors determine response and non-response?

Challenges of Implementation of Evidence-based Treatments (including MI, IHBLT, AOMs, WLS) in Clinical Settings

Mona Sharifi, M.D., M.P.H., Yale University School of Medicine

Clinical use of Anti-Obesity Medications; when to start, escalate, wean down or stop, prospect of physiological resetting, contraindications, and long- term safety.

Claudia Fox, M.D., M.P.H., University of Minnesota Medical School

Metabolic/Bariatric Surgery and the Role of Pharmacotherapy

Tom Inge, M.D., Ph.D., Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern Feinberg School of Medicine

Mental Health Considerations

Denise Wilfley, Ph.D., Washington University in St. Louis

Moderated Discussion

Sarah Armstrong, M.D., Duke University School of Medicine

Session 4: Equity and Access to Care

Barriers and Inequities to Care: the impact of weight stigma and bias and provider and student education.

Kofi Essel, M.D., M.P.H., Elevance Health

Improving Access to Care- insurance coverage, role of telemedicine and virtual platforms, and risks of using remote care platforms

Valerie O'Hara, D.O., Maine Medical Center

Moderated Discussion

Fatima Cody Sanford, M.D., M.P.H., M.P.A., Harvard Medical School

Agenda

Session 5: Design and Measurement

Clinical trial design considerations for pharmacotherapy trials: best practices and future considerations

Daniel Hsia, M.D., Pennington Biomedical Research Center

Choosing meaningful outcomes and measures including outcomes to assess success and harm; BMI and its limitations, eating behaviors, co-morbidities, and quality of life and other patient reported outcomes

Sarah Barlow, M.D., M.P.H., University of Texas Southwestern Medical School

Cost Effectiveness Study Designs

Chin Hur, M.D., M.P.H. Columbia University

Moderated Discussion

Asheley Skinner, Ph.D., Duke University School of Medicine

Lunch and Lightning Talks

Moderator: *Charlotte Pratt, PhD., National Heart, Lung, and Blood Institute*

Parent and Patient Panel Discussion

Moderator: *Ted Kyle, R.Ph., M.B.A., ConscienHealth*

Panel Discussion and Closing Remarks (90 min). Co-Chairs

Completed Meetings and Workshops



NEUROIMMUNE CROSSTALK IN THE GUT

Impact on Local, Autonomic,
and Gut–Brain Function

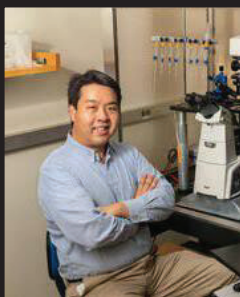
June 29–30, 2023

The Bethesda Hotel
Bethesda, Maryland



National Institute of
Diabetes and Digestive
and Kidney Diseases

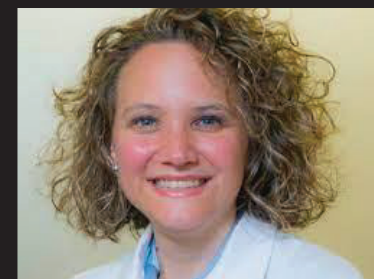
External Organizers



Isaac Chiu Ph.D.
Harvard University



Brain Gulbransen Ph.D.
Michigan State University



Kara Margolis M.D.
New York University

NIDDK

Diana Cummings Ph.D.

Patricia Greenwel Ph.D.

Dwayne Lunsford Ph.D.

Terez Shea-Donohue Ph.D.

Neuroimmune Interactions

1. The reciprocal influence between the nervous and the immune systems is central to survival as the interaction between these two systems underlies the ability to recognize, interpret, and respond to environmental stimuli.
2. Both systems also have the ability to recall earlier challenges and events and mount memory responses that anticipate and efficiently adapt to ever-changing conditions.
3. There is evidence that disruption of neuroimmune communications contributes to symptoms, severity, and chronicity of GI disorders such as IBD, IBS, celiac disease, and others.
4. Functional neuroimmune targets are at the crossroads of health and disease and are promising novel therapeutic targets for GI pathologies.

Workshop Objectives

- 1. To facilitate in-person networking among mucosal immunologists, enteric neuroscientists, and microbiologists to expand the scope of current NIDDK funding in this area.**
- 2. To explore recent advances in state-of-the-art molecular, imaging, and genetic technologies that can be leveraged across these disciplines.**
- 3. To better characterize the nature and specificity of neuroimmune interactions in the gut to allow for more precise targeting for development of novel therapeutics for GI disorders.**

Day 1 Agenda

Session 1 - Neuroimmune Perspectives

Moderators - Kara Margolis MD (New York University), Jakob von Moltke PhD (University of Washington)

1. Brian Gulbransen PhD (Michigan State University) - Immune Tuning of the Gut's Brain
2. Isaac Chiu PhD (Harvard) How Neurons Control Immunity in the Gut and Beyond

Session 2 - ENS development and Immune Interactions

Moderators - Julia Ganz PhD (Michigan State University) and Laren Becker MD, PhD (Stanford University)

1. E. Michelle Southard-Smith PhD (Vanderbilt University) – Enteric Nervous System Development - Origins, Gene Networks, and Cell Type Diversification
2. Jaime Belkind-Gerson MD, MSc (University of Colorado) – Neurogenesis and the Immune System
3. Yuuki Obata PhD (University of Texas Southwestern) – Environmental Modifications of the Enteric Nervous System

Day 1 Agenda

Session 3 - Visualizing Neuroimmune Interactions

Moderators - Eric Chang PhD (Feinstein Institutes for Medical Research) and Hongzhen Hu PhD (Washington University)

- 1. Kristen Smith-Edwards PhD (Mayo Clinic, Rochester) – Seeing is Believing: Approaches to Visualize Cell-to-Cell Communication in the Gut**
- 2. Li Ye PhD (The Scripps Research Institute) – New Approaches to Visualize and Target the Peripheral Nervous System**
- 3. Polina Anikeeva PhD (Massachusetts Institute of Technology) – Neurotechnology to Probe Brain and Gut Circuits**

Session 4 - Mechanisms of Neuroimmune Communication

Moderators - Gianluca Cipriani PhD (Mayo Clinic, Rochester) and Ruaidhri Jackson PhD (Harvard University)

- 1. Francisco Quintana PhD (Brigham and Women's Hospital) – Mechanisms of Neuroimmune Communication in the Gut**
- 2. Milena Bogunovic MD, PhD (University of Massachusetts) – Mucosal Inflammation Drives Adult Enteric Nervous System Remodeling by Muscularis Macrophages**
- 3. Colin Reardon PhD (University of California, Davis) – Neuroimmune Circuits in the Regulation of Peripheral Immunity and Inflammation**

Day 2 Agenda

Session 4 - Neuroimmune Interactions and Gut Sensation

Moderators - Kirsteen Browning PhD (Pennsylvania State University) and Alejandra Mendoza PhD (The Scripps Research Institute)

- 1. Michael Wheeler PhD (Brigham and Women's Hospital) – Deciphering Microbially Regulated Neuroimmune Interactions Via High-Throughput Genomic Tools**
- 2. Esther Borges Florsheim PhD (Arizona State University) – Innate Immune Cell Sensing**
- 3. Chuan Wu MD, PhD (NIH/NCI) - Immune Calibration of Neuroendocrine Homeostasis**

Session 6 - Neuroimmune Interactions along the Gut Brain Axis

Moderators - Timothy Sampson PhD (Emory University) and Helen Vuong PhD (University of Minnesota)

- 1. Kara Margolis MD (New York University) - Afferent Signaling in Gut-Brain Communication: An Overview with Clinical Translation**
- 2. Christoph Thaiss PhD (University of Pennsylvania) – ENS sensing of Microbiome and Gut Brain Communication**
- 3. Diego Bohórquez PhD (Duke University) – Deciphering Visceral Instincts**

Break-out Sessions

- **Increasing visibility of this area as it relates to IBD, disorders of gut brain interaction, functional gastrointestinal disorders, motility disorders, metabolic disease, neurodevelopmental disorders, and other relevant GI pathologies.**
 - **Leverage existing human studies to incorporate studies of neuroimmune communication**
 - **Increase basic and clinical collaboration**
 - **Recognition of complexity of the area including regional differences, immune context, and individual variation.**
 - **Identification of neuroimmune interactions as an important therapeutic target.**
- **Team science opportunities that support multidisciplinary research relevant to neuroimmune communication in the gut**
 - **Cross-disciplinary training opportunities and formal education**
 - **Augmented support for transition to faculty**

Break-out Sessions

■ Resources and Tools

- Development of new tools and adaptation of current state-of-the-art technologies to study neuroimmune interactions in the gut.
- Building the neuroimmune connectome
- High through-put analyses of luminal molecules and their function.
- Improved *ex vivo* and *in vitro* model systems.
- Development of mice for intersectional genetics targeting specific cell types.
- Need for mechanisms to allow sharing and distribution of available and emerging resources and technologies to investigators in this area.

Publication of Meeting Summary



Interventions for Pancreatitis:

New Approaches, Knowledge Gaps,
and Research Opportunities

JULY 26, 2023

The University Club | 123 University Place | Pittsburgh, PA



WITH THE ADDITIONAL SUPPORT OF
THE NATIONAL PANCREAS FOUNDATION

Program Review

➤ Date and Venue

- Wednesday July 26, 2023 - University Club, Pittsburgh PA
- Immediately prior to the annual PancreasFest meeting, a multidisciplinary research and clinical meeting.

➤ Attendance

- A hybrid format for both in-person and virtual attendance by Zoom
- 200 persons attended, half in-person on site.
- Meeting evaluations overwhelmingly positive

➤ Deliverables

- Conference Summary manuscript submitted for publication
- Recommendations may inform possible future funding initiatives of NIDDK

Rationale for Workshop

- Recent NIDDK Workshops have focused on the requirements for designing and conducting clinical trials in pancreatitis.
- The breadth and variety of interventions which are planned or underway include pharmacologic studies, nutritional studies and mechanical studies with devices, endoscopy and surgery.
- The purpose of this one day workshop was to inform investigators of new developments and to identify the knowledge gaps and research opportunities.

Workshop Faculty

- Adam Bell PhD Theraly Inc
- Randall Brand MD UPitt
- Greg Cote' MD OHSU
- Adriana Cowdin NPF
- Nancy Diazgranados MD NIAAA
- Vikas Dudeja MD UAB
- Sinead Duggan RD, PhD Trin Coll Dublin
- Evan Fogel MD Indiana Univ
- Chris Forsmark MD UFL
- Jay Freeman MD Nationwide/OSU
- George Gittes MD UPitt
- Phil Hart MD OSU
- Steve Hughes MD UFL*
- Christie Jeon DSc Cedars Sinai
- William Nealon MD Northwell/Hofstra
- John Neoptolemos MD Heidelberg Univ
- Tonya Palermo PhD Seattle Children
- Steve Pandol MD Cedars Sinai
- Anna Evans Phillips MD UPitt*
- Kristen Roberts PhD, RD OSU
- Martin Rosenthal MD UFL
- Vikesh Singh MD, MPH Johns Hopkins
- David Whitcomb MD, PhD UPitt
- Dhiraj Yadav MD, MPH UPitt
- Nicholas Zyromski MD Indiana Univ

* Workshop Co-chairs

Workshop Agenda

- Keynote Speakers
 - Patient Advocate, Adriana Cowdin – Patient Priorities
 - Chris Forsmark MD – Overview of Knowledge Gaps
- Promising, New or Novel Bio-Pharmacol Interventions
 - Repurposing Approved Anti-inflammatory Drugs, New Drugs Under Development, Stem Cell Treatment of Acute Pancreatitis
- Behavioral and Nutritional Interventions
 - Food as Medicine, Food as Causation, Oral versus Intrajejunal feeding, Alcohol Cessation Therapy, Whole Person Approach
- Mechanical and Device Interventions
 - Status of Therapeutic Endoscopy, Intraductal Infusion of Chemicals, Resection versus Excavation in Surgery, Timing and Subject Selection in Surgical Trials

Highlights

- HUMAN AUTOLOGOUS STEM CELLS AS POTENTIAL THERAPY IN NECROTIZING PANCREATITIS Nicholas J. Zyromski, MD, Indiana University
- REPURPOSING FDA-APPROVED ANTI-FIBROSIS AGENTS: EVOLUTION OF PIRFENIDONE FROM RODENTS TO MAN Vikas Dudeja MD, UAB
- CHEMICAL PANCREATECTOMY: A POTENTIAL NON-OPERATIVE TREATMENT FOR CHRONIC PANCREATITIS George K. Gittes, MD, U.Pitt