224th Meeting of the
NATIONAL DIABETES and DIGESTIVE and KIDNEY DISEASES ADVISORY COUNCIL
Hybrid: Virtual | In-person (Building 31C, 6th fl., Rooms F&G)
Division of Diabetes, Endocrinology, and Metabolic Diseases
Sub-committee Meeting – Open Session
January 10, 2024

DDEMD Sub-committee Members: Dr. David D'Alessio, Dr. Debra Haire-Joshu, Ms. Davida Kruger, Ms. Neicey Johnson, Dr. Philipp Scherer, Dr. Elizabeth Seaquist

DDEMD Staff Members: Dr. Kristin Abraham, Dr. Beena Akolkar, Dr. Guillermo Arreaza-Rubin, Dr. Raj Basu, Dr. Olivier Blondel, Dr. Miranda Broadney, Dr. Hank Burch, Dr. Art Castle, Dr. William Cefalu, Dr. Maureen Monaghan Center, Dr. Brad Cooke, Dr. Thomas Eggerman, Dr. Rafael Gorospe, Mr. Neal Green, Dr. Jay Gupta, Dr. Carol Haft, Dr. Albert Hwa, Dr. Teresa Jones, Dr. Maren Laughlin, Dr. Jean Lawrence, Dr. Ellen Leschek, Dr. Yan Li, Dr. Hanyu (Maggie) Liang, Dr. Barbara Linder, Dr. Chris Lynch, Mr. Louis Martey, Mr. Michael Mensah, Mrs. Heidi Otradovec, Mr. Daniel Rothwell, Dr. Salvatore Sechi, Dr. Corinne Silva, Dr. Lisa Spain, Dr. Pamela Thornton, Dr. Xujing Wang, Dr. Theresa Woo, Dr. Ashley Xia, Dr. Norann Zaghloul

NIDDK/NIH Staff: Dr. Michelle Barnard, Mr. Terry Barnes, Mr. John Bellafiore, Dr. Rebecca Cerio, Dr. John Connaughton, Dr. Greg Germino, Dr. Sophia Jeon, Mr. David Robinson, Dr. Elena Sandovich, Dr. Tori Stone

Welcome and Approval of October 2023 Sub-committee Minutes (Dr. Cefalu)

Dr. Cefalu welcomed everyone to the DEM Sub-committee Open Session meeting and provided an overview of the agenda. Minutes were moved for approval by committee members. He then acknowledged Dr. Debra Haire-Joshu for her council service extension and thanked Ms. Neicey Johnson for her service as an ad hoc member.

Heterogeneity of T2D Working Group of Council (Dr. Cefalu)

Dr. Cefalu provided updates on the Heterogeneity of T2D Working Group of Council (WGoC) and stated that the output would provide a "blueprint" to guide future initiatives to address the topic. For now, the composition and expected outcomes have been established. He mentioned the proposed publication of a global perspective. Dr. Cefalu explained the structure, the composition, and the charges for each subgroup-engagement, pre-clinical, clinical, lifestyle and innovation. More subgroups could be added as the work proceeds. The output of these subgroups will be to inform NIDDK staff on future research and to address gaps and opportunities, and to allow continued progression to a more stratified medical approach to diagnosis, prevention, management, and treatment of type 2 diabetes.

Dr. Cefalu talked about the WGoC deliverables and the expectations of the subgroups. Each subgroup will do a deeper dive into their topic and the members will have a wide diversity of interests. Each member will bring their own expertise to help address detailed, specific areas within their own subgroup. Subgroup leadership (co-chairs) and NIDDK program leads will finalize subgroup membership with global academic investigators by end of January 2024 and will outline areas to cover. Information will be assembled in a common SharePoint site that will be used by each subgroup as a central location for minutes, reports, and organization composition.

In closing, Dr. Cefalu also noted that Diabetes in America will come out next week as an online resource document rather than in hard copy. This effort led by Dr. Lawrence will enable regular updates to this "living document" moving forward. More details on this effort will be presented at the May Subcommittee meeting.

The Human Islet Research Network (HIRN) (Dr. Blondel)

Dr. Cefalu introduced Dr. Blondel who presented an update on the origin and prospects for HIRN. Dr. Blondel explained the mission, charge, and overall goals for HIRN. He stated that HIRN comprises the following consortia: Consortium on Targeting and Regeneration (CTAR), Consortium on Human Islet Biomimetics (CHIB), Consortium on Modeling Autoimmune Interactions (CMAI), Consortium on Beta Cell Death and Survival (CBDS), and Human Pancreas Analysis Consortium (HPAC). Several examples of successful CBDS projects with potential clinical applications were presented. The HIRN was expanded with the creation of the Human Pancreas Analysis Program (HPAP) in 2016 and the Human Pancreas Analysis Consortium (HPAC) in 2018, to facilitate research using primarily pancreatic tissues isolated from cadaver donors, including T1D and T2D patients, and non-diabetic individuals.

Dr. Blondel presented several metrics of success for HIRN, including many publications, the various grant programs targeting young investigators, and the success of the publicly available resources and scientific webinar produced by the network. Dr. Blondel ended by demonstrating how HIRN continues to evolve with some consortia terminating (CTAR, CHIB, CMAI), and new ones being created, including the Consortium on Modeling Autoimmune Diabetes (CMAD) and the pancreas-focused knowledgebase (PANKbase).

Dr. Cefalu asked to explain the significance of the SDP funding. The HIRN structure was developed and supported by the SDP funds and would not have been possible without this support. However, SDP funds are never guaranteed and continued support is needed to support this innovative initiative. He explained the science is constantly evolving and things are never static. This is an intellectual community that new investigators can join. HIRN has attracted new program staff who have diverse experiences.

History of Large Grant Solicitations over the Decades: Support of Team Science (Dr. Haft)

Dr. Haft explained that special funding is provided each fiscal year to DEM, KUH and DDN by the NIDDK director to fund several new, large, investigator-initiated research project grants. Historically, these large grants were program project grants (P01), and more recently P01s were replaced by inter-disciplinary team science projects (R24/RC2), and high-risk, high-reward projects, NIDDK Catalyst awards (DP1).

From the 1980s through the early 2000s program project grants were the large grant mechanism of choice to support multiple investigators who came together to address a central theme in NIDDK's mission. Program projects had a required structure of at least 3 individual subprojects and one or more shared scientific cores. Strong supporting preliminary data was required to justify P01

support, and the scientific impact of a new program project was anticipated to be greater than the cumulative contributions of its individual components. For many years the program projects supported by NIDDK were strong and very productive. However, following an NIDDK-wide P01 portfolio analysis and discussions between program staff, Council members and IC leadership it was decided that starting in 2013 NIDDK would no longer accept new program project applications and existing P01s would begin to sunset.

The movement away from support of program projects was deemed appropriate as institutional cores were now widely available to many researchers, multi-PI R01s were also possible to allow two or more PIs to work collaboratively on a project and the productivity of the current P01s in the DK portfolio were often no longer particularly synergistic. In addition, sun-setting of P01s would allow large grant resources to be slowly reutilized to support new inter-disciplinary teams looking to tackle emerging complex problems in our mission or to generate a research resources for the community that could not be accommodated with the program project structure.

For the new NIDDK inter-disciplinary team science funding opportunity announcement that followed, no pre-determined structure was required, and the initiative encouraged the establishment of new collaborations with world experts rather than colleagues at one's same institution. Over the last decade, DEM has supported several ground-breaking projects and research resources that Dr. Haft then highlighted.

Lastly, in 2018 two additional modification to the DEM large grant program took place following another large grant outcomes analysis, and discussion among staff and Council members designed to determine if we could enhance the impact of the team science projects solicited and to further attract Principal Investigators not currently in the portfolio. One strategy that resulted was to focus on specific topics over several years to generate interest in emerging areas and jump-starting emerging areas crucial to DEM. This was in addition to the broad NIDDK inter-disciplinary team science solicitation that continued to be available.

A second funding opportunity announcement was also developed called the Catalyst Award in Diabetes, Endocrinology and Metabolic Diseases. This new program was designed to support high-risk, high-reward projects in DEM's mission with the overarching objective of fostering innovation. This new program was similar in focus to the NIH Director's Pioneer and Innovative Awards except that a disease focus was required for the problem to be tackled. After several years of piloting and refining this new, large, grant program, DDN joined this effort and the outcomes of the FY24 NIDDK Catalyst Award program will be presented at the May 2024 meeting.

In closing, Dr. Haft brought up several points for discussion including What should be metrics of success for our large grant programs, how can we enhance team science, and should we accept more R01s with yearly budgets in direct cost of greater than $500K?

This was followed by open discussion. Dr. Scherer expressed doubts about the RC2 mechanism and felt the sunsetting of P01 grants may have left some gaps that haven't been filled. He believes the problem is the scientific community is confused about the correct mechanism to use. He

specifically believes the RC2 mechanism needs to be communicated better to accommodate groups of researchers coming together to bridge an understanding gap. Dr. David D'Alessio liked the idea of changing the cap that allows multi-PI grants to have more flexibility that a larger budget would allow.

Dr. Germino noted that a fair amount of time and money has been dedicated to supporting investigator initiated R01s and that there has been a surge in the number of applicants and the cost per award. The R01 part of the budget has ballooned, making it more difficult to support other initiatives. Dr. Germino explained the budget is not increasing at a fast enough rate to support the initiatives NIDDK and DEM would like to support and NIDDK must balance the different needs.

DEM FY23 Funding (Dr. Haft)

Dr. Haft delivered a comprehensive overview of the DEM funding activities fiscal year 2023. She began by showing the sources of funding for FY23, the yearly DK "use it or lose it" appropriation, as well as the Special Diabetes Program (SDP) appropriation. The DEM portfolio was shared with an analysis of the Principal Investigator (PI) success rate. The success rate for new awards (type 1s) stood at approximately 21%, while competing continuation awards (type 2s) had a much higher success rate of around 46%.

Dr. Haft included a breakdown of SDP and DK spending by different categories (Centers, research project grants, training, career development, small business, and other research). Dr. Haft also highlighted that investigator initiated R01s constituted a significant portion of the dollars spent, making up 46.5% of DEM's competing awards. Additionally, Dr. Haft shared that about half of the applications and an extended for Early-Stage Investigators (ESIs) to 25%.

Dr. Haft then shared insights for special emphasis funding, as she delineated the criteria for eligibility and provided a list of projects benefiting from multi-year special emphasis funding. The purpose of short-term awards included assisting PIs in project strengthening, bridging existing projects, offering a lifeline for at-risk PIs/projects, and covering unexpected costs.

Projects recommended for special funding consideration are typically to PIs with limited other support. To conclude, Dr. Haft shared a funding comparison between established PIs and ESIs, and the presentation concluded with a question from Ms. Kruger asking about the mechanics of R56 funding.

DEM Workshops and Events

Dr. Cefalu introduced and presented on future workshops for DEM.

Cystic Fibrosis Center Directors' Meeting
March 29, 2024, Bethesda, MD

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Understanding the Biological Mechanisms Underlying the Health Consequences of Racism, Marginalization, and Discrimination
April 2024

Targeted Mass Spectrometric Assays in Diabetes and Obesity Research (TaMADOR) Annual Meeting/Workshop
May 6, 2024, Seattle Washington and virtual

Dr. Cefalu thanked the Sub-committee members and DEM staff for their presentations and comments.