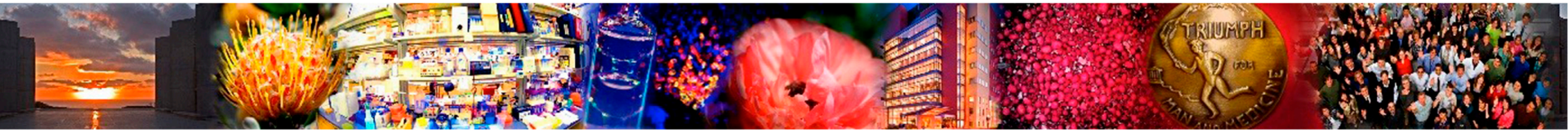
DIABETES RESEARCH CENTERS



2020 NIDDK Diabetes Research Center Directors' Annual Meeting

October 1, 2020

2020 NIDDK Diabetes Center Directors' Meeting

October 1, 2020

Virtual Meeting

Agenda

Session 1 (all times are Eastern)

10:30 - 10:45 am	Welcome and Brief Updates (Dr. Silva)
10:45-11:00	Remarks from NIDDK Director (Dr. Rodgers)
11:00-11:30	Perspectives and Opportunities (Dr. Cefalu)
11:30-12:00	Funding opportunities Mechanistic COVID RFA (Dr. Laughlin) Cystic Fibrosis Centers (Dr. Eggerman) Emerging Physicians Administrative Supplement (Dr. Silva)
12:00-12:45	Discussion on strategies regarding COVID and diabetes (DRC Directors)
12:45-1:15	**Break**

Session 2 (all times are Eastern)

1:15-3:15	Concurrent P&F presentations Two Zoom Sessions with 8 presentations each
3:15 - 3:45	NIDDK Medical Student Summer Program (Dr. Stafford) Moderator, Dr. Powers
3:45-4:15	Virtual Seminar Series (Dr. Davies) Moderator, Dr. Kahn
4:15-4:30	Wrap up (Dr. Silva)

DIABETES RESEARCH CENTERS

2020 Meeting of the Diabetes Research Centers' Directors

Table of Contents

2020 NIDDK Diabetes Research Center Directors' Annual Meeting

October 1, 2020

Participants

Domenico Accili, M.D.
Russell Berrie Foundation Professor of Diabetes
Chief, Division of Endocrinology
Director, Columbia Diabetes Research Center
College of Physicians & Surgeons
Department of Medicine
Columbia University
Russ Berrie Pavilion
1150 Saint Nicholas Avenue, Room 2-238
New York, NY 10032
Telephone: (212) 851-5332
Email: da230@columbia.edu

Eric Appel, Ph.D.
Assistant Professor
Department of Material Science and Engineering
Stanford University
eappel@stanford.edu

Graeme Bell, Ph.D.
Professor
Department of Medicine
The University of Chicago
5841 S. Maryland Avenue, MC 1027
Chicago, IL 60637
Telephone: (773) 702-5849
Email: g-bell@uchicago.edu

Carlos Bernal-Mizrachi, M.D.
Philip E. and Carolyn E. Cryer Professor in Medicine
Chief of Endocrinology at St. Louis VA Medical System
Associate Director, Washington University in St. Louis Diabetes Research Center
Endocrinology, Metabolism and Lipid Research
Washington University
St Louis, MO 63110
Office: 314-362-0947
cbernal@wustl.edu

Karin Bornfeldt, Ph.D.
Professor of Medicine
Division of Metabolism, Endocrinology and Nutrition
University of Washington
Seattle, WA
bornf@uw.edu

Matthew Brady, Ph.D.
Associate Professor
Department of Medicine
The University of Chicago
5841 S. Maryland Avenue, MC 1027
Chicago, IL 60637
Telephone: (773) 296-6063
Email: mbrady@medicine.bsd.uchicago.edu

John Buse, M.D., Ph.D.
Professor of Medicine
Director, Diabetes Center
University of North Carolina School of Medicine
CB# 7172
Burnett-Womack 8027
160 Dental Circle
Chapel Hill, NC 27599-7172
Telephone: (919) 966-0134 or (919) 923-6963
Email: jbuse@med.unc.edu

Ronald Cohen, M.D.
Associate Professor
Department of Medicine
The University of Chicago
5841 S. Maryland Avenue, MC 1027
Chicago, IL 60637
Telephone: (773) 834-7555
Email: roncohen@medicine.bsd.uchicago.edu

Robert Considine, Ph.D.
Professor of Medicine
Professor, Anatomy, Cell Biology and Physiology
Assistant Director, Center for Diabetes and Metabolic Diseases (CDMD)
Department of Medicine
Indiana University School of Medicine
635 Barnhill Drive, MS 224B
Indianapolis, IN 46202
Telephone: (317) 278-2389
Email: rconsidi@iu.edu

Nancy Cox, Ph.D.
Director, Vanderbilt Genetics Institute
Professor of Medicine
Director, Division of Genetic Medicine
Mary Phillips Edmonds Gray Professor of Genetics
Vanderbilt University Medical Center
519C Light Hall
2215 Garland Avenue
Nashville, TN 37232
Telephone: (615) 343-1689
Email: nancy.j.cox@vumc.org

David A. D'Alessio, M.D.
Professor of Medicine
Chief, Division of Endocrinology and Metabolism
Member of Duke Molecular Physiology Institute
300 North Duke Street
Durham, NC 27701
Telephone: (919) 684-4005
Email: david.d'alessio@duke.edu

Sean Davies, Ph.D.
Associate Professor of Pharmacology
Associate Director of Graduate Studies, Department of Pharmacology
Vanderbilt University
556 Robinson Research Building
2220 Pierce Avenue
Nashville, TN 37232
Email: sean.davies@vanderbilt.edu

Carmella Evans-Molina, M.D., Ph.D.
J.O. Ritchey, M.D. Professor of Medicine
Professor, Cellular and Integrative Physiology, Biochemistry and Molecular Biology
Director, Center for Diabetes and Metabolic Diseases (CDMD)
Director, Indiana Diabetes Research Center (IRDC)
Director, Pediatric Diabetes Research Group, Herman B Wells Center for Pediatric Research
Director, Indiana Diabetes Research Center Islet and Physiology Core
Staff Physician, RLR VAMC
Indiana University School of Medicine
Department of Medicine
635 Barnhill Drive, MS 2031
Indianapolis, IN 46202
Telephone: (317) 278-3177
Email: cevansmo@iu.edu

W. Timothy Garvey, M.D.
Butterworth Professor
Department of Nutrition Sciences
PI: AHA Strategically Focused Obesity Center
Director, UAB Diabetes Research Center
The University of Alabama at Birmingham
1675 University Boulevard
Birmingham, AL 35294-3360
Telephone: (205) 996-7433
Email: garveyt@uab.edu

Anna Gloyn, D.Phil.
Professor of Pediatrics and Genetics (by courtesy)
Stanford University School of Medicine
Stanford, CA 94305
Telephone: (650) 724-6080
Email: agloyn@stanford.edu

Barbara Gower, Ph.D.
DRC Associate Director
DRC Human Physiology Core
Professor, Nutrition Sciences
Telephone: (205) 934-4087
Email: bgower@uab.edu

Michelle Guney, Ph.D.
DRC Program Manager
Barbara Davis Center for Diabetes
University of Colorado Anschutz Medical Campus
1775 Aurora Court
Aurora, CO 80045
Telephone: (303) 724-8694
Email: michelle.guney@cuanschutz.edu

Meredith Hawkins, M.D., M.S.
Professor of Medicine
Harold and Muriel Block Chair in Medicine
Director, Global Diabetes Institute
Co-Director, Einstein Diabetes Research Center
Albert Einstein College of Medicine
Belfer 709
1300 Morris Park Avenue
Bronx NY 10461
Telephone: (718) 430-3186
Email: meredith.hawkins@einsteinmed.org

Kevan Herold, M.D.
CNH Long Professor of Immunobiology and Internal Medicine at Yale University.
Professor
Department of Immunobiology
Yale University School of Medicine
P.O. Box 208011
New Haven, CT 06520-8011
Telephone: (203) 785-6507
Email: kevan.herold@yale.edu

Dirk Homann, MD, MA
Professor of Medicine
Icahn School of Medicine at Mount Sinai
One Gustave L. Levy Place; Box 1152
New York, NY 10029
p (212) 241-1935
f (212) 241-2485
email: dirk.homann@mssm.edu

Mehboob A. Hussain, M.D.
Professor
Division of Metabolism, Endocrinology and Diabetes
Department of Internal Medicine
University of Michigan
NCRC B26 247S
2800 Plymouth Road
Ann Arbor, MI 48109
Telephone: (734) 647-8731
Email: mehboobh@med.umich.edu

Steven Kahn, M.B., Ch.B.
Professor of Medicine
Leonard L. and Marjorie C. Wright Chair
Division of Metabolism, Endocrinology and Nutrition
Director, Diabetes Research Center
University of Washington
VA Puget Sound Health Care System (151)
1660 S. Columbian Way
Seattle, WA 98018
Telephone: (206) 277-5515
Email: skahn@uw.edu

Seung Kim, M.D., Ph.D.
Director, Stanford Diabetes Research Center
Professor, Departments of Developmental Biology and Medicine (by courtesy)
Divisions of Endocrinology and Endocrinology
Stanford University School of Medicine
Beckman B300
279 Campus Drive
Stanford, CA 94305
Telephone: (650) 723-6230
Email: seungkim@stanford.edu

George L. King, M.D.
Chief Scientific Officer
Joslin Diabtes Center
Professor of Medicine and Ophthalmology
Harvard Medical School
One Joslin Place
Boston MA 02215
Telephone: (617) 309-2622
Email: george.king@joslin.harvard.edu

Kiran Kocherlakota, Ph.D.
Program Manager
Stanford Diabetes Research Center
JDRF Center of Excellence (at Stanford)
Stanford University
Stanford, CA 94305
Telephone: (650)497-5143
Email: kiransk@stanford.edu

Fredric B. Kraemer, M.D.
Professor of Medicine
Chief, Division of Endocrinology, Gerontology and Metabolism
Director, SDRC Pilot &Feasibility Program
Stanford University School of Medicine
VA Palo Alto Health Care System
Stanford, CA 94305-5103
Telephone: (650) 493-5000, ext. 63184
Email: fbk@stanford.edu

Rohit N. Kulkarni M.D., Ph.D.
Margaret A. Congleton Chair and Senior Investigator
Joslin Diabetes Center
Professor of Medicine
Harvard Medical School
One Joslin Place, Room 410
Boston, MA 02215
Telephone: (617) 309-3460
Email: rohit.kulkarni@joslin.harvard.edu

Brian T. Layden, M.D., Ph.D.
Associate Professor
Department of Medicine
University of Illinois at Chicago
835 Wolcott St.
Suite 625E M/C 640
Telephone: (312) 996-6060
Email: blayde1@uic.edu

Mitchell Lazar, M.D., Ph.D.
Willard and Rhoda Ware Professor in Diabetes and Metabolic Diseases
Director, Institute for Diabetes, Obesity, and Metabolism
Chief, Division of Endocrinology, Diabetes, and Metabolism
University of Pennsylvania Perelman School of Medicine
12-102 Smilow Center for Translational Research
3400 Civic Center Boulevard
Philadelphia, PA 19104
Telephone: (215) 898-0198
Email: lazar@pennmedicine.upenn.edu

Rudolph Leibel, M.D.
Christopher J. Murphy Professor of Diabetes Research
Head, Division of Molecular Genetics
Co-director, Naomi Berrie Diabetes Center
Columbia University Vagelos College of Physicians and Surgeons
1150 St. Nicholas Avenue, Room 620
New York, NY 10032
Telephone: (212) 851-5257
Email: rl232@columbia.edu

David Maahs, M.D. Ph.D.
Secretary-General of the International Society of Pediatrics and Adolescent Diabetes
Associate Director, Stanford Diabetes Research Center
The Kirkwood Distinguished Packard Fellow
Professor of Pediatrics and, by courtesy, of Health Research and Policy (Epidemiology)
Chief of Pediatric Endocrinology
Lucile Packard Children's Hospital
Stanford University School of Medicine
Stanford, CA 94305
Telephone: (650) 498-7351
Email: dmaahs@stanford.edu

Donald A. McClain. M.D., Ph.D.
Professor of Internal Medicine-Endocrinology and Metabolism
Wake Forest University Health Sciences
NRC Building, E Floor
One Medical Center Boulevard
Winston Salem, NC 27157
Telephone: (801) 550-2905
Email: dmcclain@wakehealth.edu

Owen McGuinness, Ph.D.
Professor
Department of Molecular Physiology and Biophysics
Vanderbilt University
707 Light Hall
2215 Garland Avenue
Nashville, TN 37232
Telephone: (615) 343-4473
Email: owen.mcguinness@vanderbilt.edu

Raghu Mirmira, M.D., Ph.D.
Professor
Department of Medicine
The University of Chicago
5841 S. Maryland Avenue, MC 1027
Chicago, IL 60637
Telephone: (773) 702-2210
Email: rmirmira@medicine.bsd.uchicago.edu

Martin Myers, Jr., M.D., Ph.D.
Professor of Internal Medicine and Molecular and Integrative Physiology
University of Michigan
6317 Brehm Tower
1000 Wall Street
Ann Arbor, MI 48105
Telephone: (734) 647-9515
Email: mgmyers@umich.edu

Elimelda Moige Ongeri, Ph.D.
Professor and Associate Dean for Research and Innovation
College of Health and Human Sciences
North Carolina A&T State University
219 Fort IRC
1601 E. Market Street
Greensboro NC 27411
Telephone: (336) 285-2182 or (717) 460-3551
Email: eongeri@ncat.edu

Jeffrey Pessin, Ph.D.
Judy R. & Alfred A. Rosenberg Professorial Chair in Diabetes Research
Director, Diabetes Research Center
Departments of Medicine and Molecular Pharmacology
Albert Einstein College of Medicine
375 Price Center
1301 Morris Park Avenue
Bronx, NY 10461
Telephone: (718) 678-1029
Email: jeffrey.pessin@einsteinmed.org

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 Center
7465 Medical Research Building IV
2215 Garland Avenue
Nashville, TN 37232-0475
Telephone: (615) 936-7678
Email: al.powers@vumc.org

Jane Reusch, M.D.
Professor of Medicine and Biochemistry
Division of Endocrinology, Metabolism and Diabetes
Associate Director, Center for Women's Health Research University of Colorado
University of Colorado Anschutz Medical Campus
VA Staff Physician and Merit Investigator
CCTSI-VA Liaison Denver VAMC
ENDO -111H
Room 9c120b
1055 Clermont Street
Denver, CO 80220
Telephone: (303) 399-8020x2775/3137
Email: jane.reusch@ucdenver.edu

Michael Rickels, M.D., M.S.
Professor of Medicine
Division of Endocrinology, Diabetes and Metabolism
University of Pennsylvania Perelman School of Medicine
12-134Smiow Center for Translational Research
3400 Civic Center Boulevard
Philadelphia, PA 19104
Telephone: (215) 746-0025
Email: rickels@pennmedicine.upenn.edu

Alan Saltiel, Ph.D.
Professor of Medicine and Pharmacology
Director, Institute of Diabetes and Metabolic Health
University of California, San Diego
9500 Gilman Drive
La Jolla, CA 92093-0757
Telephone: (858) 534-5974
Email: asaltiel@ucsd.edu

Jean E. Schaffer, M.D.
Associate Research Director
Joslin Diabetes Center
Member, Faculty of Medicine
Harvard Medical School
1 Joslin Place
Boston, MA 02115
jean.schaffer@joslin.harvard.edu

Clay F. Semenkovich, M.D.
Irene E. and Michael M. Karl Professor
Chief, Division of Endocrinology, Metabolism & Lipid Research
Director, Washington University in St. Louis Diabetes Research Center
Washington University
Campus Box 8127
660 South Euclid Avenue
St. Louis, MO 63110
Telephone: (314) 362-4454
Email: csemenko@wustl.edu

Anath Shalev M.D., Ph.D.
DRC Associate Director, Enrichment
Professor, Endocrinology/Medicine
Telephone: (205) 996-9546
Email: ashalev@uabmc.edu

Gerald Shulman, M.D., Ph.D.
George R. Cowgill Professor of Internal Medicine and
Cellular & Molecular Physiology
Co-Director, Yale Diabetes Research Center
Yale School of Medicine
333 Cedar St.
New Haven, CT 06520-8020
Telephone: (203) 785-5447
Email: gerald.shulman@yale.edu

Michael P. Snyder, Ph.D.
Professor
Department of Genetics
Stanford University
Stanford, CA
mpsnyder@stanford.edu

John Stafford, M.D., Ph.D.
Associate Professor
Department of Medicine
Division of Molecular Physiology and Biophysics
Vanderbilt University Medical Center
7465 MRBIV
2213 Garland Avenue
Nashville, TN 37232
Telephone: (615) 936-6113
Email: john.stafford@vumc.org

Roland Stein, Ph.D.
Professor
Department of Molecular Physiology and Biophysics and Cell and Developmental Biology
707 Light Hall 2215 Garland Avenue
Nashville, TN 37232
Telephone: (615) 322-7026
Email: roland.stein@vanderbilt.edu

Andrew Stewart, M.D.
Irene and Dr. Arthur M. Fishberg Professor of Medicine
Director, Diabetes, Obesity and Metabolism Institute
Atran 5
Mount Sinai School of Medicine
1428 Madison Avenue, Box 1152
New York, NY 10029
Telephone: (212) 241-7680
Email: andrew.stewart@mssm.edu

Lori Sussel, Ph.D.
Professor, Pediatrics and Cell and Developmental Biology
Sissel and Findlow Family Chair
Director of Basic and Translational Research
Barbara Davis Center for Diabetes
University of Colorado Anschutz Medical Campus
1775 Aurora Court
Aurora, CO 80045
Telephone: (303) 724-9119 or (212) 729-8439
Email: lori.sussel@cuanschutz.edu

Peter Tontonoz, M.D., Ph.D.
Professor of Pathology and Laboratory Medicine
Professor of Biological Chemistry
Frances an Albert Piansky Chair
University f California, Los Angeles
675 Charles Young Drive, MRL 6-770
Los Angeles, CA 90095-1662
Telephone: (310) 206-4546
Email: ptontonoz@mednet.ucla.edu

NIDDK STAFF

William Cefalu, M.D.
Director
Division of Diabetes, Endocrinology, and Metabolic Diseases
Two Democracy Plaza, Room 6037
6707 Democracy Boulevard, MSC 5460
Bethesda, MD 20892-5460
Telephone: (301) 435-1011
Email: william.cefalu@nih.gov

Thomas Eggerman, Ph.D. M.D.
Program Director
Division of Diabetes, Endocrinology, and Metabolic Diseases
Two Democracy Plaza, Room 6057
Telephone: (301) 594-8813
Email: thomas.eggerman@nih.gov

Carol Renfrew Haft, Ph.D.
Program Director
Cell Biology and Adipocyte Biology
Division of Diabetes, Endocrinology, and Metabolic Diseases
Telephone: (301) 594-7689
Carol.haft@nih.gov

Maren Laughlin, Ph.D.
Program Director
Division of Diabetes, Endocrinology, and Metabolic Diseases
Two Democracy Plaza, Room 7205
Telephone: (301) 594-8802
Email: maren.laughlin@nih.gov

Griffin P. Rodgers, M.D., M.A.C.P.
Director
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Building 31, Room 9A52
31 Center Drive, MSC 2560
Bethesda, MD 20892-2560
Telephone: (301) 496-5741
Email: griffin.rodgers@nih.gov

Corinne M. Silva, Ph.D.
Program Director
Signaling and Nutrient Sensing
Division of Diabetes, Endocrinology and Metabolic Diseases
Two Democracy Plaza, Room 7221
Telephone: (301) 451-7335
Email: silvacm@niddk.nih.gov

Philip Smith, Ph.D.
Deputy Director
Division of Diabetes, Endocrinology, and Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Two Democracy Plaza, Room 6047
6707 Democracy Boulevard, MSC 5460
Bethesda, MD 20892-5460
Telephone: (301) 594-8816
Email: philip.smith@nih.gov

Karen Teff, Ph.D.
Program Director
Division of Diabetes, Endocrinology, and Metabolic Diseases
Telephone: (301) 594-8803
Karen.teff@nih.gov

Pilot and Feasibility Awardees/Presenters

Petter Bjornstad, M.D.
Assistant Professor
Pediatric Endocrinology
Children's Hospital Colorado
University of Colorado Anschutz Medical Campus
Petter.Bjornstad@childrenscolorado.org

Justin Gregory, M.D.
Assistant Professor of Pediatrics
Ian M. Burr Division of Pediatric Endocrinology and Diabetes
Vanderbilt University School of Medicine
justin.m.gregory.1@vumc.org

Kirk Habegger, Ph.D.
Associate Professor
Department of Medicine
Division of Endocrinology Diabetes & Metabolism
University of Alabama at Birmingham
kirkhabegger@uabmc.edu

Peter K. Jackson, Ph. D.
Baxter Laboratory
Department of Microbiology & Immunology
Department of Pathology
Stanford University School of Medicine
pjackson@stanford.edu

Kennita Johnson, Ph.D.
Research Assistant Professor
Director of Diversity and Equity
UNC/NCSU Joint Department of Biomedical Engineering
Chapel Hill, NC 27599
Email: kennita@email.unc.edu

Jenny Kanter, Ph.D.
Research Associate Professor
Department of Medicine
Division of Metabolism, Endocrinology and Nutrition
University of Washington
jenka@uw.edu

Sarah Lessard, MSc, PhD
Assistant Professor of Medicine
Harvard Medical School
Joslin Diabetes Center
Sarah.Lessard@joslin.harvard.edu

Jeffrey R. Millman, Ph.D.
Assistant Professor
Departments of Medicine and Biomedical Engineering
Washington University School of Medicine in Saint Louis
jmillman@wustl.edu

Sirimon Reutrakul, M.D.
Professor
Division of Endocrinology, Diabetes and Metabolism
University of Illinois at Chicago
sreutrak@uic.edu

Celine Riera, Ph.D.
Assistant Professor,
Center for Neural Science and Medicine
Department of Biomedical Sciences
Board of Governors Regenerative Medicine Institute
Cedars-Sinai Medical Center
Celine.Riera@cshs.org

Kosaku Shinoda, Ph.D.
Assistant Professor
Departments of Medicine and Molecular Pharmacology
Albert Einstein College of Medicine
kosaku.shinoda@einsteinmed.org

Emily K. Sims, M.D.
Assistant Professor
Department of Pediatrics
Indiana University School of Medicine
eksims@iu.edu

Jinsook Son, Ph.D.
Associate Research Scientist
Naomi Berrie Diabetes Center
Department of Medicine,
Columbia University
js4730@cumc.columbia.edu

Paul M. Titchenell, Ph.D.
Assistant Professor
Department of Physiology
Institute for Diabetes, Obesity, and Metabolism
Perelman School of Medicine at the University
of Pennsylvania
ptitc@pennmedicine.upenn.edu

Daniel F. Vatner, M.D., Ph.D.
Assistant Professor of Medicine
(Endocrinology)
Yale School of Medicine
daniel.vatner@yale.edu

Jun Wu, Ph.D.,
Assistant Professor,
Department of Molecular & Integrative Physiology,
Life Sciences Institute,
University of Michigan
wujunz@umich.edu

UPCOMING MEETINGS AND WORKSHOPS

Joint CIHR-INMD and NIDDK Diabetes Symposium Commemorating the 100th Anniversary of the Discovery of Insulin

Spring 2021

2021 Cystic Fibrosis Related Diabetes NIH Cystic Fibrosis Foundation Workshop

June 24 – 25, 2021

NIH Campus, Building 35

Bethesda, MD

Obstacles and Barriers to Treatment and Prevention of Impaired Awareness of Hypoglycemia (IAH) and Counter-Regulatory Responses in Patients with Type 1 Diabetes

Fall 2021

Location TBD

2020 DRC Administrative Changes

Change in Director Leadership

Indiana Diabetes Research Center

(from Dr. Raghu Mirmira)

Carmella Evans-Molina, M.D., Ph.D.

Washington University in St. Louis

Diabetes Research Center

(from Dr. Jean Schaffer)

Clay F. Semenkovich, M.D.

FY2020 Two New Centers

- *North Carolina Diabetes Research Center*

  Duke University (Duke)

  The University of North Carolina at Chapel Hill (UNC)

  Wake Forest School of Medicine (WF)

  North Carolina A&T (NC A&T)

Center Director: Donald A McClain MD PhD

https://ncdiabetesresearch.org/

- *University of Colorado Denver*

  CU Anschutz Medical Campus

Center Director: Lori Sussel PhD

https://medschool.cuanschutz.edu/diabetes-research-center

Budget Update

September 2020

National Institute of Diabetes and Digestive and Kidney Diseases

FY 2020 Appropriations

NIH

2019 Final	2020 Approp	Increase/%
$39.084B	$41.459B	$2.375B/6.08%

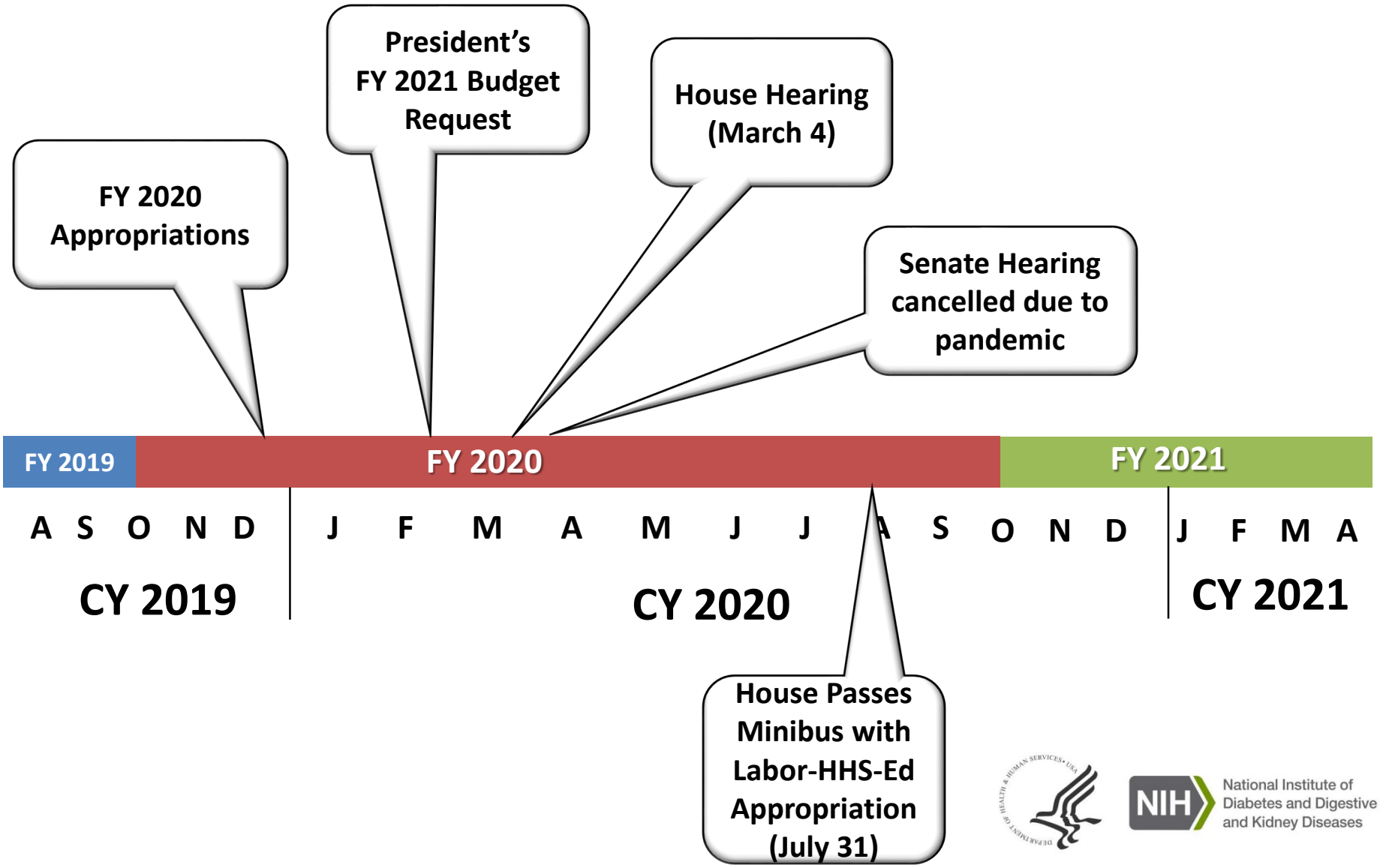
NIDDK

2019 Final	2020 Approp	Increase/%
$2.030B	$2.114B	$84.5M/4.2%

*All dollars exclude Special Diabetes Program funds

National Institute of Diabetes and Digestive and Kidney Diseases

FY 2021 Budget Events



National Institute of Diabetes and Digestive and Kidney Diseases

FY 2021 President's Budget Request*

NIH

2020 Enacted	2021 PBR	Δ/% 2020-2021
$41.459B	$38.016B	-$3.443B/-8.3%

NIDDK

2020 Enacted	2021 PBR	Δ/% 2020-2021
$2.114B	$1.924B	-$190M/-9.0%

**All dollars exclude Special Diabetes Program funds.*

National Institute of Diabetes and Digestive and Kidney Diseases

FY 2021 House L-HHS-Ed Appropriations Bill*

NIH

2020 Enacted	H.R. 7614	Δ/% 2020-2021
$41.459B	$42B**	$0.5B/1.2%

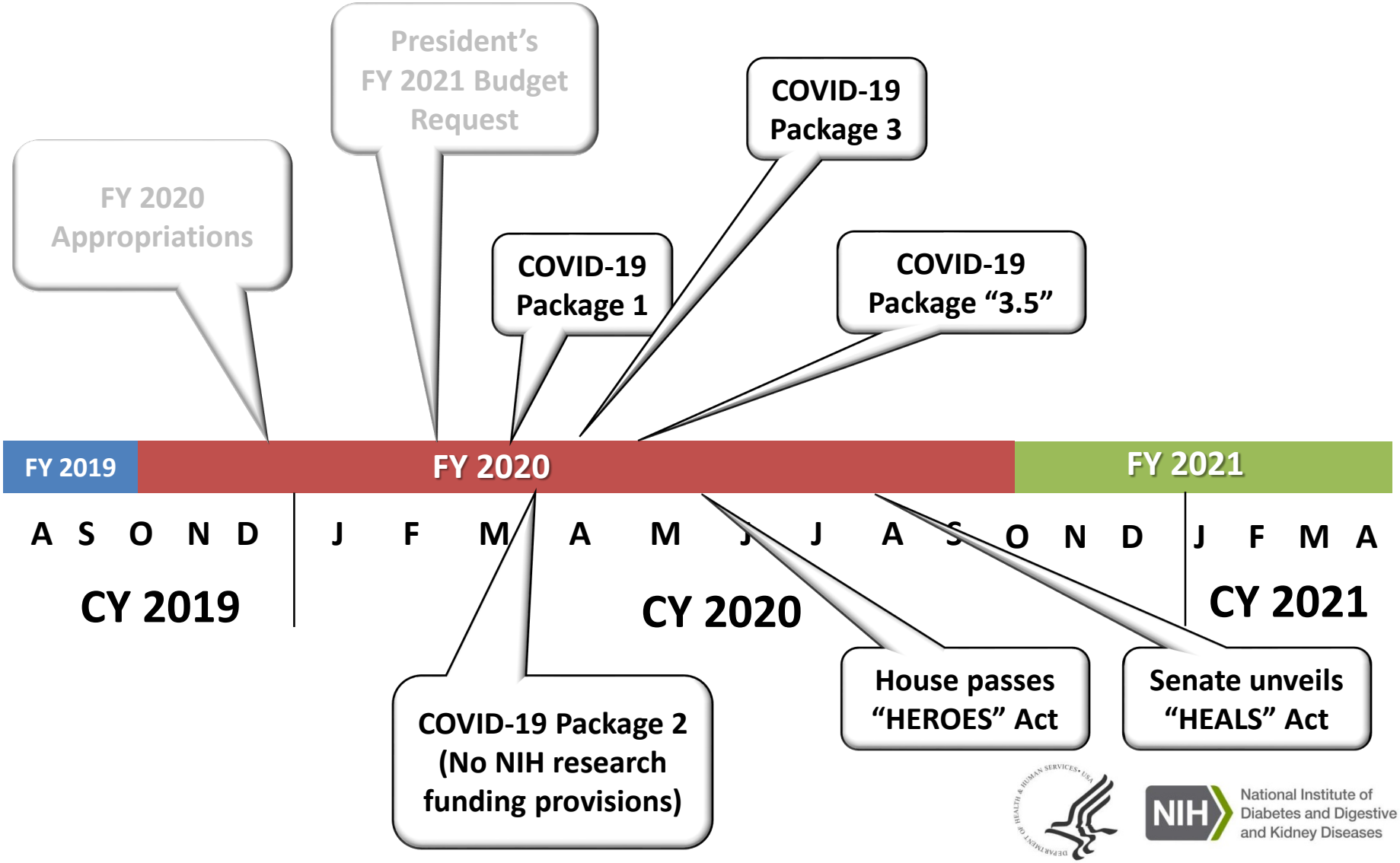
NIDDK

2020 Enacted	H.R. 7614	Δ/% 2020-2021
$2.114B	$2.132B	$18M/0.85%

*All dollars exclude Special Diabetes Program funds
**An additional $5 billion was included in emergency spending for NIH

National Institute of Diabetes and Digestive and Kidney Diseases

COVID-19-related Supplemental Packages



National Institute of Diabetes and Digestive and Kidney Diseases

NIH Funding in Early COVID-19 Supplemental Packages

Coronavirus Preparedness and Response Supplemental Appropriations Act (Package 1) -- March 6, 2020

- $8.3 billion total for NIH; funds included $836 million to NIAID, with $10 million of those funds to be transferred to NIEHS

Coronavirus Aid, Relief, and Economic Security (CARES) Act (Package 3) -- March 27, 2020

- almost $950 million for NIH
- authorized the remaining FY20 and partial FY21 funding for the Special Statutory Funding Program for Type 1 Diabetes Research

Paycheck Protection Program and Health Care Enhancement Act (Package “3.5”) – April 24, 2020

- $1.8 billion for NIH, with a focus on coronavirus testing and development of new testing platforms and technologies

Health and Economic Recovery Omnibus Emergency Solutions (HEROES) Act

- $3 trillion bill passed by the House on May 15, 2020, largely along party lines
- Wide range of areas, including economic assistance to governments at the state, local, tribal, and territorial levels; expanded unemployment benefits; stimulus checks to individuals; and many health care-related benefits.
- The bill provides $4.7 billion overall funding to NIH

ICO	Amount
NIAID	$500 million
NIMH	$200 million
NIH Office of the Director	$4 billion

Health, Economic Assistance, Liability Protection and Schools (HEALS) Act

- $1 trillion bill unveiled by Senate Republicans on July 27, 2020
- Quite different from HEROES Act. The bill similarly included stimulus checks to individuals and unemployment benefits; but included liability protections for employers; deferred student loan payments; increased funding for schools, educational institutions, and hospitals
- The bill provides $15.5 billion overall funding across the NIH

ICO	Amount
NIDDK	$200 million
NHLBI	$290 million
NIAID	$480.56 million
NICHD	$172.68 million
NIMH	$200 million
NIMHD	$64.33 million
NCATS	$1.22 billion
NIH Office of the Director	$12.91 billion

National Institute of Diabetes and Digestive and Kidney Diseases

NIDDK Advisory Council: COVID Discussion

- Policy Flexibility
- Policy Accommodations
- Targeted Investments

Budget Update

September 2020

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Diabetes and Digestive and Kidney Diseases

1950 70 years 2020

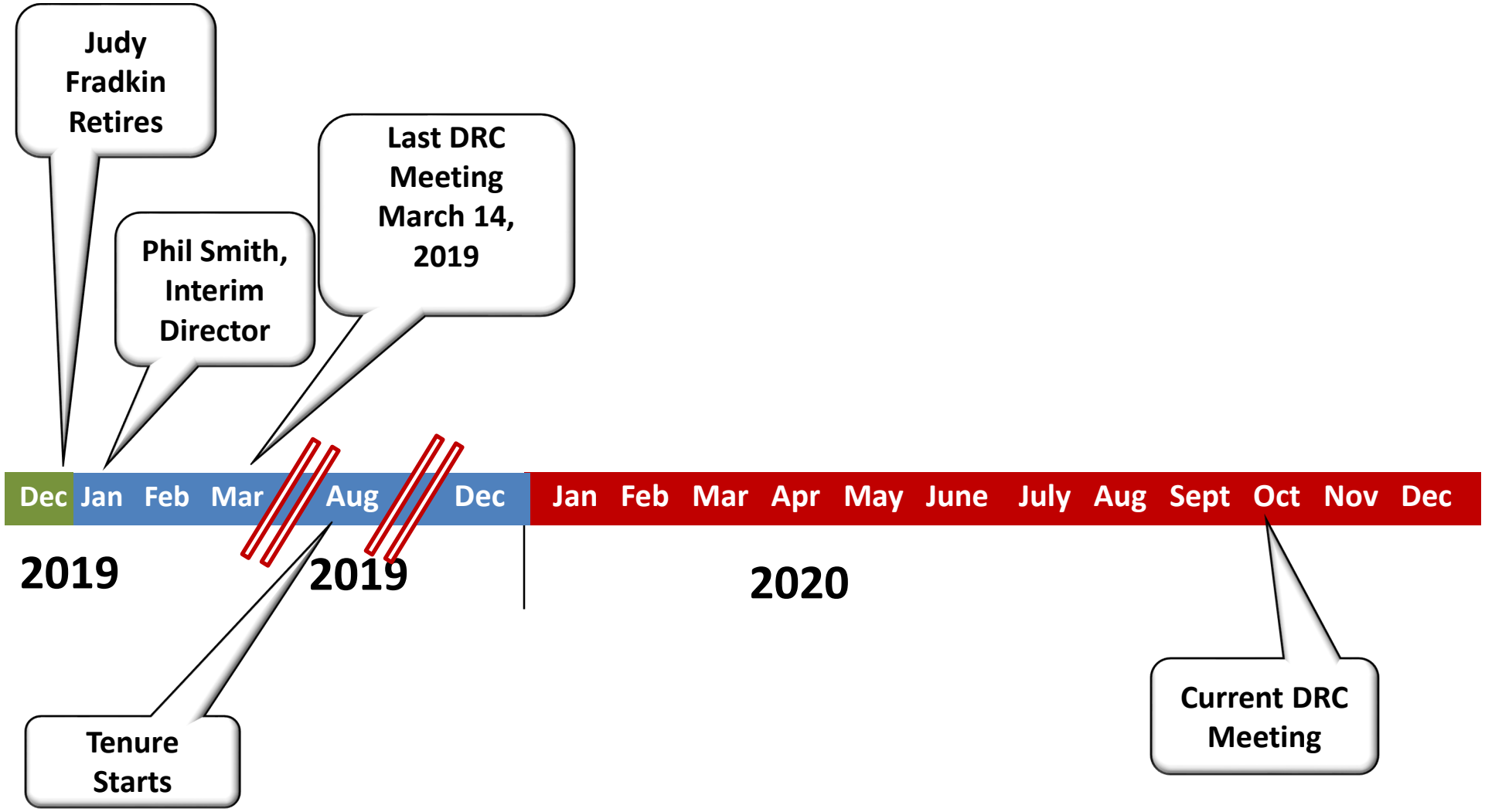
“Perspectives & Opportunities” NIDDK-DEM

William T. Cefalu, M.D.

Director, Division of Diabetes, Endocrinology, & Metabolic Diseases

October 1, 2020

Timeline of Events



NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) Perspectives

- **Opportunities and Challenges**
- **Addressing Urgent Needs and Areas of Emphasis**
- **Evolving Role of Diabetes Research Centers**

NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) Perspectives

➢ Opportunities and Challenges

- ***NIH/NIDDK & Special Diabetes Program Budget***
- COVID-19 Research Disruptions
- Future of landmark NIDDK studies

The Special Diabetes Program

$150 M/Year

- Supports ambitious, large-scale, high-risk, high-reward projects that would not otherwise be performed
- Enables stable, long-term investment in research

First FDA-authorized interoperable, automated insulin dosing controller, 12/13/19

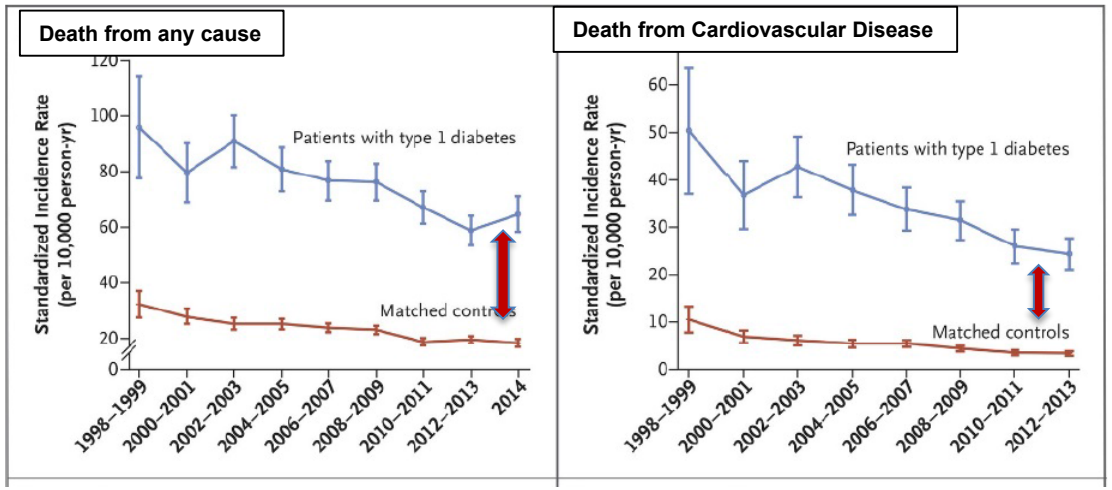
Control-IQ Technology (Tandem Diabetes)

FDA-approved new soluble, stable glucagon formulation, 9/10/19

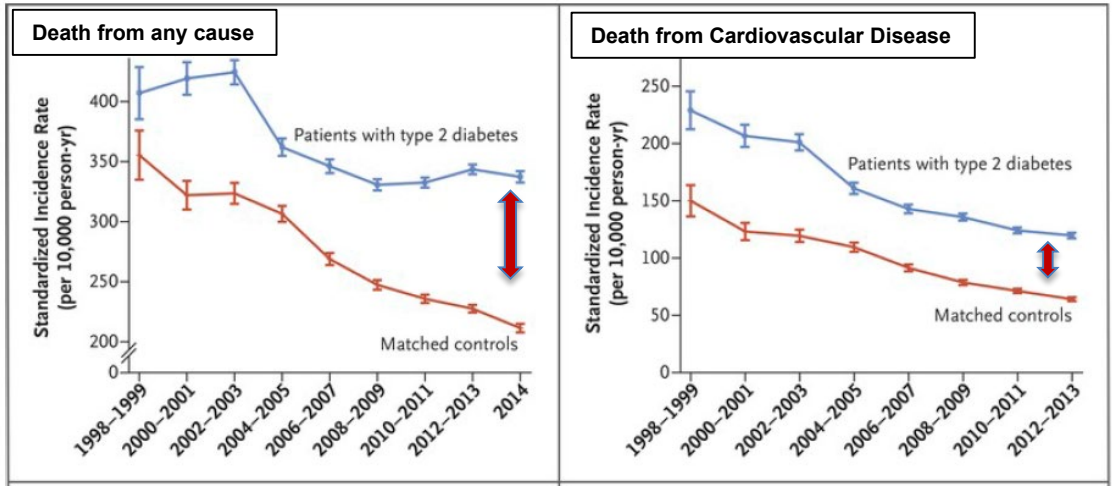
Glucagon Gvoke™ rescue pen (Xeris)

Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes

Patients with Type 1 DM



Patients with Type 2 DM



"…data from 1998 to 2014 showed marked reductions in mortality and in the incidence of cardiovascular complications among adults with either type 1 diabetes or type 2 diabetes".

"Residual Risk"

"There remains a substantial excess overall rate of all outcomes analyzed among persons with either type 1 diabetes or type 2 diabetes as compared with the general population.

Rawshani A, Rawshani A, Franzén S, et al.. **N Engl J Med**. 2017 Apr 13;376(15):1407-1418.

NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) Perspectives

➢Opportunities and Challenges

- NIH/NIDDK & Special Diabetes Program Budget

- *COVID-19 Research Disruptions*

- Recruitment, Retention, Compliance with protocols
- Issues with in-person clinic visits, and converting to virtual visits
- Increasing costs (Medications, PPEs, COVID-19 testing)
- Staff issues (Social distancing, COVID cases, etc)

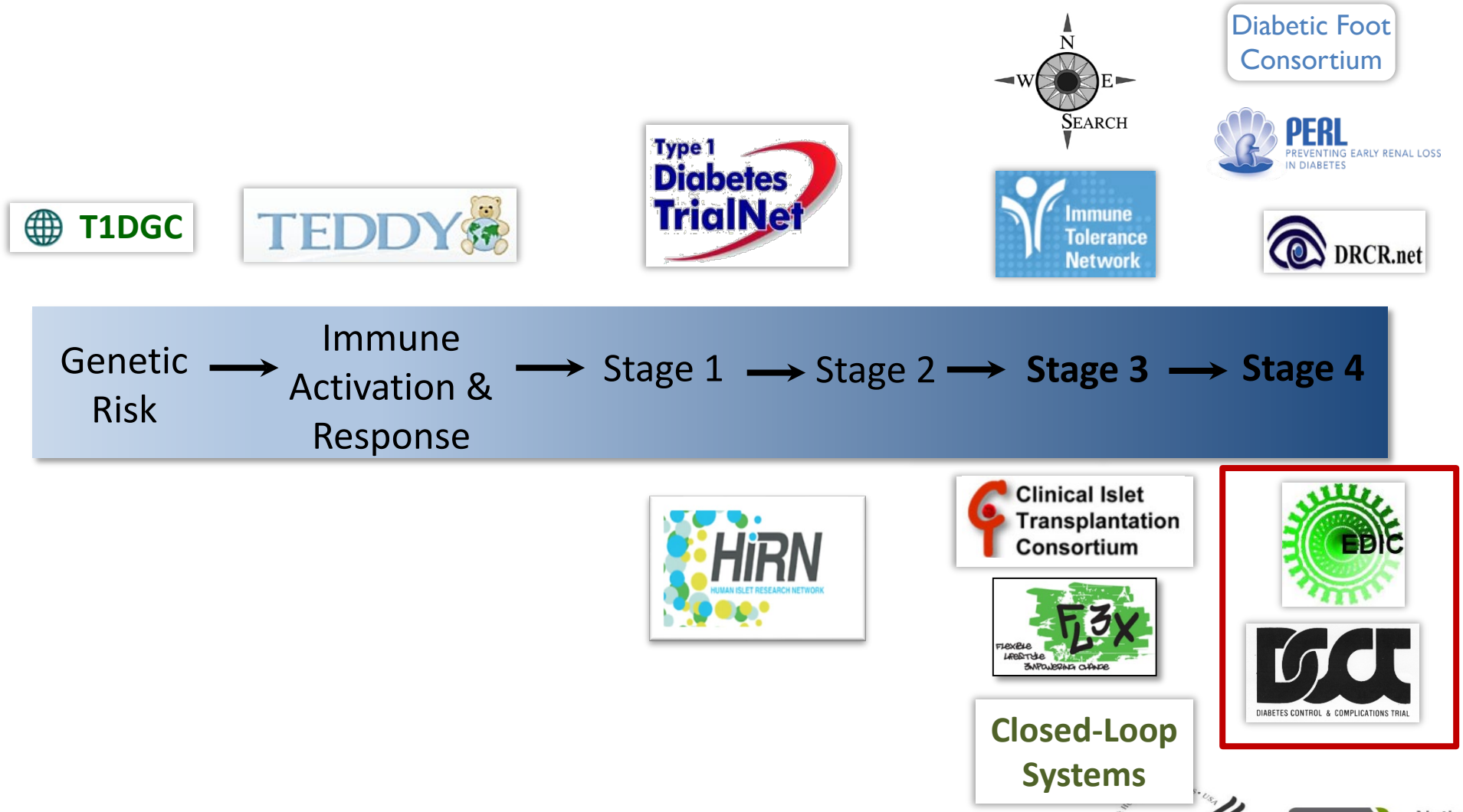
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html?utm_source=dlvr.it&utm_medium=twitter

NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) Perspectives

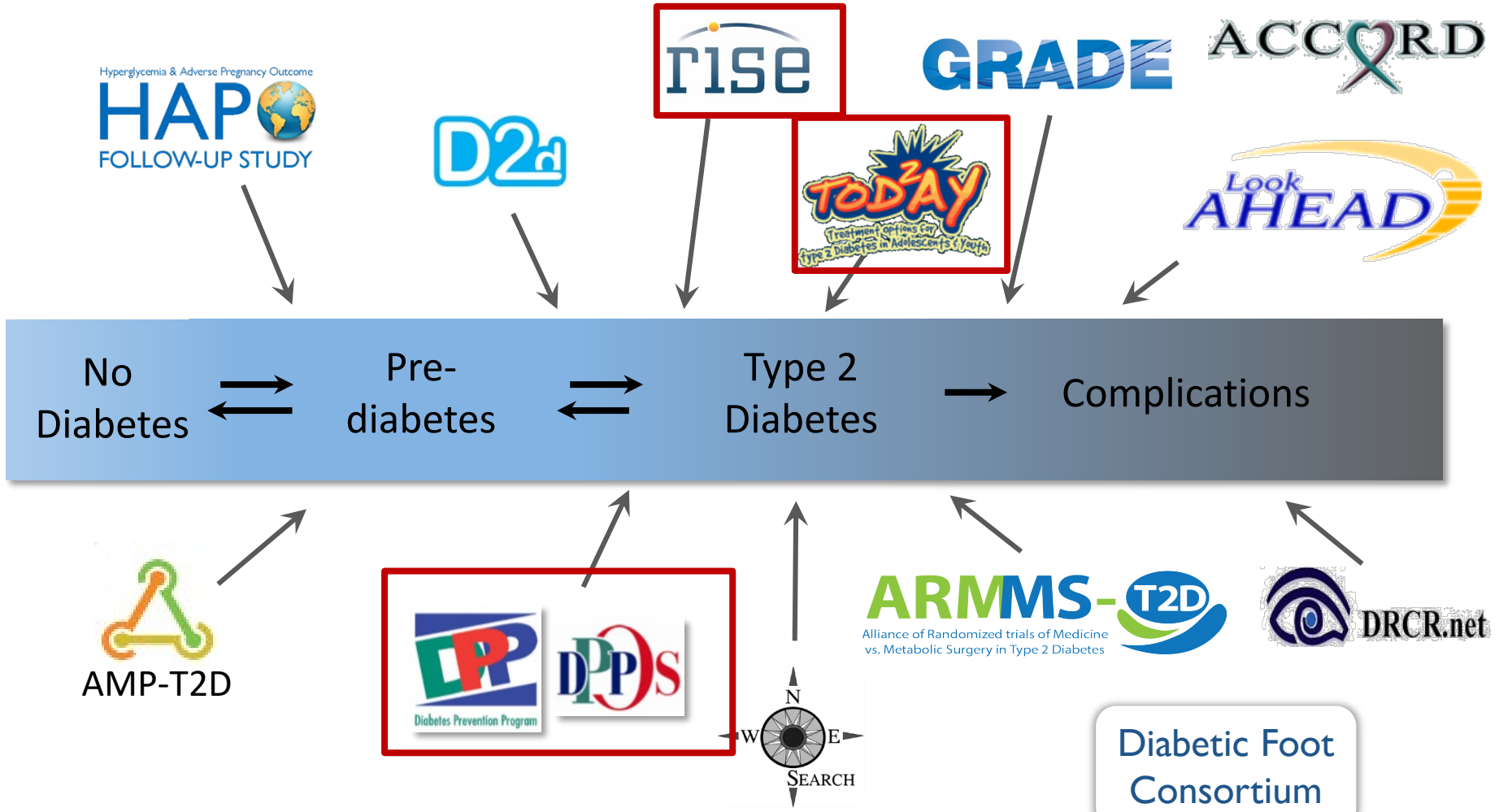
➢ Opportunities and Challenges

- NIH/NIDDK & Special Diabetes Program Budget
- COVID-19 Research Disruptions
- *Future of landmark NIDDK studies*

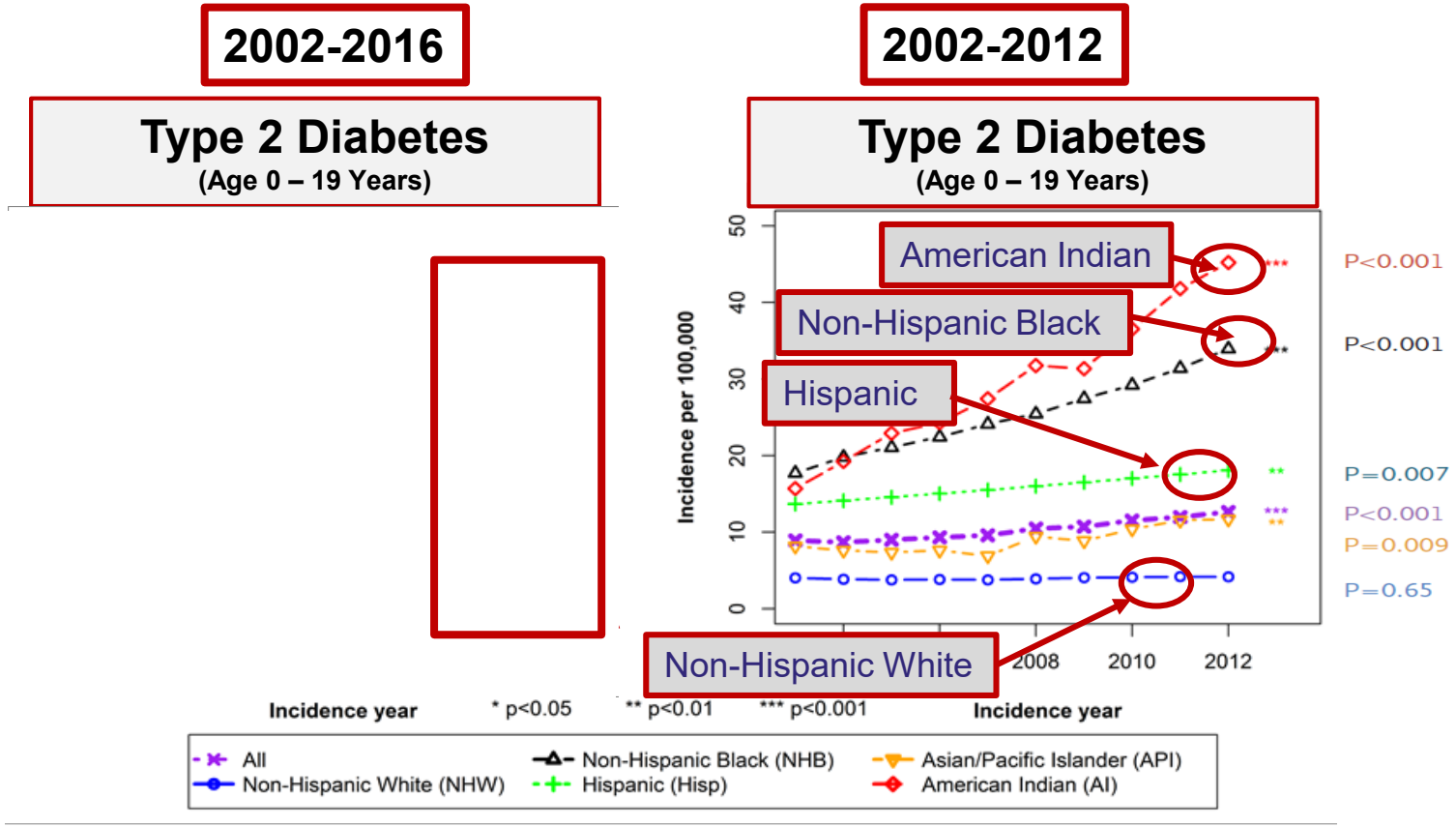
NIDDK Funds Research on All Stages of Type 1 Diabetes Research



NIDDK Funds Research on All Stages of Type 2 Diabetes Research



Incidence Trends of Type 2 Diabetes Among Youths



Mayer-Davis EJ, Lawrence JM, Dabela D. N Engl J Med 2017; 376: 1419-29.

Divers J et al. MMWR Morb Mortal Wkly Rep 2020; 69:161-165

Glycemic Observation and Metabolic Outcomes in Mothers and Offspring (GO MOMs)

GO MOMs

Characterization of Maternal Glucose

- Continuous glucose monitoring (10-14, 16-20, 24-28, 32-36 weeks' gestation)
- Early OGTT (10-14 weeks gestation)
- Evaluation of other biomarkers

Mothers: GDM at 24-28 weeks' gestation

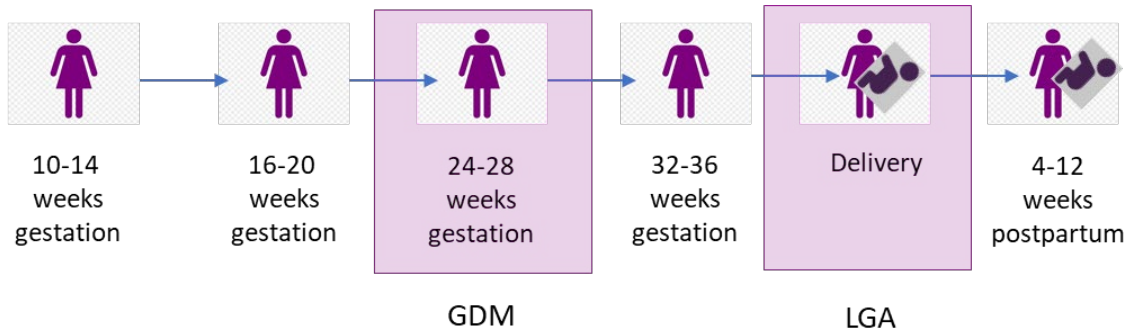
- 3hr 100g oral glucose tolerance test (OGTT)

Primary Outcomes

Offspring: large for gestational age (LGA) birth

- Birthweight >90th percentile for gestational age

Comprehensive, longitudinal characterization of maternal glucose over the course of pregnancy



Heterogeneity of Disease (Diabetes)

Interest In Diabetes Subtypes

Risk of diabetes-associated diseases in subgroups of patients with recent-onset diabetes: a 5-year follow-up study

Oana P Zaharia, Klaus Strassburger, Alexander Strom, Gidon J Bönhof, Yanislava Karusheva, Sofia Antoniou, Kálmán Bódis, Daniel F Markgraf, Volker Burkart, Karsten Müssig, Jong-Hee Hwang, Olof Asplund, Leif Groop, Emma Ahlqvist, Jochen Seissler, Peter Nawroth, Stefan Kopf, Sebastian M Schmid, Michael Stumvoll, Andreas F H Pfeiffer, Stefan Kabisch, Sergey Tselmin, Hans U Häring, Dan Ziegler, Oliver Kuss, Julia Szendroedi, Michael Roden, for the German Diabetes Study Group*

METABOLISM

Refining diabetes into five types

SCIENCE sciencemag.org

Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables

Emma Ahlqvist, Petter Storm, Annemari Käräjämäki*, Mats Martinell*, Mozhgan Dorkhan, Annelie Carlsson, Petter Vikman, Rashmi B Prasad, Dina Mansour Aly, Peter Almgren, Ylva Wessman, Nael Shaat, Peter Spégel, Hindrik Mulder, Eero Lindholm, Olle Melander, Ola Hansson, Ulf Malmqvist, Åke Lernmark, Kaj Lahti, Tom Forsén, Tiinamaija Tuomi, Anders H Rosengren, Leif Groop

Clusters provide a better holistic view of type 2 diabetes than simple clinical features

*Emma Ahlqvist, Tiinamaija Tuomi, *Leif Groop*

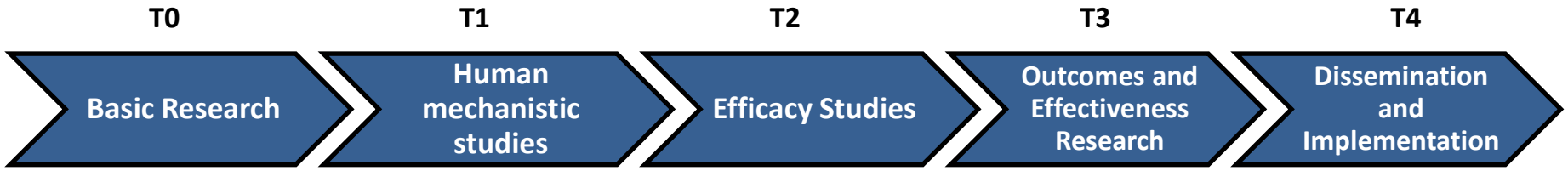
Disease progression and treatment response in data-driven subgroups of type 2 diabetes compared with models based on simple clinical features: an analysis using clinical trial data

John M Dennis, Beverley M Shields, William E Henley, Angus G Jones, Andrew T Hattersley

Novel subgroups of patients with adult-onset diabetes in Chinese and US populations

Xiantong Zou, Xianghai Zhou, Zhanxing Zhu, *Linong Ji
jiln@bjmu.edu.cn

NIDDK Research to Understand Heterogeneity of Diabetes



Define and test mechanisms
Understand pathophysiology
Identify molecular targets
Facilitate therapeutic development

Controlled studies leading to effective care

Observational or pragmatic studies to evaluate healthcare interventions on outcomes

Studies to adapt, implement broadly, and sustain efficacious care

HiRN
HUMAN ISLET RESEARCH NETWORK

TEDDY
The Environmental Determinants of Diabetes in the Young

DPP DPPOS
Diabetes Prevention Program

RADIANT
Rare and Atypical Diabetes Network

CENTERS for DIABETES TRANSLATION RESEARCH

TYPE 2 DIABETES KNOWLEDGE PORTAL
type2diabetesgenetics.org

GRADE
Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE)

NIH
Small Business Innovation Research (SBIR)
Small Business Technology Transfer (STTR)

Rare and Atypical DIAbetes NeTwork: Objectives

RADIANT
Rare and Atypical Diabetes Network

- Identify patients and families with novel rare/atypical forms of diabetes and **characterize the underlying molecular mechanisms**
  - Outreach and inclusivity of minority and underrepresented populations
- Perform **genetic** and **phenotypic** characterization of participants
- Construct an access-controlled **biorepository and database**
- Make data and biosamples available to the scientific community to **advance research** in this area

NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) Perspectives

- Opportunities and Challenges
- **Addressing Urgent Needs and Areas of Emphasis**
  - **Workforce Development**
  - **COVID 19 Research in diseases of interest to NIDDK**

nters

Work Force Development

- **Special emphasis on supporting Early Stage Investigators**

  - Higher payline, not reducing years of grant, bridge funding.

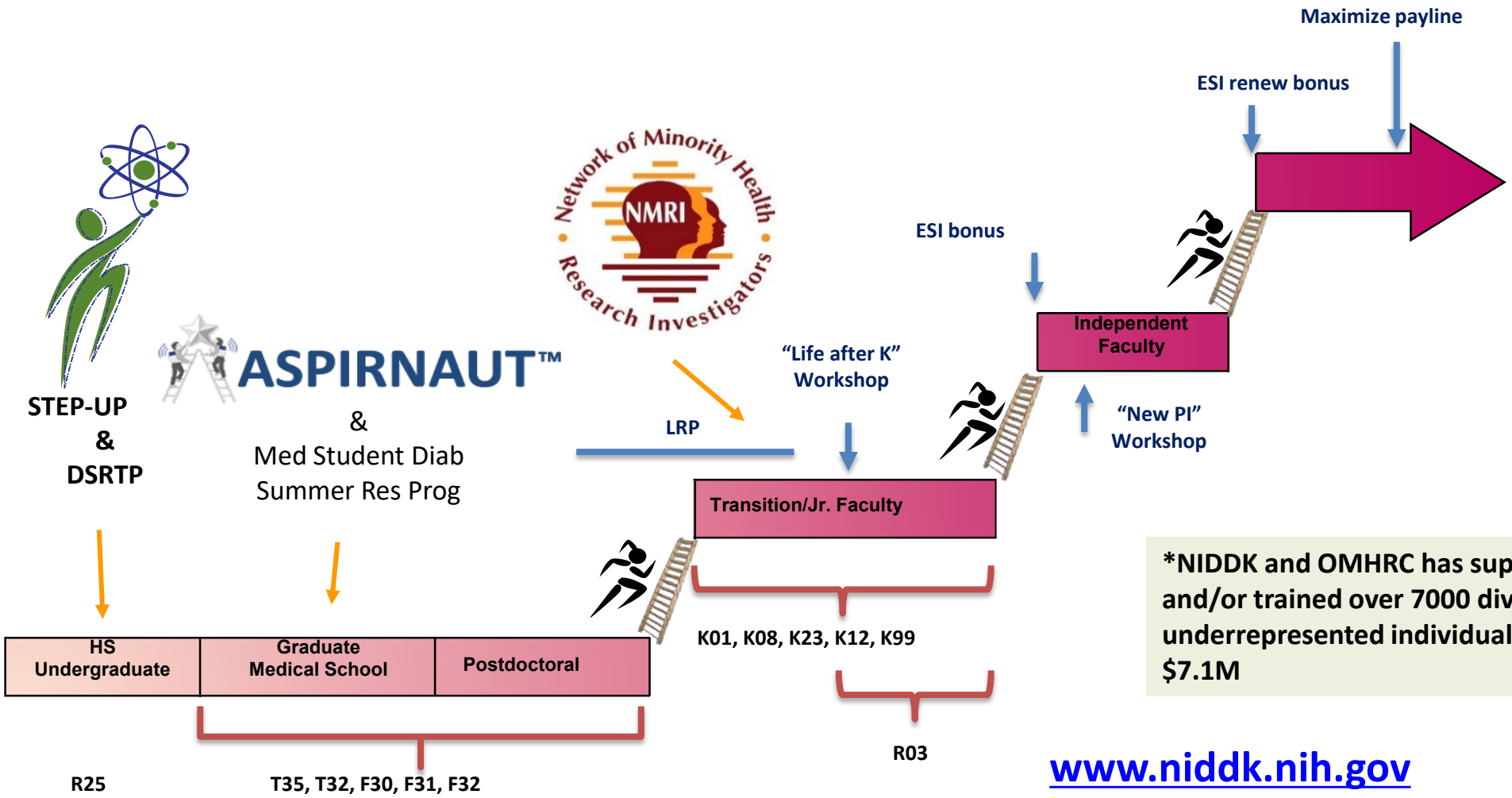
- **Providing opportunities to support emerging physician scientists via Administrative Supplements**

  - **NOT-DK-20-040:** to provide MDs or MD/PhDs with 2 years of **additional research experience** in diabetes, endocrinology or metabolic diseases to allow candidates more time for research productivity to be competitive for individual career development awards

  - **Clinical P&F opportunity through Diabetes Research Centers:** to provide MDs or MD/PhDs with supplemental funds to co-support clinical research opportunities to allow candidates to expand clinical research experience and productivity to be competitive for independent research funding

- **Diversification of the NIDDK Biomedical Research Workforce**

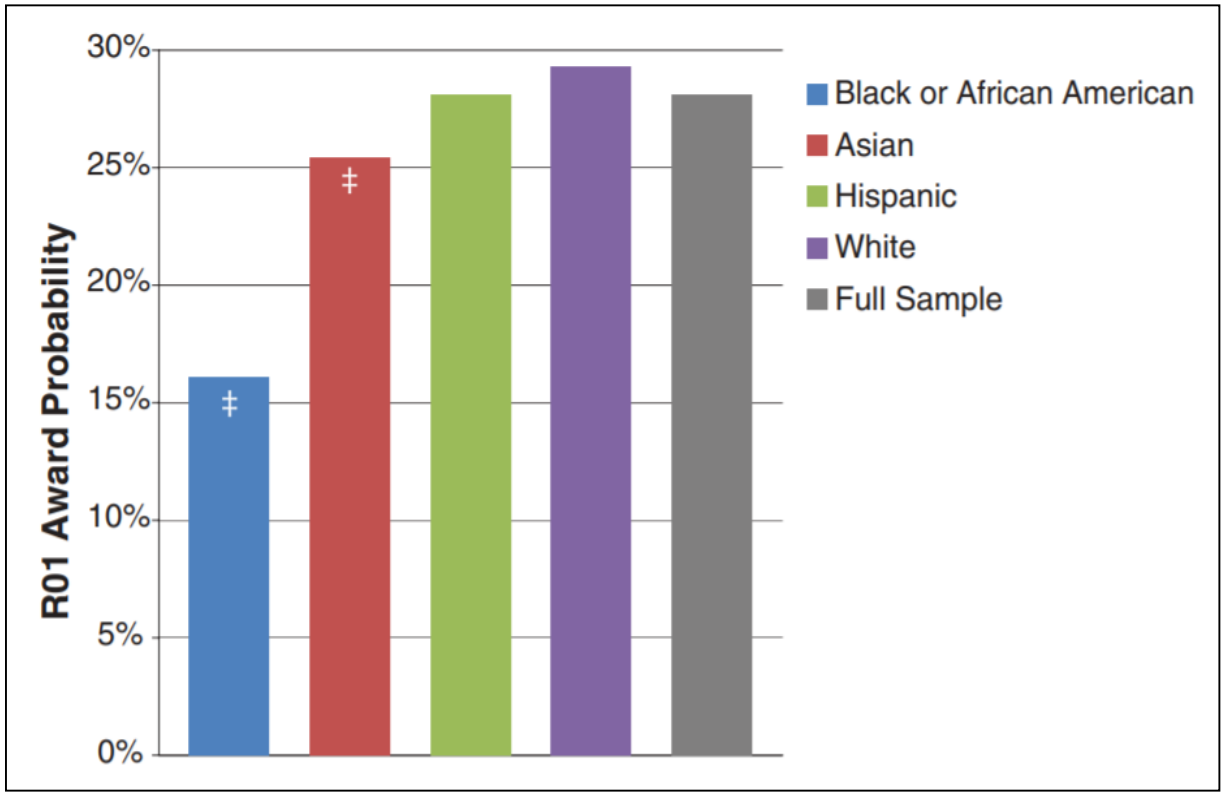
NIDDK Promotion of Scientific Workforce Diversity from HS Student through R01

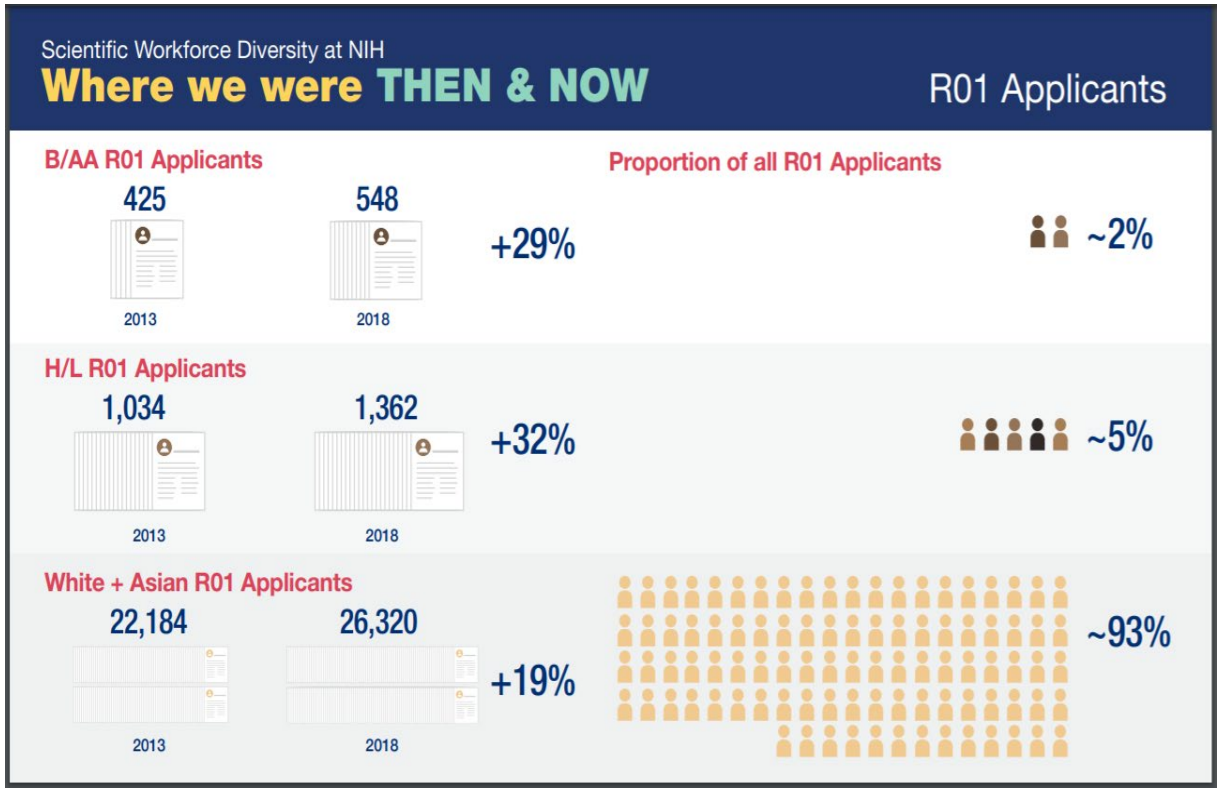


*NIDDK and OMHRC has supported and/or trained over 7000 diverse and underrepresented individuals with $7.1M

www.niddk.nih.gov

NIH R01 Award Probability and Applications by Race/Ethnicity

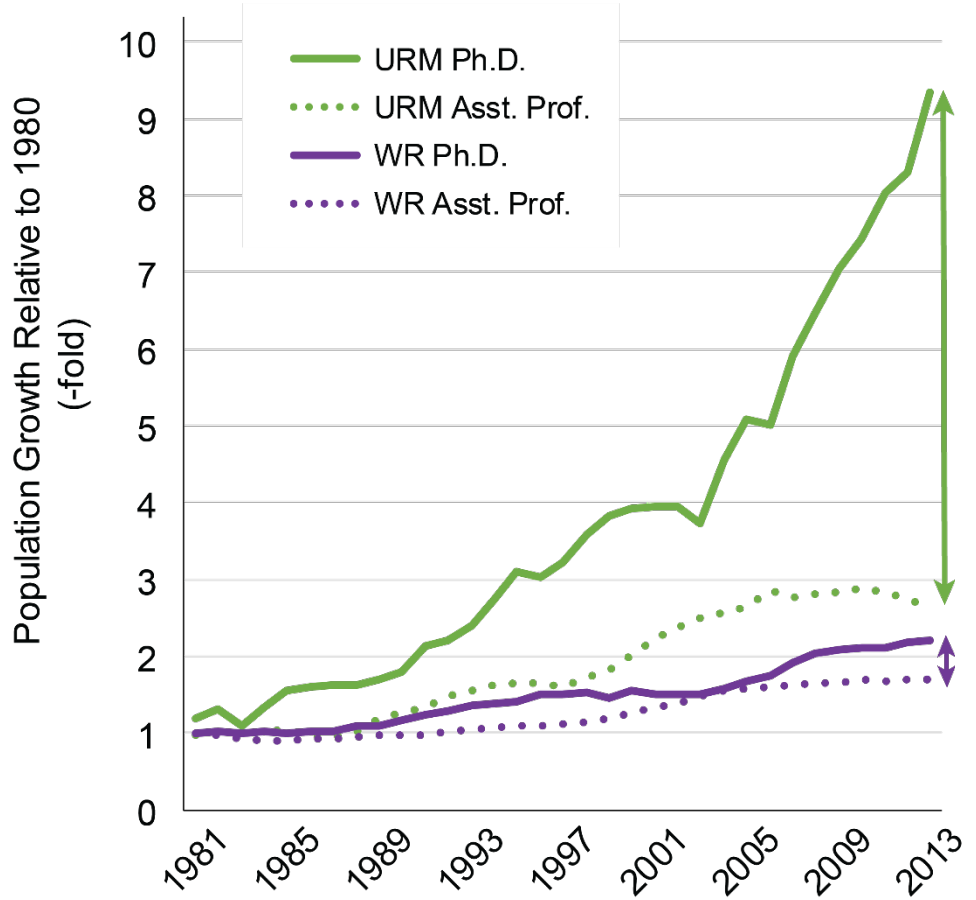




Source: Ginther, D.K., et al. (2011). *Race, ethnicity, and NIH research awards.* FY2000-FY2006

Source: NIH Office of the Director, Scientific Workforce Diversity FY2013 & FY2018

Opportunities and Challenges: Talent Pool Exists

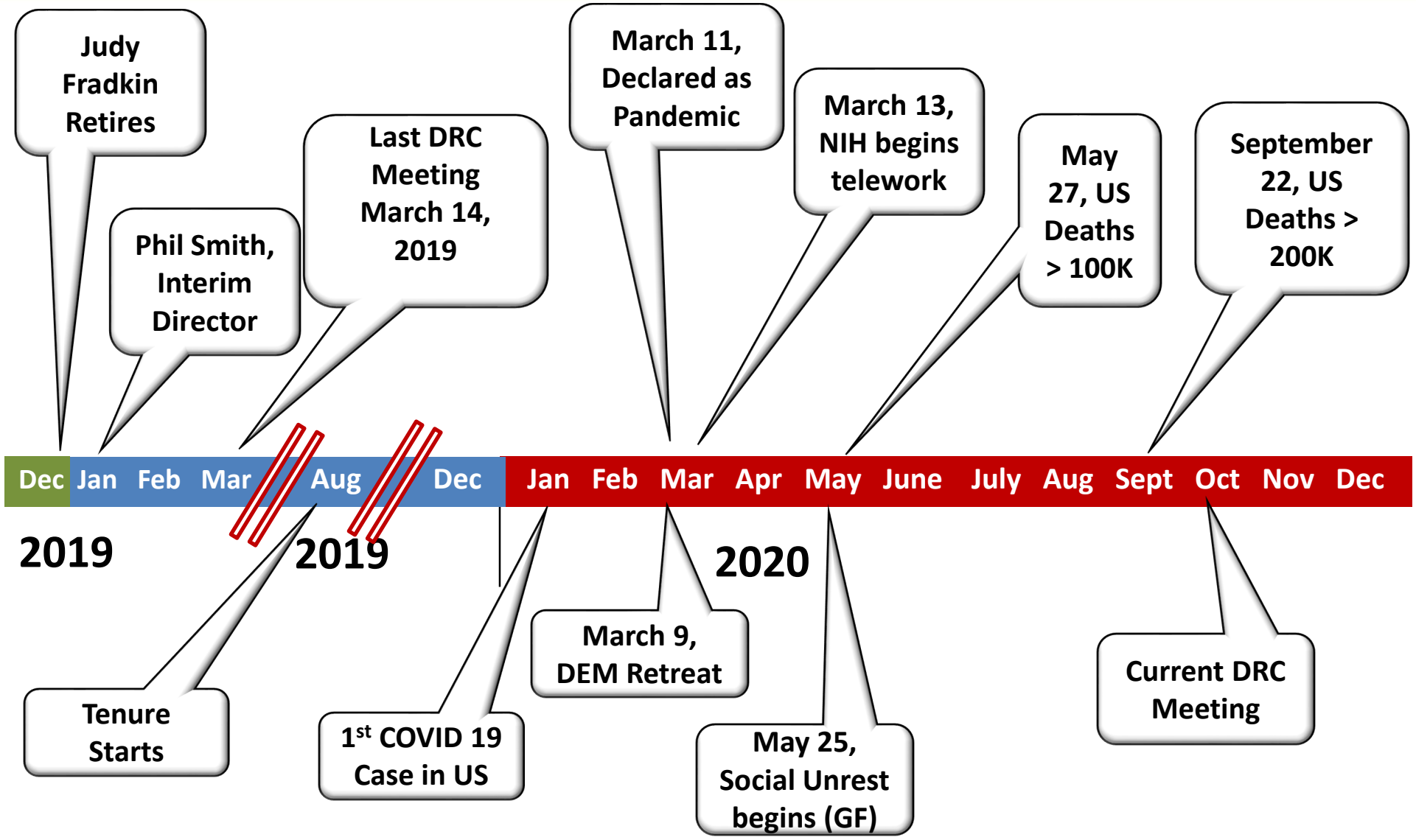


- **Institutional Research Base**
- **Attract and Retain Investigators with Diverse Backgrounds:**
- **P and F Program**

URM = Underrepresented Minority (AA/Black, Latinx, AI/AN)
WR = Well-Represented (White, Asian)

Gibbs, K. D., et al. (2016). *Decoupling the minority PhD talent pool and assistant professor hiring in the medical school basic science departments in the US*.

Timeline of Events



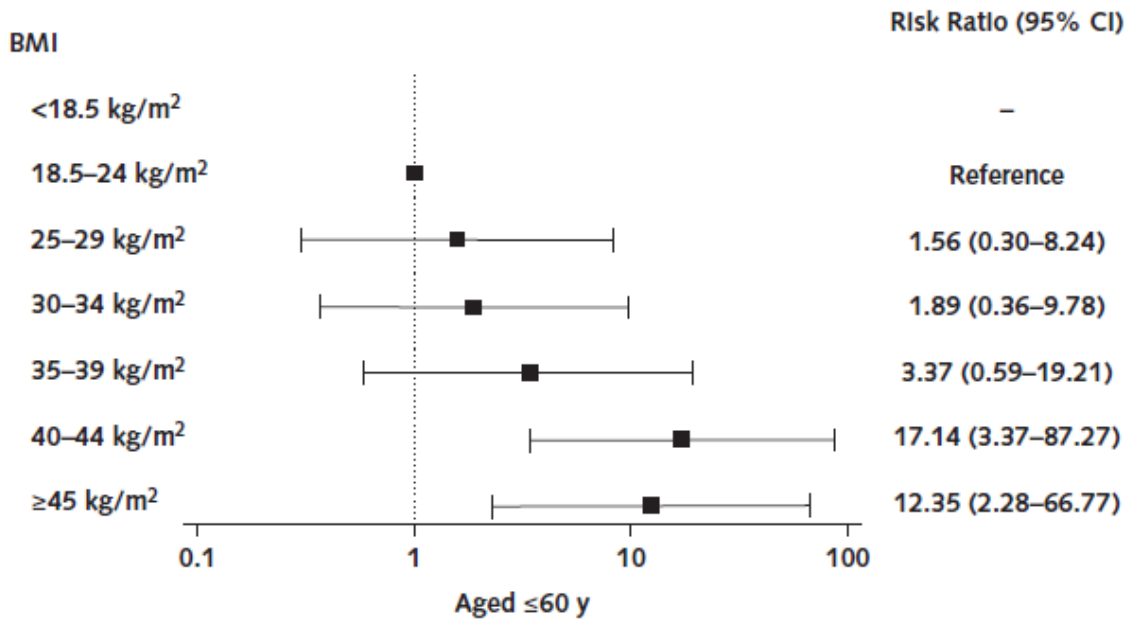
COVID 19 Outcomes: Pre-existing Diabetes & Obesity

	Article type	Study population	Prevalence of diabetes	Outcome	Risk
Zhang et al[3]	Retrospective	258	24%	Mortality	3·64 (1·08–12·21)*
Kumar et al[4]	Meta-analysis	16 003	9·8%	Severe disease	2·75 (2·09–3·62)*
Kumar et al[4]	Meta-analysis	16 003	9·8%	Mortality	1·90 (1·37–2·64)*
Guan et al[10]	Retrospective	1590	NA	Composite†	1·59 (1·03–2·45)‡
Li et al[11]	Meta-analysis	1525	9·7%	ICU admission§	2·21 (0·88–5·57)¶
Fadini et al[12]	Meta-analysis	1687	NA	Severe disease	2·26 (0·98–4·82)‖
Fadini et al[12]	Meta-analysis	355	35·5%	Mortality	1·75‖
Petrilli et al[13]	Retrospective	5279	22·6%	Hospital admission	2·24 (1·84–2·73)*
Roncon et al[14]	Meta-analysis	1382	NA	ICU admission	2·79 (1·85–4·22)*
Roncon et al[14]	Meta-analysis	471	NA	Mortality	3·21 (1·82–5·64)*
Zhou et al[15]	Retrospective	191	19%	Mortality	2·85 (1·35–6·05)*
Zhu et al[16]	Retrospective	7337	13%	Mortality	1·49 (1·13–1·96)‡
Yan et al[17]	Retrospective	193	25%	Mortality	1·53 (1·02–2·3)‡
Sardu et al[18]	Retrospective	59	44%	Survival	0·172 (0·051–0·576)‡
Yang et al[19]	Meta-analysis	4648	NA	Severe disease	2·07 (0·88–4·82)*
Barron et al[20]	Cohort study	61 414 470	0·4% type 1 diabetes	Mortality	3·50 (3·15–3·89)*
Barron et al[20]	Cohort study	61 414 470	4·7% type 2 diabetes	Mortality	2·03 (1·97–2·09)*

ICU=intensive care unit. NA=not given. *Odds ratio (95% CI). †ICU admission, or invasive ventilation, or death. ‡Hazard ratio (95% CI). §Calculated for 1056 patients (in three of six studies). ¶Risk ratio (95% CI). ‖Rate ratio (95% CI not given).

Table 1: **COVID-19 outcomes according to pre-existing diabetes**

BMI and Mortality



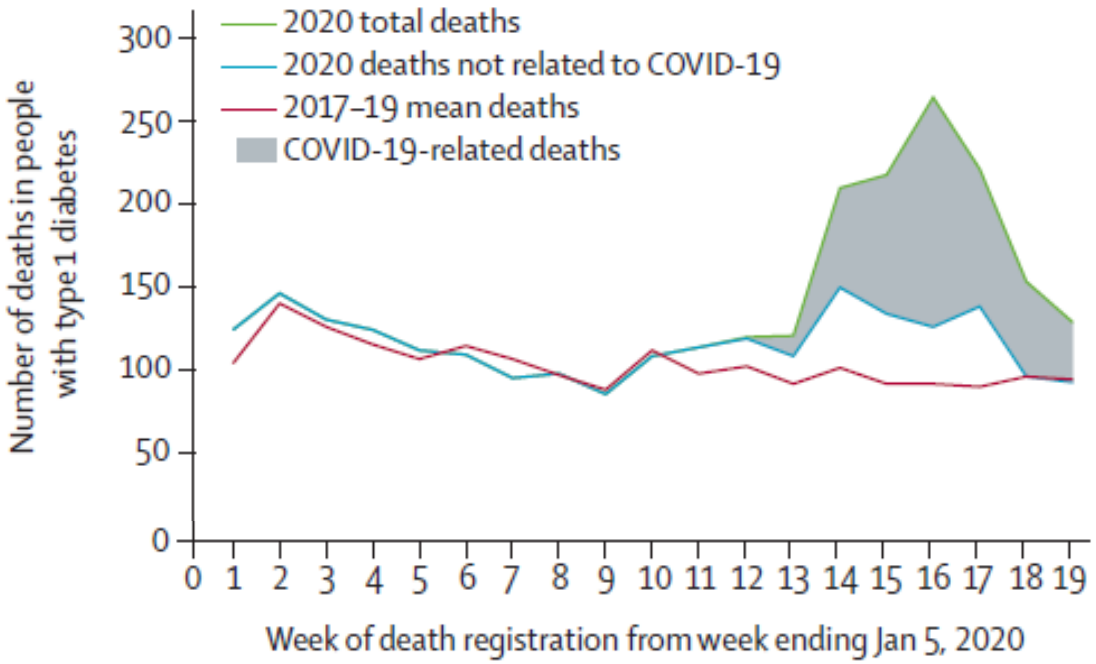
Diabetes is associated with a **2-fold increased risk of death** and other adverse outcomes from COVID-19

Tartof et al. Ann Int Med 2020

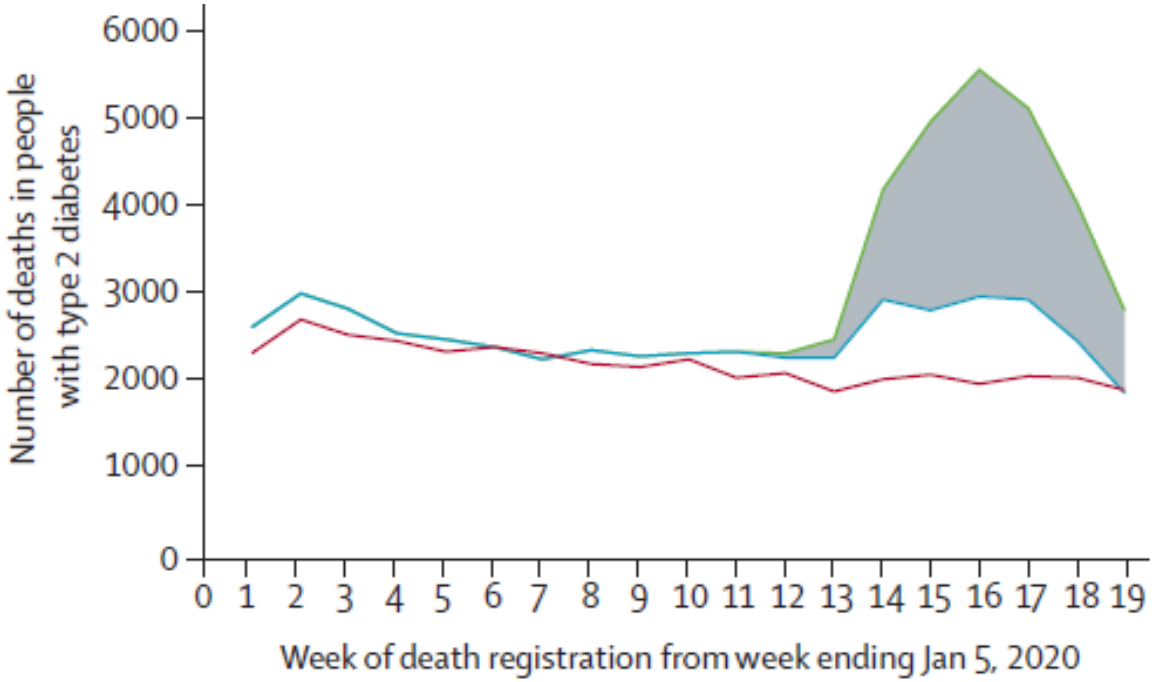
Lancet Diabetes Endocrinolol 2020, 8:782-792

COVID 19 Mortality: Type 1 and Type 2 DM

Type 1 Diabetes



Type 2 Diabetes



Holman N, et al. The Lancet Diabetes & Endocrinology DOI: (10.1016/S2213-8587(20)30271-0

COVID 19 Cases, Hospitalization and Death by Race/Ethncity

Rate ratios compared to White, Non-Hispanic Persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
CASES[1]	2.8x higher	1.1x higher	2.6x higher	2.8x higher
HOSPITALIZATION[2]	5.3x higher	1.3x higher	4.7x higher	4.6x higher
DEATH[3]	1.4x higher	No Increase	2.1x higher	1.1x higher

Race and ethnicity are risk markers for other underlying conditions that impact health — including socioeconomic status, access to health care, and increased exposure to the virus due to occupation (e.g., frontline, essential, and critical infrastructure workers).

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html (accessed 8/24/20)

Observations and Research Gaps

- Diabetes is associated with a **2-fold increased risk of death** and other adverse outcomes from COVID-19.
- Diabetes and obesity **disproportionally affects minorities** (race/ethnicities or lower socio-economic status) and there is clear evidence that some **racial and ethnic minority groups with these co-morbidities are being disproportionately affected by COVID-19.**
- There is evidence supporting associations between **hyperglycemia and poor outcomes** in patients with diabetes hospitalized with COVID-19
- **Glycemic management** of diabetes (either outpatient or inpatient) in individuals with COVID **has not been adequately studied**
- **Mechanisms** explaining the increased morbidity/mortality in individuals with diabetes, obesity and in racial and ethnic groups with diabetes and obesity are **still not precisely known**, and if known, could greatly inform on effective interventions
- Role of COVID 19 **in unmasking diabetes or inducing new cases**

NIDDK COVID-19 Funding Opportunities

- **NOT-20-018: Availability of Urgent Competitive Revision Supplements on Coronavirus Disease 2019 (COVID-19)**

  - Consider applications that propose projects that may lead to rapid translation and impact in the COVID-19 emergency)

- **RFA-DK-20-021: Mechanistic Studies of the Interaction between SARS-CoV-2/COVID-19 and Diseases and Organ Systems of Interest to NIDDK**

  - Support mechanistic oriented work on the pathways responsible for increased adverse outcomes, either due to diseases of interest to NIDDK or that result in damage to organs of interest to NIDDK, in cells, tissues, animal models and human subjects)

NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) Perspectives

- Opportunities and Challenges
- Scientific Priorities, Research Gaps & Opportunities
- Addressing Urgent Needs and Areas of Emphasis
- **Evolving Role of Diabetes Research Centers**

Thanks!

National Institute of Diabetes and Digestive and Kidney Diseases

1950 70 years 2020

National Institute of Diabetes and Digestive and Kidney Diseases

RFA-DK-20-021
Mechanistic Studies of SARS-CoV-2/COVID-19 in NIDDK Diseases and Organ Systems

Maren R. Laughlin

Division of Diabetes, Endocrinology and Metabolic Diseases

David Saslowsky and Bonnie Burgess-Beusse

Division of Digestive Diseases and Nutrition

Ivonne Schulman and Afshin Parsa

Division of Kidney, Urologic, and Hematologic Diseases

September 9, 2020

National Institute of Diabetes and Digestive and Kidney Diseases

1950 70 years 2020

Background

Obesity, older age and male sex are all associated with poor COVID-19 outcomes.

Diseases, including diabetes (odds ratio 1.48, 16 studies) and chronic kidney disease (odds ratio 3.25, 9 studies) are associated with a significantly greater risk of mortality from COVID-19.
(metanalysis by Paddy Ssentongo et al, PLoS One, August 2020)

Among other organs, COVID-19 infection is resulting in acute and possibly chronic damage and dysfunction in heart, kidney and liver.
(review by Dominik Wolff et al, Infection, August 2020)

Minority and disadvantaged populations are particularly adversely affected by COVID-19, with elevated incidence, severity and mortality.

Purpose

To provide information leading to treatment and prevention of severe outcomes in COVID-19 patients with NIDDK diseases, or in tissues of interest to NIDDK

RFA-DK-20-021

Support new basic and clinical mechanistic research on SARS-CoV-2 and COVID-19 within NIDDK's interests

diabetes and other metabolic diseases, obesity, and endocrine, digestive, liver, pancreas, kidney, urological, and hematologic tissues and diseases

Identify biological mechanisms surrounding

- Role of pre-existing diseases
- Adverse acute or chronic outcomes in NIDDK tissues / diseases, including new onset of disease

RFA-DK-20-021
Diabetes, Metabolic and Endocrine Diseases

- Mechanisms for any increased susceptibility or altered course of COVID-19 due to **type 1 or type 2 diabetes or diabetic complications;**
- **Roles of dysregulated glycemia, insulin resistance**, insulin secretion, etc. in severity of response to COVID-19 infection;
- Mechanisms whereby COVID-19 infection results in acute or chronic metabolic dysfunction, or the **onset of diabetes or other endocrine diseases;**
- Mechanisms involved in **alterations in the course of existing type 1 or type 2 diabetes** or the complications of diabetes following COVID-19 infection.

RFA-DK-20-021
Obesity and Nutrition

- Tissues, biological systems and pathways involved in increased susceptibility, greater severity, or diminished response to treatment for COVID-19 in **obesity**;
- Aspects of **adipose tissue biology** involved in the severity of COVID-19 infection, disease course, response to treatment, and outcomes in obesity;
- Mechanisms for impact of **nutritional status** on variability in COVID-19 susceptibility, course, and response to treatment;
- Do **diet-host-microbiome interactions** impact the course of COVID-19 infection?

Why Issue an RFA?

- Many publications on COVID-19 and SARS-CoV-2 already
- Applications can be submitted in the normal R01 competition.
- Adverse impact of diabetes, obesity, kidney diseases, etc. in COVID-19 outcomes are well recognized and of high priority, with many interested researchers.

BUT

- Many of the publications are observational studies
- Few animal models exist
- Low access to tissues from COVID patients or the facilities to work with virus; mechanistic data are scarce
- **A mechanism is needed for small or risky studies that have few preliminary data to support them**

RFA-DK-20-021

RFA-DK-20-021

Mechanistic Studies of the Interaction between SARS-CoV-2/COVID-19 and Diseases and Organ Systems of Interest to NIDDK (R01 Clinical Trial Optional)

Trans-NIDDK RFA	Budget: $250,000 DC/year
Issued: July 10, 2020	Duration: 3 years
Due: December 16, 2020	$5M/year (11-13 awards)
Council: May, 2021	reduced emphasis on preliminary data

Will support studies in human subjects or model organisms, using isolated tissues, cells, or in vivo approaches

P and F Studies Involving Cystic Fibrosis Related Diabetes (CFRD) at the Diabetes Centers

Thomas Eggerman

Cystic Fibrosis Program Director

NIDDK/DEM

October 1, 2020

Cystic Fibrosis Background

- Autosomal recessive mutation in the cystic fibrosis transmembrane conductance regulatory protein (CFTR)
- Affects 1/3000 of Northern European descent
- Involves lungs, pancreas, liver, kidney and intestines
- 80% die of pulmonary complications
- Life expectancy now in 40s
- About half of adults have diabetes
  - 25% of adults with diabetes survive to age 30
  - 60 % of adults without diabetes survive to age 30

FY2020 Locations of Cystic Fibrosis Centers

Institution (grant year #)	Partners
U. Alab Birm (14)	Southern Res. Inst.
U. N Carolina (16)	
Dartmouth (3)	
U. Cincinnati (3)	
Seattle Children's Hospital (11)	University of Washington
U. Iowa (21)	
U. Cal SF (16)	U. California Davis
Emory (1)	Augusta U, Georgia Tech

Cystic Fibrosis P and Fs at Diabetes Centers

- Plan to fund 2 two-year P and F's every other year beginning in 2020-21 fiscal year.
- Research must involve Cystic Fibrosis Related Diabetes
- Excludes Institutions with Cystic Fibrosis Centers
- Can be either basic or clinical
- $50,000 Direct costs/yr maximum
- Review through usual Center specific process
- One P and F/Center forwarded to NIDDK for review
- Formal announcement forthcoming

P and F Investigator Eligibility

- New investigators without current or past NIH research support as a PD/PI
- Established investigators with no previous work in ~~diabetes~~ **Cystic Fibrosis** who wish to apply their expertise to a problem in this area
- Investigators developing new research techniques/technologies that could be used in a DRC Core facility.
- All eligible investigators, however, must have faculty appointments and be independent investigators.
- Postdoctoral fellows or their equivalent are not eligible.
- P and F awards are not intended to serve as 'bridge' funding for established ~~diabetes~~ **Cystic Fibrosis** researchers who may be experiencing a gap in research funding.
- Applications from historically underrepresented Investigators are strongly encouraged.

Upcoming Cystic Fibrosis Related Diabetes Workshop

- June 24-25 2021 (just before ADA meeting in Washington DC)
- NIH Campus Bldg. 35, Room 620/630

National Institute of Diabetes and Digestive and Kidney Diseases

1950 70 years 2020

Administrative Supplements for Diabetes Research Centers to enable Clinical Pilot and Feasibility Studies for Emerging Physician Scientists

Corinne M. Silva, PhD.

Program Director, Diabetes Research Centers

Division of Diabetes, Endocrinology and Metabolic Diseases

NIDDK/NIH

Clinical Pilot and Feasibility Studies for Emerging Physician Scientists-Purpose

- Allow candidates to expand their clinical research experience and productivity *to help them successfully compete* for *independent research funding* in the next stage of their research careers as physician-scientists

- Augment the level of funding to allow human subjects research activities that might have been too expensive under the Center's standard funding policies

Administrative Supplements for Diabetes Research Centers to enable Clinical Pilot and Feasibility Studies for Emerging Physician Scientists

- Only ***one supplement application*** from each DRC
- Supplement ***cannot be used to replace*** Center P&F funding of the candidate's project
- Eligible Centers will have end date of ***September 2022*** or later
- P&F candidate must have ***MD*** (or equivalent) or an ***MD/PhD*** degree w/ ***no more than 4 years*** of postdoc research experience
- P&F project must be ***patient-oriented research***

Administrative Supplement Application Details

- solicit new 2-year patient-oriented clinical P&Fs with a maximum budget of $200K Direct Costs ($100K/year)
- P&F project must have undergone the Center P&F Program review process and already be approved for funding by Center
- starting a new P&F award no later than September 2021
- P&F candidates from groups that are underrepresented in health-related research as defined by NIH-are strongly encouraged

Application Due Date—April 1, 2021

Award Date—Summer 2021

Discussion on Strategies Regarding COVID19 & Diabetes (Moderators, Drs. Pessin and Leibel)

An opportunity to discuss how the DRCs-as a strong network of diabetes researchers and programs across the country-could facilitate addressing the COVID-19 pandemic and related challenges such as health disparities

COVID-19 & Diabetes: A Research Road Map

Verena van der Heide, Michael Schotsaert, Rachel Brody, Adolfo Garcia-Sastre, Carmella Molina-Evans, Mark Atkinson, Dirk Homann

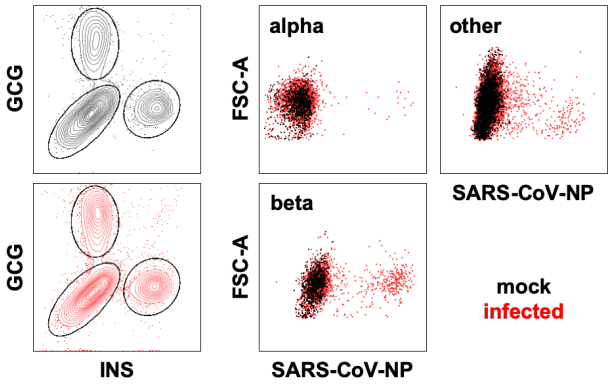
Icahn School of Medicine at Mount Sinai, New York, NY

In response to growing concerns by the NIDDK that SARS-CoV-2 infection may trigger diabetes, we have assembled a team of investigators and collaborators in July 2020 to interrogate this possibility in a series of complementary investigations.

1., expression of viral entry factors in the non-diabetic, T1D and T2D human pancreas: using a combination of scRNAseq (re-analysis of public data sets) as well as *in situ* hybridization (ISH) and multiplexed immunohistochemistry (IHC) conducted with pancreatic tissue sections from the nPOD Consortium, we have found that ACE2 is minimally expressed by islet endocrine cells and largely restricted to microvascular and ductal structures. This work has now been posted on a preprint server (https://doi.org/10.1101/2020.08.31.270736) together with very similar findings reported by the group of Dr. A. Powers (https://doi.org/10.1101/2020.08.31.275719).

2., virus traces and inflammatory signatures in pancreatic autopsy tissue from fatal COVID-19 cases: drawing on the Mount Sinai Pathology Biorepository and other sources, we are employing multiplexed IHC and ISH techniques to delineate expression of SARS-CoV-2 protein and message as well as immune cell infiltrates and other markers of inflammation.

3., in vitro SARS-CoV-2 infection studies: using isolated islets from non-diabetic donors, we employ flow cytometry, mass cytometry, scRNAseq and other methodologies to assess the consequences and mechanisms of *in vitro* SARS-CoV-2 infection. Our preliminary findings indicate that a subset of beta cells can be readily infected, and we are now extending these investigations to pancreatic slice studies.



Human islets were cultured for 48h in the absence (mock) or presence of SARS-CoV-2 (infection with the Seattle strain [BEI Resources] at an MOI of ~0.05), subsequently dispersed and analyzed by flow cytometry. Left contour plots: distinction of alpha cells (GCG+), beta cells (INS+) and other cells (GCG-/INS-) following mock treatment (top) and infection (bottom). Right dot plots: SARS-CoV-NP staining of mock (black) and infected (red) islet cell subsets.

4., complementary animal studies: based on emerging insights in the above and other work reported in the literature, we are harnessing the hamster model as well as mouse-adapted SARS-CoV-2 and human islet cell transplants to determine the potential for beta cell damage accrued in the wake of *in vivo* viral infection.

In other lines of investigation not outlined here, we are also pursuing questions about the role of high fat diet, obesity and T2D in promoting an aggravated disease course after SARS-CoV-2 infection.

2020 NIDDK Diabetes Research Center Directors' Annual Meeting

October 1, 2020

Pilot and Feasibility Presentations

Session I: Moderator, Dr. Michael Rickels, Professor, University of Pennsylvania Perelman School of Medicine

1:15-1:30 Spatial metabolomics for human kidney interrogation of early diabetic kidney disease
Petter Bjornstad, M.D., University of Colorado Anschutz Medical Campus

1:30-1:45 Iatrogenic Hyperinsulinemia, not Hyperglycemia, Drives Insulin Resistance in Type 1 Diabetes as Revealed by Comparison to GCK-MODY (MODY2).
Justin Gregory, M.D., Vanderbilt University School of Medicine

1:45-2:00 Glycemic and Energetic Effects of Glucagon-Receptor Agonism
Kirk Habegger, Ph.D., University of Alabama at Birmingham

2:00-2:15 Ciliary GPCRs regulate glucose-regulated insulin and glucagon secretion in pancreatic islets
Peter K. Jackson, Ph. D., Stanford University School of Medicine

2:15-2:30 Assessment of Kidney Function in Diabetic Non-Human Primates by Contrast-Enhanced Ultrasound and Metabolomic Profiling
Kennita Johnson, Ph.D., UNC/NCSU Joint Department of Biomedical Engineering

2:30-2:45 Apolipoprotein C3 in complications of diabetes
Jenny Kanter, Ph.D., University of Washington

2:45-3:00 Mechanisms of exercise resistance in metabolic disease
Sarah Lessard, MSc, PhD, Joslin Diabetes Center

3:00-3:15 Stem Cell-Derived Islet Organoids for Diabetes Therapy
Jeffrey R. Millman, Ph.D., Washington University School of Medicine in Saint Louis

ABSTRACTS

Spatial metabolomics for human kidney interrogation of early diabetic kidney disease
Petter Bjornstad, M.D., University of Colorado Anschutz Medical Campus

The goal of Dr. Petter Bjornstad's DRC P&F grant is to comprehensively detail the metabolic and energetic patterns of early diabetic kidney disease (DKD) in type 1 diabetes (T1D). The grant provides support to add untargeted and targeted spatial metabolomics analyses of kidney tissues by matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) from young adults with (n=20) and without (n=20) T1D. Our central objective is to quantify metabolite data in discrete kidney compartments and establish a regulatory hierarchy of intrarenal metabolic changes that closely correlate with structural and hemodynamic alterations of diabetic kidney injury, in order to define the metabolic pathways that may drive early DKD in T1D.

Iatrogenic Hyperinsulinemia, not Hyperglycemia, Drives Insulin Resistance in Type 1 Diabetes as Revealed by Comparison to GCK-MODY (MODY2)
Justin Gregory, M.D., Vanderbilt University Medical Center

Although insulin resistance consistently occurs with type 1 diabetes, its predominant driver is uncertain. We therefore determined the relative contributions of hyperglycemia and iatrogenic hyperinsulinemia to insulin resistance using hyperinsulinemic-euglycemic clamps in three participant groups (n=10/group) with differing insulinemia and glycemia: healthy controls (euinsulinemia, euglycemia), glucokinase maturity-onset of the young (GCK-MODY; euinsulinemia, hyperglycemia), and type 1 diabetes (hyperinsulinemia, hyperglycemia matching GCK-MODY). We assessed the contribution of hyperglycemia by comparing insulin sensitivity in control and GCK-MODY and the contribution of hyperinsulinemia by comparing GCK-MODY and type 1 diabetes. HbA1c was normal in controls and similarly elevated for type 1 diabetes and GCK-MODY. Basal insulin levels in control and GCK-MODY were nearly equal but were 2.5-fold higher in type 1 diabetes. Low-dose insulin infusion suppressed endogenous glucose production similarly in all groups and suppressed nonesterified fatty acids similarly between control and GCK-MODY, but to a lesser extent for type 1 diabetes. High-dose insulin infusion stimulated glucose disposal similarly in control and GCK-MODY, but was 29% and 22% less effective in type 1 diabetes, respectively. Multivariable linear regression showed insulinemia—but not glycemia—was significantly associated with muscle insulin sensitivity. These data suggest iatrogenic hyperinsulinemia predominates in driving insulin resistance in type 1 diabetes.

Glycemic and Energetic Effects of Glucagon-Receptor Agonism
Kirk Habegger, Ph.D., University of Alabama at Birmingham

Glucagon is an essential regulator of glucose and lipid metabolism that also promotes weight loss. Thus, novel therapeutics that stimulate glucagon-receptor (GCGR) signaling are promising targets for treatment of obesity; however, the mechanism(s) underlying these effects are yet to be fully elucidated. We have recently observed that mice deficient for liver Fgf21 (Fgf21ΔLiver) are partially resistant to the anti-obesity effects of GCGR agonism, clearly implicating hepatic FGF21 as an essential component of glucagon's weight-loss effects. FGF21 signals through the canonical FGF-receptors coupled with an obligate co-receptor (□Klotho, Klb). Expression of KLB, and therefore FGF21 signaling, is limited to adipose tissue, liver, and neurons of the hypothalamus. As the hypothalamus has crucial roles in regulating energy balance, we hypothesized that the anti-obesity action of the glucagon-FGF21 system signals through a central mechanism. To test this hypothesis, we generated diet-induced obese mice with neuronal Klb deficiency (Klbflox x Synapsin1Cre: KlbΔCNS). Following chronic GCGR activation via the selective GCGR agonist IUB288, KlbΔCNS mice exhibit a partial reduction in body weight (11%) in comparison to control mice (18%) ($p<0.001$), suggesting that FGF21 mediates glucagon's anti-obesity properties through central action. Consistent with GCGR-stimulated, neuronal FGF21 signaling, we found that neuronal activation, measured via immunohistochemical analysis of

FOS expression, was increased in the SCN of the hypothalamus following IUB288 injection. Taken together, these data suggest that glucagon mediates part of its anti-obesity properties through FGF21-KLB signaling in the CNS and has implications for future treatments against obesity and the metabolic syndrome. Moreover, while the best-known roles of glucagon are as the key counter-regulatory hormone opposing insulin; we recently found that daily treatment with IUB288 enhanced glucose disappearance (kg) during an insulin tolerance test. Confirming these initial observations, we likewise observed enhanced insulin sensitivity and glucose uptake following GCGR-agonism in a hyperinsulinemic-euglycemic clamp. Finally, glucagon and insulin co-treatment in primary hepatocytes, synergistically enhanced insulin signaling through Akt. Taken together, these data reveal that GCGR agonism stimulates enhanced glucose homeostasis that is mediated in part by enhanced insulin action. This heretofore-unappreciated aspect of glucagon biology has implications for GCGR agonism in therapeutic strategies for diabetes.

Discovery of ciliary G protein-coupled receptors regulating pancreatic islet insulin and glucagon secretion

Peter K. Jackson, Ph. D., Stanford University School of Medicine

Multiple G protein coupled receptors (GPCRs) are expressed in pancreatic islet cells but the majority have unknown functions. We observe specific GPCRs localized to primary cilia, a prominent signaling organelle, in pancreatic α- and β-cells. Loss of cilia disrupts β-cell endocrine function, but the molecular drivers are unknown. Using functional expression, we identified multiple GPCRs localized to cilia in mouse and human islet α- and β-cells, including FFAR4, PTGER4, DRD5, ADRB2, KISS1R, and P2RY14. Free fatty acid receptor 4 (FFAR4) and prostaglandin E receptor 4 (PTGER4) agonists stimulate ciliary cAMP signaling and promote glucagon and insulin secretion by α- and β-cell lines, and by mouse and human islets. Transport of GPCRs to primary cilia requires TULP3, whose knockdown in primary human and mouse islets depleted ciliary FFAR4 and PTGER4, and impaired regulated glucagon or insulin secretion, without affecting ciliary structure. Our findings provide index evidence that regulated hormone secretion by islet α- and β-cells is regulated by ciliary GPCRs.
(Chien-Ting Wu, Keren I. Hilgendorf, Romina J. Bevacqua, Yan Hang, Janos Demeter, Seung K. Kim, Peter K. Jackson)

Assessment of Kidney Function in Diabetic Non-Human Primates by Contrast-Enhanced Ultrasound and Metabolomics Profiling

Kennita Johnson, Ph.D., UNC/NCSU Joint Department of Biomedical Engineering

Although detection methods of Diabetic kidney disease (DKD) have improved, a large fraction of people with diabetes still progress to renal insufficiency. A tool to predict which patients will progress rapidly from microalbuminuria to kidney failure will help clinicians determine who will benefit from aggressive treatment. The formation of an interdisciplinary collaboration from the four NCDRC universities (Wake Forest, Duke, North Carolina A&T and University of North Carolina Chapel Hill) has combined our expertise in pursuit of a sensitive biomarker for DKD utilizing contrast-enhanced ultrasound (CEUS) and metabolomics. We propose to use an old world non-human primate model that spontaneously develops Type 2 diabetes in mid-life after a long period of insulin resistance, rising fasting blood glucose values, and chronic central adiposity. We will compare kidney function and perfusion of those models with groups of healthy and insulin resistant nondiabetic primates. The microbubble contrast agent used in CEUS is safe for compromised kidneys and acts as an effective tracer for measuring perfusion in the kidney. Metabolomics evaluates a much larger number of solutes in biofluids than those detectable by standard clinical chemistry and therefore, may reveal biomarkers for earlier progression of disease. CEUS perfusion imaging and metabolomics profiling of biofluids will be performed at 3 time points over the course of the year. Demonstration of biofluid changes detected by metabolomics and kidney perfusion differences detected by CEUS, between the normal and disease state

in a model similar to human DKD, will facilitate exploration of these techniques in humans in clinical studies.

Apolipoprotein C3 in complications of diabetes
Jenny E. Kanter, University of Washington

Diabetes is a significant risk factor for atherosclerotic cardiovascular disease (CVD) and kidney disease. Here we explore the relationship between atherosclerosis and diabetic kidney disease and whether apolipoprotein C3 (APOC3)-mediated dyslipidemia plays a mechanistic role. Reducing APOC3 levels using an antisense to APOC3 dramatically reduces circulating APOC3 levels and plasma triglycerides in a mouse model of type 2 diabetes with atherosclerosis and kidney disease. APOC3 inhibition results in protection against diabetes-accelerated atherogenesis and improvement in albumin excretion and glomerular hypertrophy, potentially suggesting a role for APOC3 and the dyslipidemia it represents not only in diabetes-accelerated atherosclerosis but also diabetic kidney disease.

Mechanisms for exercise resistance in metabolic disease
Sarah Lessard, MSc, PhD, Joslin Diabetes Center

High aerobic exercise capacity is one of the best predictors of health and longevity. However, individuals with impaired glucose tolerance and diabetes have blunted improvements in aerobic exercise capacity with standardized exercise training. This "exercise resistance" likely leads to persistently low levels of exercise capacity in people with metabolic disease. Our work in animal models identified increased activation of the C-Jun N-terminal kinase (JNK) in skeletal muscle during exercise as a potential mechanism leading to exercise resistance. The aim of our DRC pilot project was to determine if impaired glucose tolerance is associated with altered JNK activation with exercise in human participants. We studied 23 participants and found that low aerobic exercise capacity was correlated with impaired glucose tolerance and insulin resistance. Moreover, we demonstrated that JNK activation during exercise was significantly higher in participants with impaired glucose tolerance. These results demonstrate that mechanisms for exercise resistance identified in animal models may also underlie impaired aerobic capacity in humans.

Stem Cell-Derived Islet Organoids for Diabetes Therapy
Jeffrey R. Millman, Ph.D., Washington University School of Medicine in Saint Louis

Cellular and tissue engineering promises new therapeutic options for people suffering from a wide range of diseases. Differentiation of stem cells is a powerful renewable source of these functional replacement cells and tissues that can be grown in the laboratory. Diabetes is cause by the death or dysfunction of insulin-secreting islets, which are a tissue type found in the pancreas that contain β cells and other endocrine cell types. We have recently developed approaches combining modulating the actin cytoskeleton and signal transduction pathways during differentiation to produce stem cell-derived islets (SC-islets) capable of undergoing glucose-stimulated insulin secretion, their primary function. We have further expanded this approach to make SC-islets from patients with diabetes and used CRISPR-Cas9 to correct their diabetes-causing mutations. Upon transplantation into mice with severe pre-existing diabetes, these SC-islets rapidly restore normoglycemia and can maintain this functional cure for a year. Our hope is that one day this technology can be used to replace unhealthy islets in patients for therapy and provide a better disease-in-a-dish model to discover new drugs to prevent, stop, or reverse diabetes progression.

2020 NIDDK Diabetes Research Center Directors' Annual Meeting

October 1, 2020

Pilot and Feasibility Presentations

Session II: Moderator, Dr. Jane Reusch, Professor, University of Colorado Anschutz Medical Campus

1:15-1:30 Circadian Regulation, Sleep and Metabolic Characteristics in Diabetic Retinopathy
Sirimon Reutrakul, M.D., University of Illinois at Chicago

1:30-1:45 CGRP sensory afferents in energy metabolism
Celine Riera, Ph.D., Cedars-Sinai Medical Center

1:45-2:00 Single Beige Adipocyte Transcriptomics
Kosaku Shinoda, Ph.D., Albert Einstein College of Medicine

2:00-2:15 The Ins and Outs of Beta Cell miR-21 During Islet Inflammatory Stress
Emily K. Sims, M.D., Indiana University School of Medicine

2:15-2:30 *Reversibility of beta cell failure in type 2 diabetes*
Jinsook Son, Ph.D., Columbia University

2:30-2:45 Regulation of Muscle Metabolism by Insulin Signaling
Paul M. Titchenell, Ph.D., Perelman School of Medicine at the University of Pennsylvania

2:45-3:00 Insulin action and lipogenesis in hepatic insulin resistance
Daniel F. Vatner, M.D., Ph.D., Yale School of Medicine

3:00-3:15 A novel metabolic circuitry through acetylcholine and nAChR
Jun Wu, Ph.D., University of Michigan

ABSTRACTS

Circadian Regulation, Sleep and Metabolic Characteristics in Diabetic Retinopathy
Sirimon Reutrakul, M.D., University of Illinois at Chicago

Background: Intrinsically photosensitive retinal ganglion cells (ipRGCs) control non-visual light responses (e.g. pupillary light reflex and circadian entrainment). Patients with diabetic retinopathy (DR) show reduced ipRGC function, as inferred by abnormalities in the post illumination pupil response (PIPR). We explored whether ipRGC function in DR is associated with circadian outputs and sleep/wake behavior. Methods: Forty-five participants (15 without diabetes, 15 with type 2 diabetes (T2D) and no DR, 15 with T2D and DR) participated. ipRGC function was inferred from the PIPR (pupil size following stimulus offset). Circadian outputs were melatonin amplitude (overnight urinary 6-sulfatoxymelatonin (aMT6s)) and timing (dim light melatonin onset (DLMO)), and evening salivary cortisol levels. Sleep/wake patterns were measured with wrist actigraphy and insomnia symptoms were assessed subjectively. Results: Patients with T2D and DR had smaller PIPR and lower urinary aMT6s than other groups ($p<0.001$). In adjusted regression models, smaller PIPR was associated with lower urinary aMT6s ($\beta=4.552$, $p=0.005$). Patients with DR were more likely to have no detectable DLMO ($p=0.049$), higher evening salivary cortisol, greater insomnia symptoms and greater sleep variability compared to other groups. Sleep duration, efficiency and rest-activity rhythms were similar. Conclusion: Reduced ipRGC function in DR is associated with circadian dysregulation and sleep disturbances, although causal relationship cannot be established in this cross-sectional study. Prospective mechanistic and intervention studies examining circadian and sleep health in these patients are warranted. [Reutrakul et al; Sci Rep. 2020 Jan 31;10(1):1560. doi: 10.1038/s41598-020-58205-1.]

CGRP sensory afferents in energy metabolism
Celine E Riera, Ph.D., Cedars-Sinai Medical Center

Sensory nociceptor fibers arising from the dorsal root ganglion (DRG) form a dense network in many tissues, where they release neuropeptides to communicate painful signals from the periphery to the central nervous system. Here, we characterized the role of nerve fibers expressing calcitonin gene-related peptide α (CGRP) in mouse models of obesity and diabetes. Loss of CGRP nerves and inhibition of circulating CGRP peptide promote increased energy expenditure and improved glucose homeostasis in obese and diabetic mice. These data highlight an unprecedented role for these neurons in neuroendocrine communication to adjust energy dissipation processes with sensory and dietary signals.

Single Beige Adipocyte Transcriptomics
Kosaku Shinoda, Ph.D., Albert Einstein College of Medicine

Thermogenic fat is a heterogeneous tissue, but only four cell types have been identified to date: brown, beige, g-beige, and white adipocytes.
Despite transformative advances in single cell genomics, the application to adipose tissue has been challenging because of the large cell size and fragile nature of lipid-filled adipocytes.
We have developed a robust protocol to isolate single nuclei from adipose tissue for downstream application to RNA-sequencing.
We have applied this technique to a genetic beige-adipocyte deficiency model as well as UCP1 knockout mice to reveal the cellular mechanism of cold adaptation.

The Ins and Outs of Beta Cell miR-21 During Islet Inflammatory Stress
Emily K. Sims, M.D., Indiana University School of Medicine

Improved biomarkers are acutely needed for the detection of developing type 1 diabetes, prior to critical loss of beta cell mass. We previously demonstrated that elevated beta cell microRNA 21-5p (miR-21-5p) in rodent and human models of type 1 diabetes increased beta cell apoptosis. In this pilot and feasibility award project, we hypothesised that the inflammatory milieu of developing diabetes may

also increase miR-21-5p in beta cell extracellular vesicle (EV) cargo and that circulating EV miR-21-5p would be increased during type 1 diabetes development. Cytokine treatment in beta cell lines and human islets resulted in a 1.5- to threefold increase in miR-21-5p. However, corresponding EVs were further enriched for this miRNA, with a three- to sixfold EV miR-21-5p increase in response to cytokine treatment. Nanoparticle tracking analysis showed cytokines to have no effect on the number of EVs, implicating specific changes within EV cargo as being responsible for the increase in beta cell EV miR-21-5p. Sequential ultracentrifugation to separate EVs by size suggested that this effect was mostly due to cytokine-induced increases in exosome miR-21-5p. Longitudinal serum collections from NOD mice showed that EVs displayed progressive increases in miR-21-5p beginning 3 weeks prior to diabetes onset. Finally, serum EV miR-21-5p was increased threefold in children with new onset type 1 diabetes compared to non-diabetic individuals. These data suggest that circulating EV miR-21-5p may be a promising marker of islet inflammatory str3ess and developing type 1 diabetes. Data generated from this pilot and feasibility project were used as justification for subsequent extramural awards for the principal investigator, including an R03 and R01 through NIDDK focused on pathophysiologic mechanisms and relevance of changing beta cell EV cargo, and their potential as biomarkers in human populations relevant to diabetes.

Reversibility of β-cell failure in type 2 diabetes through BACH2 inhibition

Jinsook Son, Ph.D., Columbia University

Type 2 diabetes is associated with defective insulin secretion and reduced β–cell mass. Available treatments provide a temporary reprieve, but secondary failure rates are high, making insulin supplementation necessary. Reversibility of β-cell failure is a key translational question. Using single-cell analyses of cadaveric islets from normal controls or type 2 diabetic donors, we reverse engineered and interrogated accurate, pancreatic islet-specific regulatory networks to identify master regulators (MR) of the diabetic islet cell state. Algorithmic predictions were experimentally validated in single primary islet β-cells using gene gain- and CRISPR-mediated loss-of-function experiments and confirmed by glucose-induced Ca++ flux analysis. We identified aberrant, diabetes-enriched states, including β- to α-cell transitional states characterized by metabolic-inflexibility, as well as endocrine-progenitor/stem cell features. bZIP transcription factor BACH2 and associated epigenetic effectors emerged as master regulators controlling β- to α-like-cell reprogramming and transition to an endocrine progenitor-like cell. BACH2-immunoreactive islet cells increased ~4-fold in islets of diabetic patients. BACH2 inhibition in primary diabetic β-cells reversed the cellular features of the disease and restored a non-diabetic phenotype. Treatment of diabetic mice with a BACH2 inhibitor lowered glycemia in vivo. The findings suggest that β-cell failure can be effectively reversed and indicate actionable pathways for pharmacological intervention, including via BACH2 inhibition. (Jinsook Son, Hongxu Ding, Thomas B. Farb, Alexander Efanov, Julie L. Gore, Samreen K. Syed, Zhigang Lei ,Jiajun Sun, Qidi Wang, Andrea Califano)

Regulation of Muscle Metabolism by Insulin Signaling

Paul M. Titchenell, Ph.D., Perelman School of Medicine at the University of Pennsylvania

Skeletal muscle insulin signaling is a major determinant of muscle growth and glucose homeostasis. Protein kinase B/Akt plays a prominent role in mediating many of the metabolic effects of insulin. Mice and humans harboring systemic loss-of-function mutations in Akt2, the most abundant Akt isoform in metabolic tissues, are glucose intolerant and insulin resistant. Since the skeletal muscle accounts for a significant amount of postprandial glucose disposal, a popular hypothesis in the diabetes field suggests that a reduction in Akt, specifically in skeletal muscle, leads to systemic glucose intolerance and insulin resistance. Despite this common belief, the specific role of skeletal muscle Akt in muscle growth and insulin sensitivity remains undefined. Here, we test this hypothesis by generating several novel mouse models of Akt deficiency specially in skeletal muscle. Surprisingly, mice lacking Akt2 alone in skeletal muscle displayed normal skeletal muscle insulin signaling, glucose tolerance, and insulin sensitivity despite a dramatic reduction in phosphorylated Akt. In contrast, deletion of both Akt

isoforms (M-AktDKO) prevented downstream signaling and resulted in muscle atrophy. Despite the absence of Akt signaling, in vivo and ex vivo insulin-stimulated glucose uptake were normal in M-AktDKO mice. Mechanistically, chronic ablation of Akt induced mitochondrial dysfunction and activation of AMPK, which was required for insulin-stimulated glucose uptake in the absence of Akt. Together, these data indicate that chronic reduction in Akt activity alone in skeletal muscle is not sufficient to induce insulin resistance or prevent glucose uptake in all conditions. Therefore, since insulin-stimulated glucose disposal in skeletal muscle is markedly impaired in insulin-resistant states, we hypothesize that alterations in signaling molecules in addition to skeletal muscle Akt are necessary to perturb glucose tolerance and insulin sensitivity in vivo.

Insulin action and lipogenesis in hepatic insulin resistance
Daniel F. Vatner, M.D., Ph.D., Yale School of Medicine

A deeper understanding of the regulation of insulin metabolism in insulin resistant subjects will be critical for the development of new therapeutics to prevent and treat atherosclerotic cardiovascular disease and nonalcoholic fatty liver disease (NAFLD). In this presentation, we will specifically address an as-yet unanswered question: to what degree does the insulin action explain increased de novo lipogenesis (DNL) in the insulin resistant organism? DNL was measured by the deuterated water method in mice and humans. We took advantage of the sequential development of hepatic vs peripheral insulin resistance in high fat diet (HFD) fed mice, wherein hepatic insulin resistance develops after short term (8-9 d) HFD, while peripheral insulin resistance develops after several weeks (4w) HFD feeding. In contrast with globally insulin resistant humans, hepatically insulin resistant mice demonstrate significantly decreased rates of DNL, which recovers after the development of peripheral insulin resistance (*2D HFD*: 22.2% ± 3.5; *9D*: 7.4% ± 1.3; *4W*: 15.9% ± 2.3). The in vivo occupancy of lipogenic target gene promoters by SREBP1c and ChREBP was determined using chromatin immunoprecipitation experiments in the same three groups of mice. SREBP1c was not bound to the *Fasn* or *Srebpf1* promoters in insulin resistant livers, while ChREBP was bound to the *Fasn* and *Pklr* promoters equally in all three groups of mice. In contrast with wild type mice, $Insr^{T1160A}$ mice (a mutant protected against the development of diet-induced hepatic insulin resistance) did not demonstrate a significant decrease in DNL after 9 days HFD (*2D*: 24.3% ± 3.6; *9D*: 16.4% ± 2.4; *4W*: 19.3% ± 2.6). In a collaboration with the Academic Medical Center in Amsterdam, we assessed DNL contribution to VLDL triglyceride in obese humans, comparing subjects with and without NAFLD and hepatic insulin resistance. NAFLD subjects demonstrated increased DNL in VLDL after meals as compared with non-NAFLD subjects. Patients were given glucose of fructose tolerance tests: glucose failed to stimulate additional DNL in NAFLD subjects (in contrast with non-NAFLD subjects); while fructose, which enters hepatocyte metabolism in an insulin-independent fashion, stimulated DNL in all subjects. Prior studies of the regulation of fatty acid esterification into triglyceride by insulin and substrate will be reviewed. DRC core facilities have allowed me as an early career investigator to do cutting-edge physiology, and DRC pilot funding has allowed me to expand into new areas, developing new and familiar animal models for use in my laboratory. In sum, changes in insulin action are unlikely to be responsible for dysregulation of triglyceride synthesis seen in insulin resistant patients; a more nuanced view is in order, wherein we examine individual substrate fluxes that change in insulin resistant individuals, alongside the activation of several lipogenic transcription factors. We plan to address these models in my nascent laboratory.

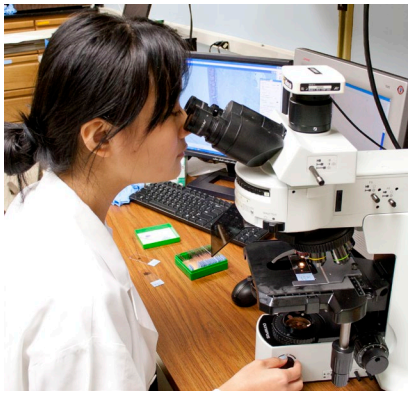
A Novel Metabolic Circuitry through Acetylcholine and nAChR
Jun Wu, Ph.D., University of Michigan, Ann Arbor, MI, USA.

Obesity epidemic has significantly increased the widespread occurrence of its associated metabolic disorders, including type II diabetes. A few years ago, we made the intriguing observation that one of the subunits of nicotinic acetylcholine receptor, the alpha 2 subunit (CHRNA2) is among the genes that are increasingly expressed in activated thermogenic beige adipocytes. Supported by a

pilot/feasibility grant from the Diabetes Research Center at the University of Michigan (P30-DK020572), we went on to demonstrate that acetylcholine-producing immune cells regulate thermogenic beige adipocytes via CHRNA2 signaling within the subcutaneous adipose tissue. CHRNA2 functions selectively in beige adipocytes and this signaling is conserved in both mice and humans. Inactivation of Chrna2 in mice compromised the cold-induced thermogenic response selectively in subcutaneous fat and exacerbated high-fat diet-induced obesity and associated metabolic disorders (Nature Medicine 2018, Mallinckrodt Grant, ADA 1-16-JDF-099, R01DK107583). In particular, CHRNA2 signaling may activate glycolytic beige fat, a newly identified subpopulation of beige adipocytes (Developmental Cell 2020). Further investigation led to our hypothesis that this novel non-neuronal cholinergic circuitry also exists in the liver between ChAT+ (choline acetyltransferase, rate limiting enzyme for acetylcholine production) non-parenchymal cells (NPCs) and CHRNA2-expressing hepatocytes. This pathway is activated in the liver by both physiological and pathological stimulations and plays an important adaptive role to protect the liver against alcohol consumption caused liver injury (R01AA028761, pending) and other metabolic dysregulations. The P/F grant enabled us to build the foundation and accelerated our discovery of the novel function of nicotinic acetylcholine receptors in energy metabolism and may eventually lead to identification of therapeutic targets to counteract human metabolic diseases.

NIDDK Medical Student Research Program in Diabetes

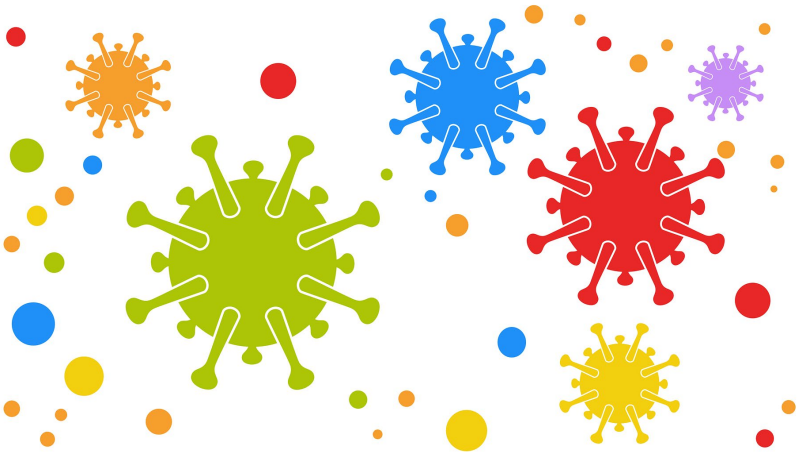
- Medical students between 1st and 2nd year
- Goals:
  - Inspire careers in discovery in diabetes, obesity, GI, and kidney disease Providing intensive mentored research early in their career
  - Provide exposure to key clinical concepts and knowledge gaps
- Started in 2009
- 80-90 students per year (33 this year)
- 4-10 students at each Diabetes Center
- Funding
  - Supplement to T32s at Diabetes Centers
  - Diabetic Complications Consortium



DIABETES RESEARCH CENTERS

Today, two challenges

- The world we live in
- Lower application numbers



DIABETES RESEARCH CENTERS

Access to careers in discovery

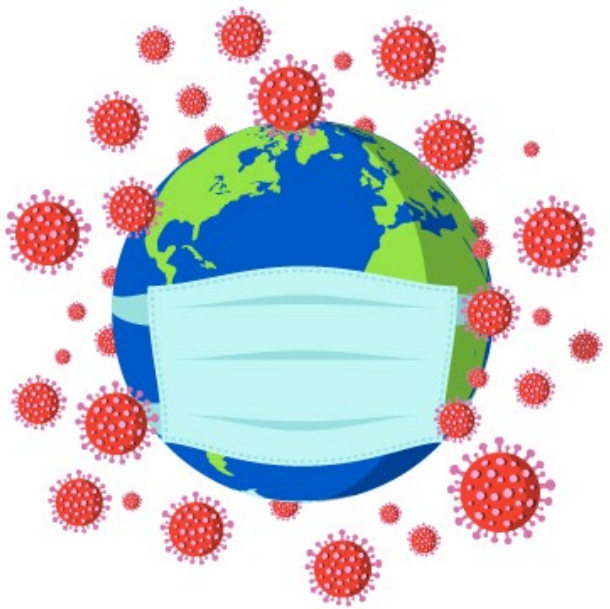
2009-present

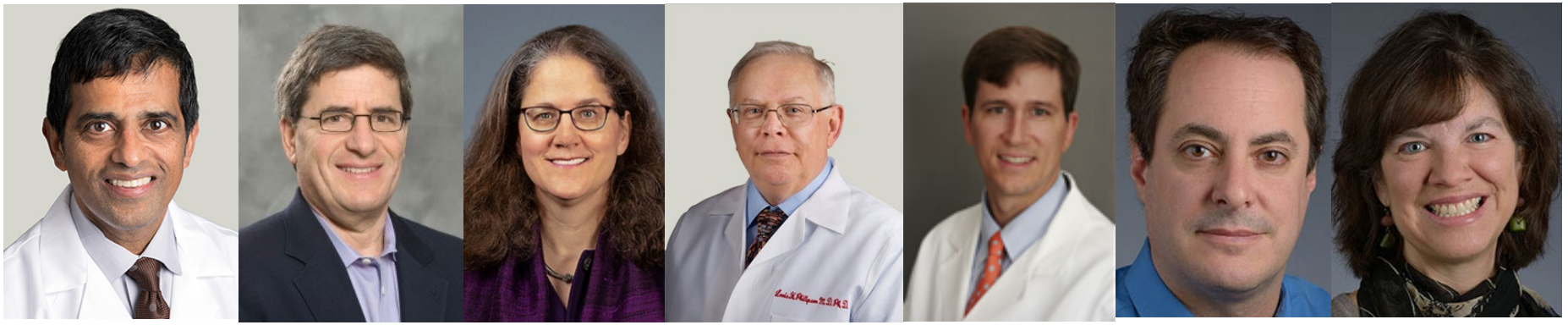
- 1258 students
- 142 medical schools
- 43 from DO programs
- 45 states including Hawaii and Puerto Rico

DIABETES RESEARCH CENTERS

A major pivot

- Surveyed which centers could take students
- Meetings with NIDDK and advisory panel
- Re-design a virtual program for 33 students
  - Research Projects: Virtual and in person
  - A virtual seminar series
  - Virtual symposium

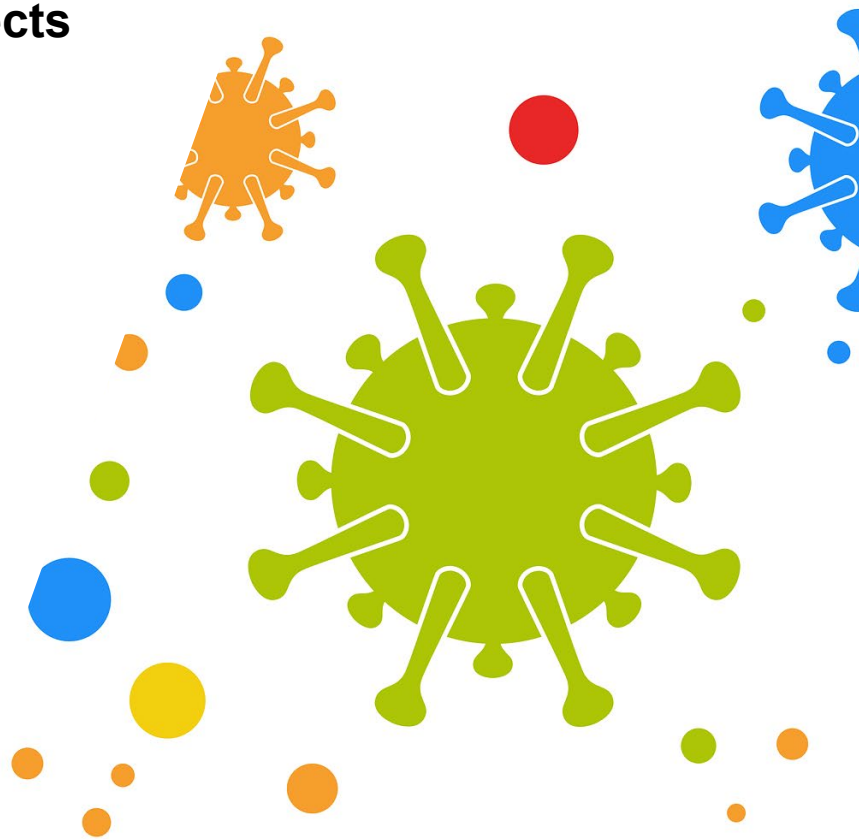




Some unusual challenges

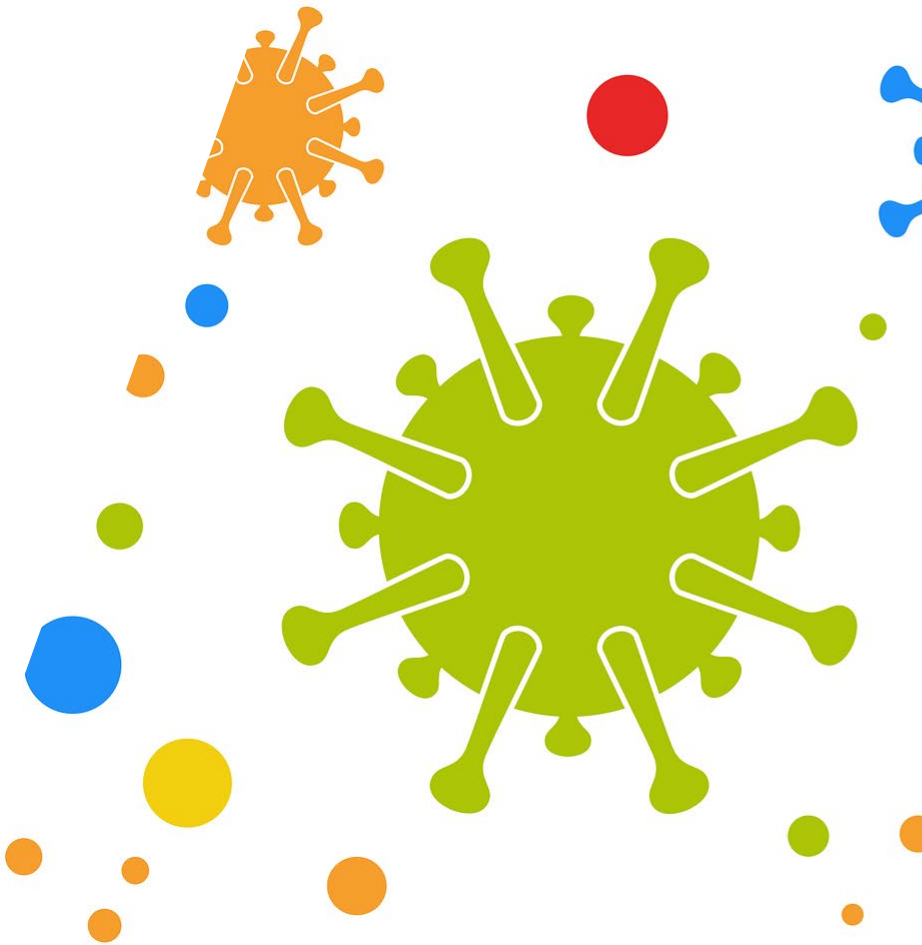
Center	# of Students
Chicago	1
Indiana-Purdue	4
Joslin	5
Kaiser	4
Michigan	10
UCSD	5
Wash St. Louis	3
Yale	1
Total	**33**

- **Several centers could not take students, or only took local students**
- **A mix of virtual and in-person projects**
- **A scramble to come up with virtual projects**



A 5-star virtual seminar series

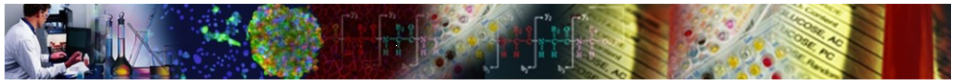
- Lou Phillipson
  - DM 101 and Monogenic DM
- Mary Elizabeth Patti
  - Gastric Bypass and DM
- Mike Rickels
  - Hypoglycemia
- Lori Laffel
  - DM1
- Arshiya Baig
  - Diabetes in the Underserved
- Corinne Silva and Art Castle
  - NIDDK perspective on DM research
- John Stafford
  - DM associated CVD
- Al Powers
  - Diabetes Advocacy



DIABETES RESEARCH CENTERS

Summer | 2020

DIABETES RESEARCH CENTERS



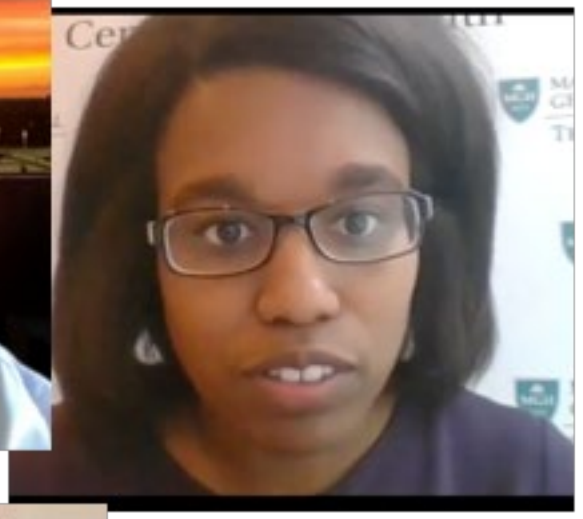
12th Annual NIDDK Medical Student
Virtual Research Symposium
July 29th, 2020

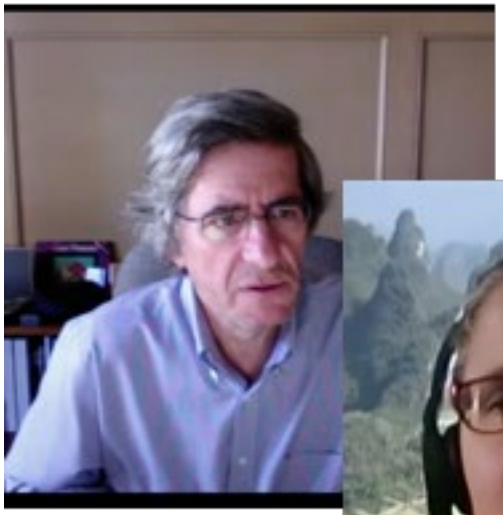
Our first virtual symposium

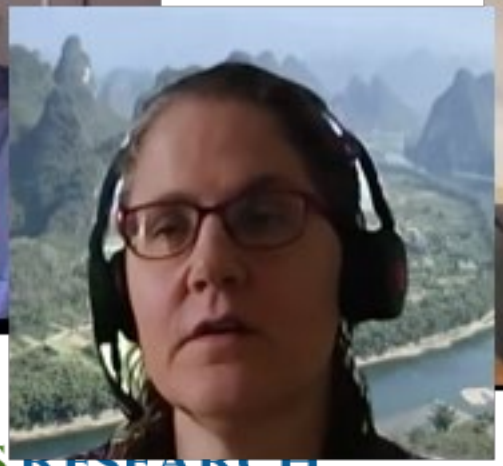
- Welcome and Intro
  - Al Powers
- Monica Peek MD, MPH: Univ Chicago
  - Social Environment and Health Disparities
- Breakouts for Student Presentations
  - All students gave 10-minute presentation
- Camille Powe MD: MGH
  - Career Path and GDM
- Career Panel

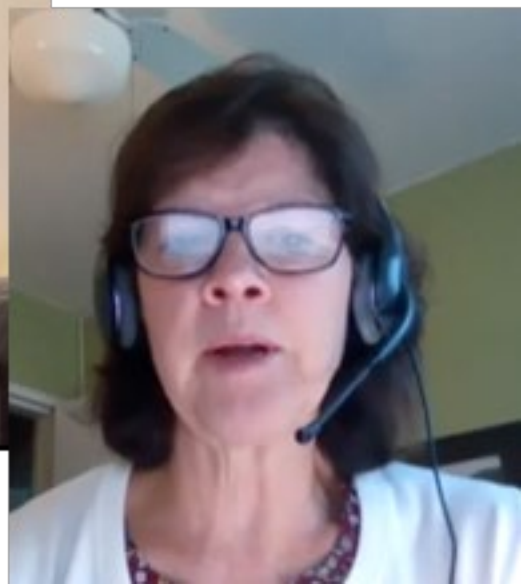
DIABETES RESEARCH CENTERS

Engaged Faculty / Career Panel



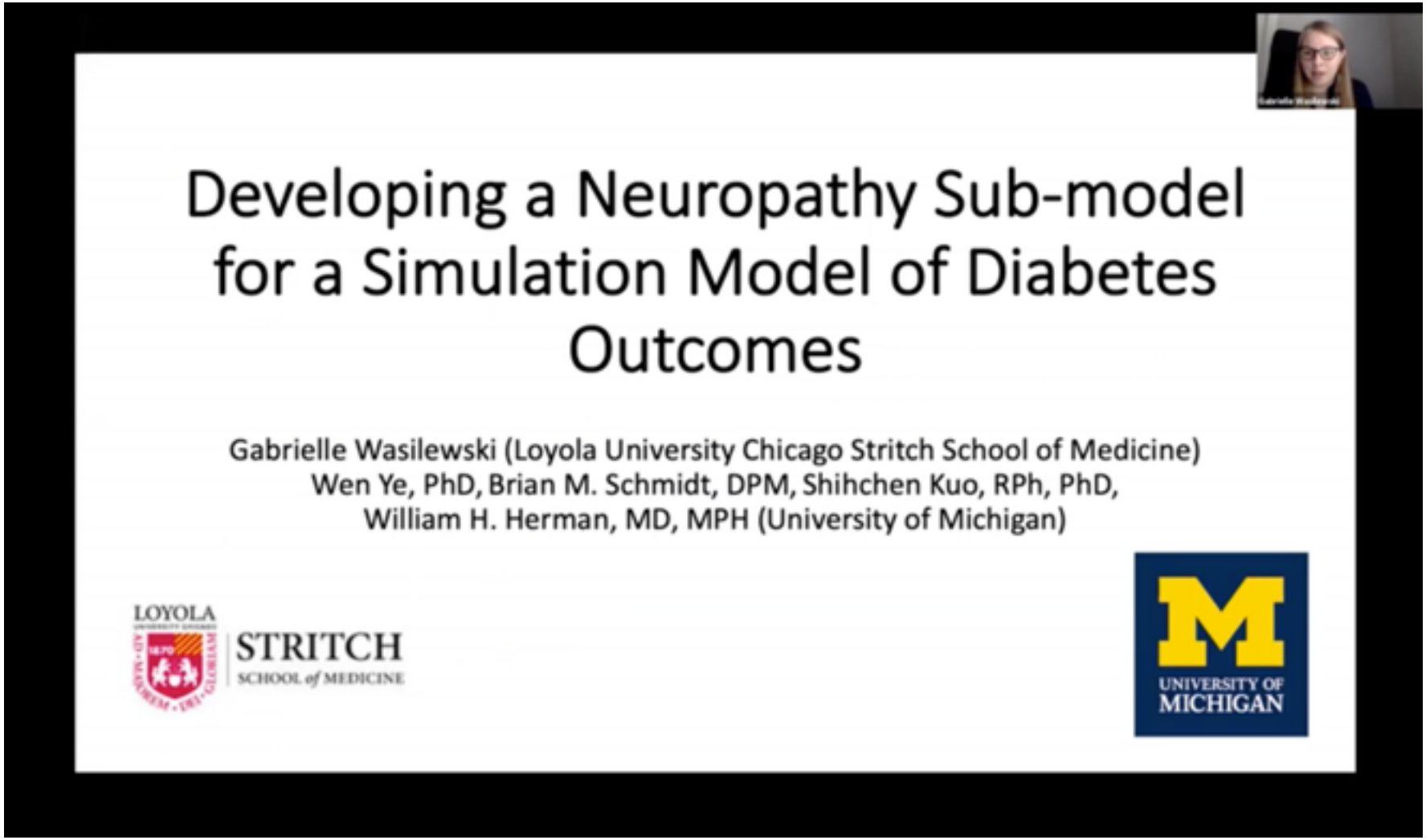






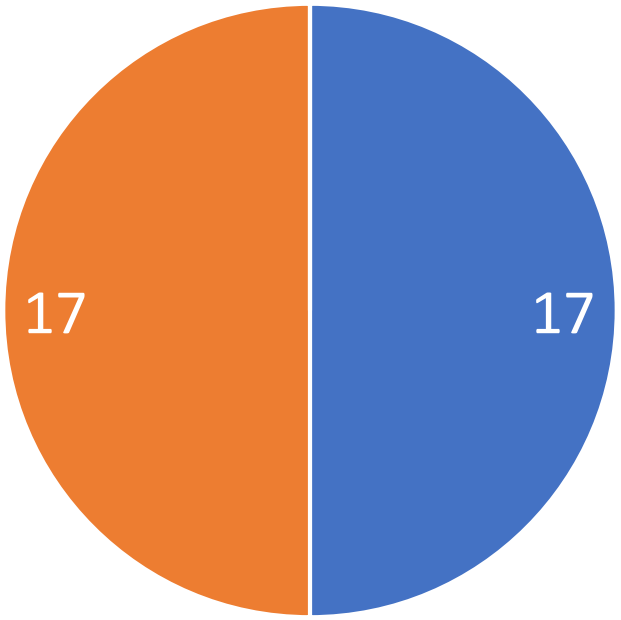
DIABETES RESEARCH CENTERS

Student talks

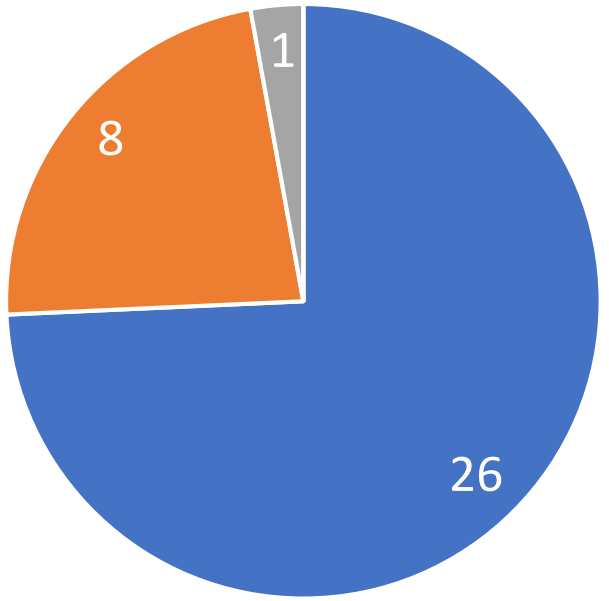


Survey Results

- **How would you rate the symposium?**



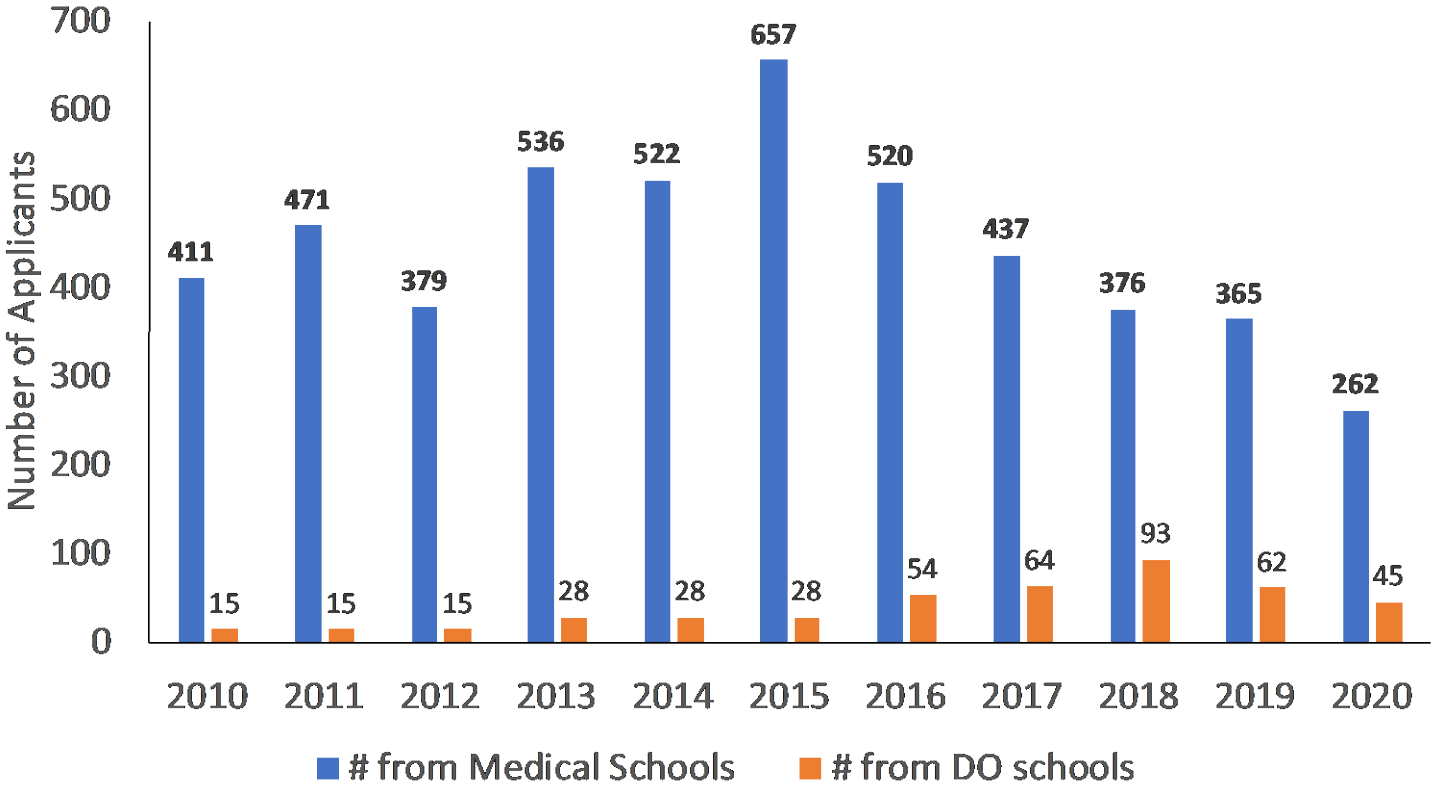
- **I found the overall program of high value**



DIABETES RESEARCH CENTERS

What do we do going forward?

- **Despite aggressive marketing, lower application numbers**



DIABETES RESEARCH CENTERS

Discussion for 2021 and onward

The world we live in

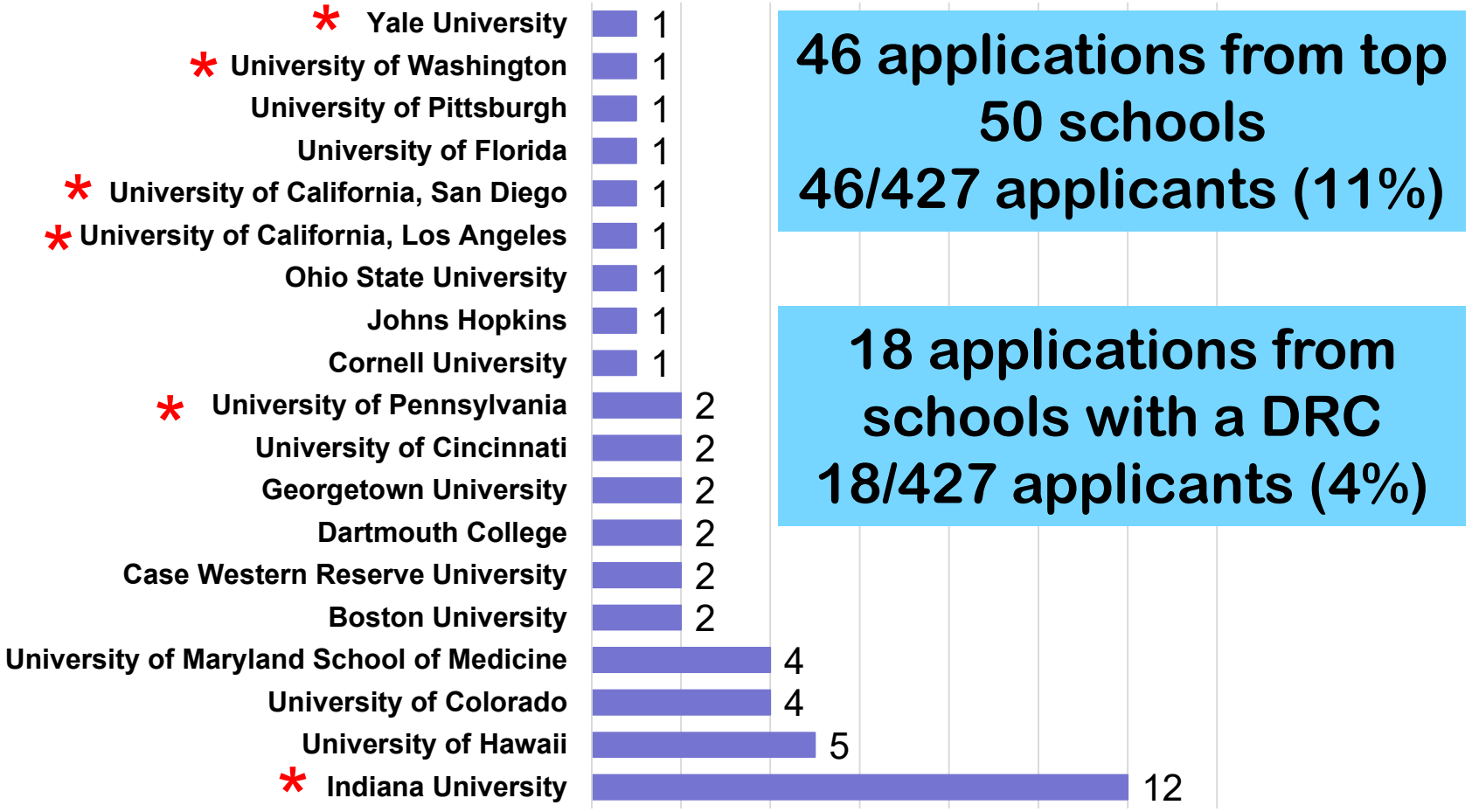
- In person, virtual, hybrid?
- Does the research component at a DRC need to be synchronous with the summer program?
- How do we develop virtual projects of value?

Lower application numbers

- Advertise to Gen-Z?
- Twitter @diabetesMSRP
- YouTube videos testimonials
- Instagram
- LinkedIn account
- New program webpage
- DRCs to promote
- dkNet to promote
- Focus Group

Applicants From Top 50 Medical Schools

(2019)



46 applications from top 50 schools
46/427 applicants (11%)

18 applications from schools with a DRC
18/427 applicants (4%)

DIABETES RESEARCH CENTERS

Updated webpage

vumc.org/niddk/welcome

NIDDK Medical Student Research Program in Diabetes

Search

Home

Opportunities for first- & second-year medical students to conduct mentored research in one of 16 diabetes centers across the US

2020 Program Lectures

Program Centers

Program Announcement

Application for Summer 2020

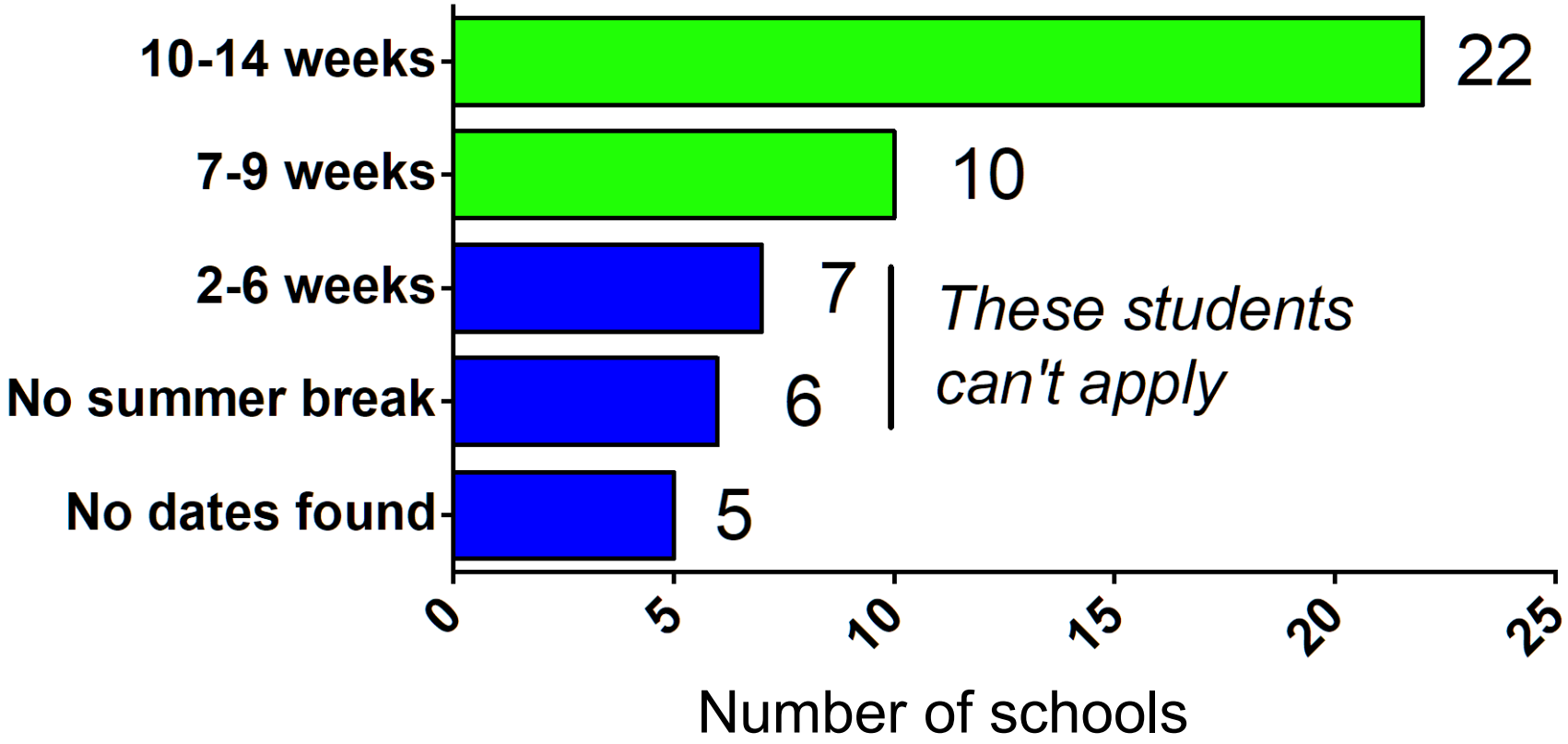
FAQ

In the News

DIABETES CENTERS

Top 50 Medical Schools Summer Break

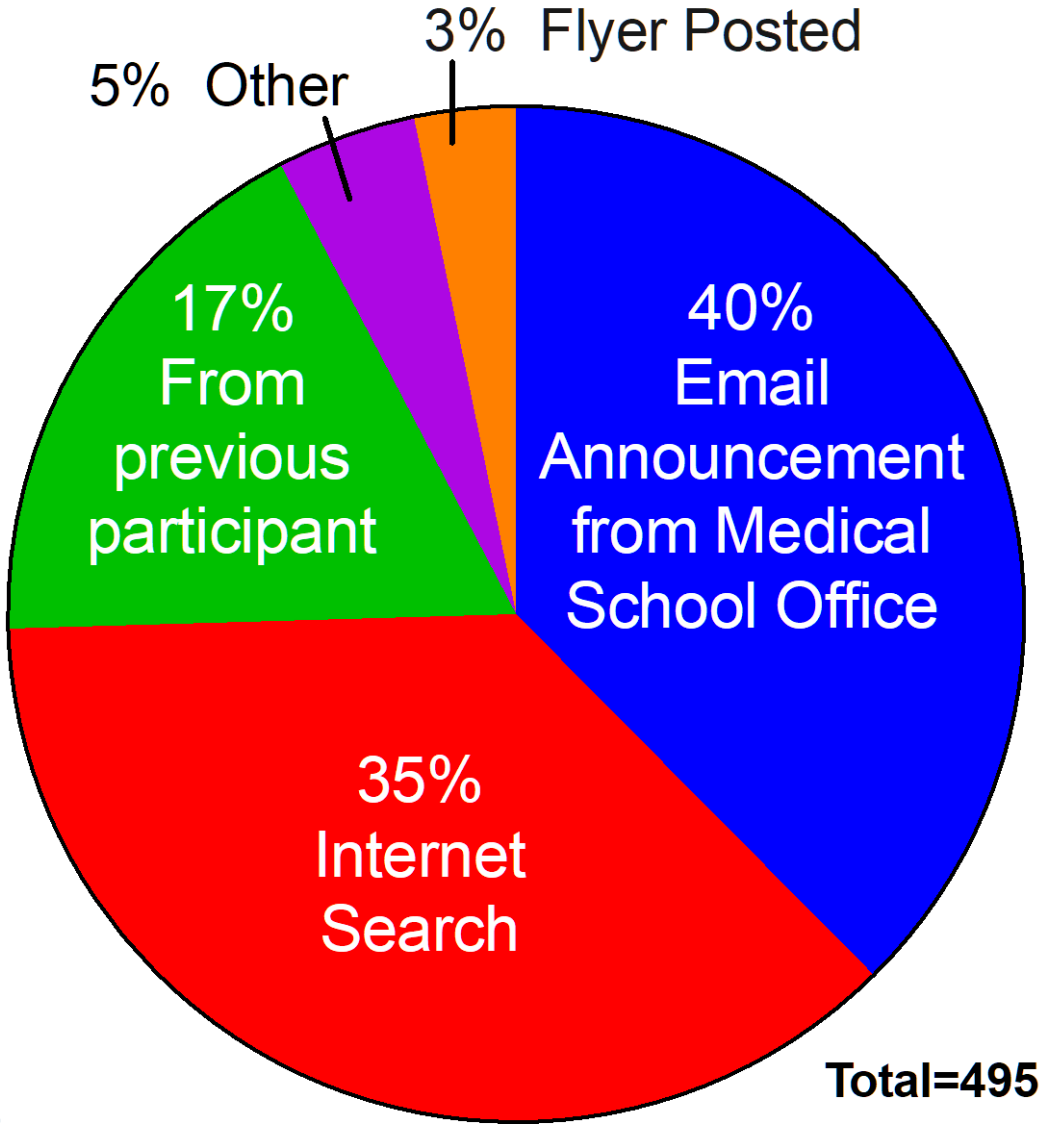
(Impact of curriculum redesign?)



DIABETES RESEARCH CENTERS

NIDDK Program Advertising - 2019

"How did you hear about us?"



DIABETES RESEARCH CENTERS

The Diabetes Research Centers Virtual Seminar Series:

a new approach to building research networks and fostering interaction

March 2020: Staring at the abyss

- Most academic travel banned
- Meetings >10 people banned
  External seminar series cancelled !!!
- Trainees doing “non-essential” / non-Covid19 research banned from lab

What to do?

Since all DRCs and CDTRs similarly affected, why not a virtual series by the DRCs/CDTRs?

North Rim of the Grand Canyon
PHOTOGRAPH BY **AWL IMAGES**

Diabetes Research Centers

Virtual Seminar Series

Weekly Seminar

Wednesdays April 8th – July 1, 2020
11 AM CT / 12 PM MT / 1 PM CT / 2 PM ET

- Rotated the center providing the speaker.
- Plenary-style seminar (45 min + 15-min Q&A)
- Internal advertising only

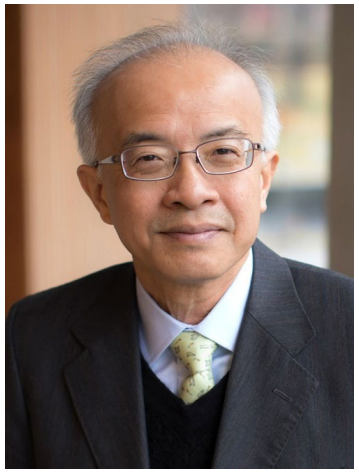
Phase I April to July 2020

Date and Time	Speaker	Title	Watch Lecture
04/08 at 1:00 P.M. CST	Dr. Steven Kahn, MB, ChB (University of Washington)	"Unraveling Beta-cell Dysfunction in Type 2 Diabetes: From the Unpredicted to the Unknown"	
04/15 at 1:00 P.M. CST	Victor L. Schuster, M.D. (Albert Einstein College of Medicine)	"To burn, or not to burn: fat is the question"	
04/22 at 1:00 P.M. CST	Anath Shalev, MD (UAB)	"Preservation of islet function in type 1 diabetes - from bench to bedside"	
04/29 at 1:00 P.M. CST	Carey N. Lumeng, MD, PhD (University of Michigan)	"Adipose tissue macrophage function in diabetes and obesity"	
05/06 at 1:00 P.M. CST	Nancy Cox, PhD (Vanderbilt University)	"Working toward a translation of polygenic liability"	
05/13 at 1:00 P.M. CST	William Herman, MD, MPH (University of Michigan)	"Closing the Gap: Diabetes Prevention and Treatment – Take 2"	
05/20 at 1:00 P.M. CST	Michael Weiss, MD, PhD, MBA (Indiana University)	"Adventures with Insulin: From Structural Biology to Novel Therapeutics"	
05/27 at 1:00 P.M. CST	Lindsay Mayberry, PhD (Vanderbilt University)	"Leveraging Family and Social Contexts to Sustain Diabetes Self-care Behavior Change"	
06/03 at 1:00 P.M. CST	Don McClain, MD, PhD (Wake Forest)	"Diabetes and Iron: Can't Live With It, Can't Live Without It"	
06/10 at 1:00 P.M. CST	Seung Kim, MD, PhD (Stanford)	"Alpha cell and glucagon regulation in development and diabetes"	
06/17 at 1:00 P.M. CST		*No Lecture Scheduled Due to ADA Virtual Meeting*	
06/24 at 1:00 P.M. CST	Jane Reusch, MD (Colorado)	"Microvascular Contributions to Exercise Intolerance in Diabetes"	
07/01 at 1:00 P.M. CST	Jeffrey Gonzalez, PhD (Albert Einstein College of Medicine)	"Tangled Up In Blue: Depression, Distress and Diabetes"	

Weekly Virtual Seminar Series Evaluation/Observations

- Significant enthusiasm.
- Robust Q&A following seminar.
- Resulted in new collaborations.
- Despite only advertising within participating DRCs/CDTRs:
  - -drew registration/attendees outside participating institutions
  - -typically ~225 attendee
- 25-30% attendees were trainees, but few asked questions.
- No issues with Zoom bombing.
- Strong desire to continue seminar series in some form.

Formation of an advisory committee



Streamson Chua
(Albert Einstein)

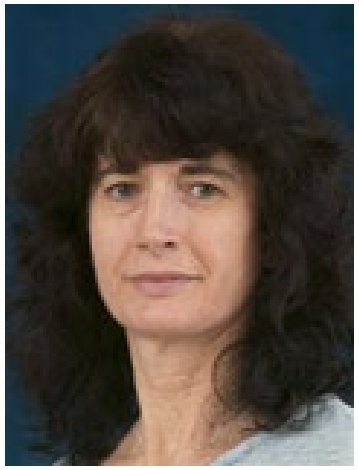
Sean Davies
(Vanderbilt)

Rebecca Hull
(Washington)

Kiran Kocherlakota
(Stanford)

Lindsay Mayberry
(Vanderbilt)

Don McClain
(Wake Forest)



Nuria Morral
(Indiana)

Jane Reusch
(Colorado)

Scott Soleimanpour
(Michigan)

Anath Shalev
(UAB)

Questions to consider

- What is vision for continuing the series?
- How frequently to hold seminars?
- Continue same format or revise?
- How to better engage trainees?
- What “types” of speakers should we have?
- How can we use the seminar series to facilitate collaborations?

Our vision:

Diabetes Research Centers
provide global access
to cutting-edge diabetes research findings.

Committee Recommendations

- Monthly seminars
- Plenary-style speakers
- Facilitate engagement of trainees with speaker
- Experiment with new meeting formats
- Compliment local seminar series
- Evaluate impact of seminar series

Monthly Seminar Series

Wednesday, September 9, 2020
2:00 PM EST | 1:00 PM CST | 11:00 AM PST| 12:00 PM MST
Please register here:
https://redcap.link/Seminar.Registration.09.09
Connection information will be provided after registration.

Anna L. Gloyn, DPhiL

Professor of Pediatrics
(Endocrinology) & Genetics
(by Courtesy)
Stanford University

Using Human Genetics to Unravel Mechanisms of Pancreatic Islet-Cell Dysfunction in Type 2 Diabetes

- Began Sept. 9th.
- Had 967 people (~100 institutions) register for first seminar.
- 420 actual attendees.
- 17 trainees met with Anna in two sessions.

Diabetes Research Centers
Virtual Seminar Series

EINSTEIN Albert Einstein College of Medicine
SCHOOL OF MEDICINE CENTER FOR DIABETES AND METABOLIC DISEASES
UAB Diabetes Research Center
VANDERBILT UNIVERSITY MEDICAL CENTER
Washington University in St. Louis SCHOOL OF MEDICINE
Michigan Diabetes Research Center
Diabetes Research Center UNIVERSITY of WASHINGTON
NCDRC
Diabetes Center University of California San Francisco
Stanford Diabetes Research Center
UCSD-UCLA Diabetes Research Center
Joslin Diabetes Center
THE UNIVERSITY OF CHICAGO
Yale SCHOOL OF MEDICINE
COLUMBIA UNIVERSITY IRVING MEDICAL CENTER
University of Colorado Anschutz Medical Campus

Upcoming Seminars

Wednesday, October 14, 2020
2:00 PM EST | 1:00 PM CST | 11:00 AM PST| 12:00 MT

https://redcap.link/DRC-Manson-10.14.20

Spero M. Manson, PhD

Distinguished Professor of Public Health and Psychiatry
Director, Centers for American Indian and Alaska Native Health
Colorado Trust Chair in American Indian Health

Behavioral Health Problems and Diabetes: Risk, Prevention, and Management Among Native Peoples

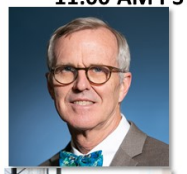
Wednesday, November 4, 2020
2:00 PM EST | 1:00 PM CST | 11:00 AM PST| 12:00 MT
Please register here:
https://redcap.link/Seminar.Registration.11.04
Connection information will be provided after registration.

Karin Bornfeldt, PhD

Edwin L. Bierman Professor of Medicine
Division of Metabolism, Endocrinology and Nutrition
Professor of Laboratory Medicine and Pathology
Director, Diabetes Complications Program, UW Medicine
Diabetes Institute

A human-first approach to identify mechanisms of cardiovascular complications of diabetes

"Future approaches for Type 1 Diabetes Therapy"
DRC Virtual Seminar Series Panel Discussion
Wednesday, December 9, 2020 – 90 Minute Panel with Q&A
11:00 AM PST | 12:00 PM MST | 1:00 PM CST | 2:00 PM EST



Panel Chair and Moderator:
David Harlan, MD
William & Doris Krupp Professor of Medicine
University of Massachusetts

Treating T1D with Stem Cells
Matthias Hebrok, PhD
Director, UCSF Diabetes Center
University of California

Predicting the diagnosis of T1D for preventative therapy
William Hagopian, MD, PhD
Director of Diabetes Programs, Pacific Northwest Research Institute, Seattle WA

Anath Shalev, M.D.
Professor of Medicine
University of Alabama at Birmingham

Targeting the immune system in T1D
Kevan Herold, MD
C.N.H. Long Professor of Immunobiology and of Medicine Deputy Director, Yale Center for Clinical Investigation, Yale University

Discussion Questions

A. Center representation and long-term governance?
B. What types of speakers should we have?
C. Honorarium?
D. How to publicize?
E. Will there be an audience after the pandemic?
F. How to better engage trainees and junior faculty?
    1. “Careers in diabetes research” seminar?
    2. “New faces in diabetes research” seminar?
    3. “DRC Interest groups” ?
G. How to use to facilitate new collaborations?

Wrap Up

- DCO web page updates
- Next RFA
- Upcoming meetings
- DRC Meeting booklet will be on https://www.diabetescenters.org/

Webpage updates

- P&F awardees-list and highlight
- P&F application reviewers-update
- Encourage to link directly from your DRC webpage to DCO https://www.diabetescenters.org/
- ORCID iDs (Open Researcher and Contributor Identifiers).
  - helps track the career outcomes of DRC Pilot & Feasibility Awardees
  - DCO website provides a link to the P&F awardee's ORCID web page
  - close to fifty percent of the P&F awardees have known ORCID IDs
  - hope to link all of the center P&F awardees on the Diabetes Centers website to their ORCID IDs

jodee.allen@diabetescenters.org

Next RFA Timeline

- Anticipate publication of RFA before end of 2020
- Applications likely due in May/June 2021

  (*review* in fall 2021; *second level of review* in January 2022 Advisory Council meeting; *earliest funding* in April 2022)
- Renewal applications expected:
  - Joslin Diabetes Center
  - Stanford University
  - University of Pennsylvania
  - Vanderbilt University

DIABETES RESEARCH CENTERS

2019 Institutional Diabetes Center Websites

Albert Einstein College of Medicine: http://www.einstein.yu.edu/centers/diabetes-research/

Columbia University: https://www.derc.cumc.columbia.edu/

Indiana University: https://medicine.iu.edu/research/centers-institutes/diabetes-metabolic-diseases/

Joslin Diabetes Center: https://www.joslin.org/research/diabetes-research-center

North Carolina Diabetes Research Center: https://ncdiabetesresearch.org/

Stanford University: https://sdrc.stanford.edu/

University of Alabama at Birmingham: http://www.uab.edu/shp/drc/

UCSD/UCLA: http://drc.ucsd.edu/index.shtml

University of Chicago: http://drtc.bsd.uchicago.edu/

University of Colorado Denver: https://medschool.cuanschutz.edu/diabetes-research-center

University of Michigan: http://diabetesresearch.med.umich.edu/

University of Pennsylvania: http://www.med.upenn.edu/idom/

University of Washington: http://depts.washington.edu/diabetes/

Vanderbilt University: https://labnodes.vanderbilt.edu/drtc

Washington University in St. Louis: https://diabetesresearchcenter.dom.wustl.edu/

Yale University: http://derc.yale.edu/

2020 Diabetes Centers' Directors Meeting Publications

Center	Publications
Albert Einstein College of Medicine	GLP-1 Receptor Agonists Synergize With DYRK1A Inhibitors to Potentiate Functional Human β Cell Regeneration Multifaceted Secretion of htNSC-derived Hypothalamic Islets Induces Survival and Antidiabetic Effect via Peripheral Implantation in Mice Central KATP Channels Modulate Glucose Effectiveness in Humans and Rodents
Columbia University	Pparγ Deacetylation Confers The Anti-Atherogenic Effect And Improves Endothelial Function In Diabetes Treatment Bile Acid Composition Regulates Gpr119-Dependent Intestinal Lipid Sensing And Food Intake Regulation In Mice Identification Of C2Cd4A As A Human Diabetes Susceptibility Gene With A Role In B Cell Insulin Secretion
Indiana University	A Versatile, Portable Intravital Microscopy Platform for Studying Beta-cell Biology In Vivo Noninvasive glucose detection in exhaled breath condensate T1D Exchange Residual C-peptide Study Group. Proinsulin Secretion Is a Persistent Feature of Type 1 Diabetes
Joslin Diabetes Center	A signature of circulating inflammatory proteins and development of end-stage renal disease in diabetes Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism Residual β cell function and monogenic variants in long-duration type 1 diabetes patients
Stanford University	A co-formulation of supramolecularly stabilized insulin and pramlintide enhances mealtime glucagon suppression in diabetic pigs In vivo studies of glucagon secretion by human islets transplanted in mice Molecular Choreography of Acute Exercise
UCSD / UCLA	Immune-evasive human islet-like organoids ameliorate diabetes ER Stress Drives Lipogenesis and Steatohepatitis via Caspase-2 Activation of S1P Estrogen receptor α controls metabolism in white and brown adipocytes by regulating Polg1 and mitochondrial remodeling
University of Alabama at Birmingham	Bone marrow-derived cells restore functional integrity of the gut epithelial and vascular barriers in a model of Ddabetes and ACE2 deficiency A gene expression network analysis of the pancreatic islets from lean and obese mice identifies complement 1q like-3 secreted protein as a regulator of β-cell function A small molecule, UAB126, reverses diet-induced obesity and its associated metabolic disorders
University of Chicago	The Impact of Biomarker Screening and Cascade Genetic Testing on the Cost-Effectiveness of MODY Genetic Testing Integrated Pancreatic Blood Flow: Bidirectional Microcirculation Between Endocrine and Exocrine Pancreas Precision Medicine in Diabetes: A Consensus Report From the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Center	Publications
University of Michigan	Ventromedial hypothalamic nucleus neuronal subset regulates blood glucose independently of insulin Risk Factors for Diabetic Peripheral Neuropathy and Cardiovascular Autonomic Neuropathy in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Cells Deploy a Two-Pronged Strategy to Rectify Misfolded Proinsulin Aggregates
University of Pennsylvania	Dietary fructose feeds hepatic lipogenesis via microbiota-derived acetate Identification of a mesenchymal progenitor cell hierarchy in adipose tissue Multiplexed In Situ Imaging Mass Cytometry Analysis of the Human Endocrine Pancreas and Immune System in Type 1 Diabetes
University of Washington	Increased apolipoprotein C3 drives cardiovascular risk in type 1 diabetes TFPa/HADHA is required for fatty acid beta-oxidation and cardiolipin re-modeling in human cardiomyocytes Hyaluronan deposition in islets may precede and direct the location of islet immune-cell infiltrates
Vanderbilt University	Iatrogenic Hyperinsulinemia, Not Hyperglycemia, Drives Insulin Resistance in Type 1 Diabetes as Revealed by Comparison With GCK-MODY (MODY2) Coregulator Sin3a Promotes Postnatal Murine β-Cell Fitness by Regulating Genes in Ca2+ Homeostasis, Cell Survival, Vesicle Biosynthesis, Glucose Metabolism, and Stress Response Human islets expressing HNF1A variant have defective β cell transcriptional regulatory networks
Washington University in St Louis	Targeting the cytoskeleton to direct pancreatic differentiation of human pluripotent stem cells Primary cilia control glucose homeostasis via islet paracrine interactions Acetyl-CoA Derived from Hepatic Peroxisomal β-Oxidation Inhibits Autophagy and Promotes Steatosis via mTORC1 Activation
Yale University	Mitochondrial GTP Links Nutrient Sensing to β Cell Health, Mitochondrial Morphology, and Insulin Secretion Independent of OxPhos Lower Insulin Clearance Parallels a Reduced Insulin Sensitivity in Obese Youths and Is Associated With a Decline in β-Cell Function Over Time. Diabetes Glucagon stimulates gluconeogenesis by INSP3R1-mediated hepatic lipolysis