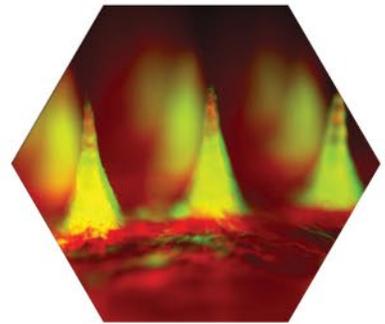
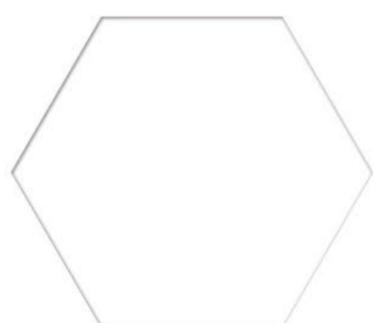
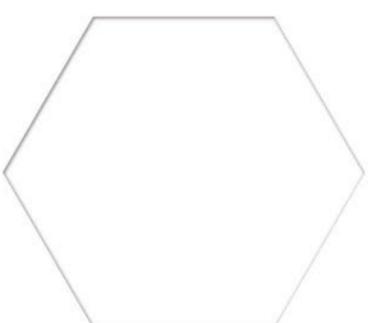
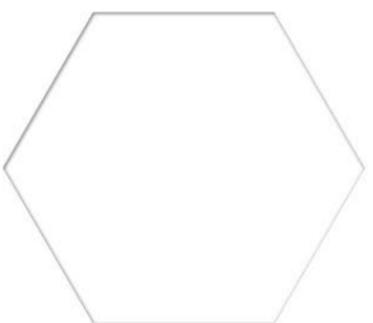
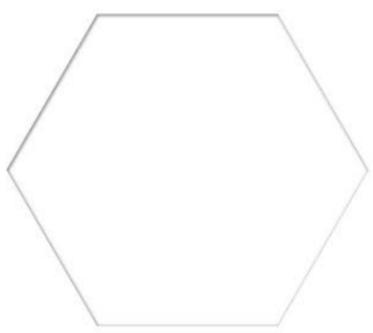


 American Diabetes Association.  
2015 *PATHWAY* ANNUAL REPORT



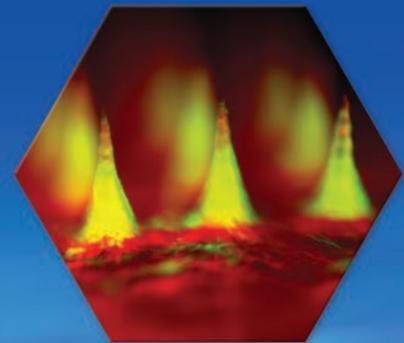
American Diabetes Association  
2015 PATHWAY ANNUAL REPORT



“When you have **an exciting idea** and you want to pursue it, you need someone to **take a chance on you.** That’s exactly what the American Diabetes Association is doing with the Pathway program.”

— JOSHUA THALER, MD, PHD  
PATHWAY ACCELERATOR  
AWARD RECIPIENT

# next



## Pathway to Stop Diabetes®

Diabetes is a serious global health crisis. An estimated 415 million people worldwide are living with diabetes. One in 11 Americans has diabetes and 86 million more are at high risk of developing the disease. Managing diabetes and its complications is a tremendous challenge for individuals and families. The economic burden of diabetes threatens to overwhelm our society and our health care system. Despite the scope of the problem, diabetes research remains critically underfunded and talented researchers are choosing other areas of focus. As a result, innovations in diabetes prevention, treatments and cures have been limited. Unless these circumstances change, the next generation of diabetes researchers may be lost forever.

To address this crisis, the American Diabetes Association established Pathway to Stop Diabetes, a transformational approach to discovering and supporting a new generation of exceptional diabetes researchers. The prestigious, nomination-only Pathway awards are designed to attract and cultivate brilliant scientists at the peak of their creativity and to accelerate research progress by:

- Providing substantial and sustained funding that is unrestricted and transferable between institutions,
- Guiding the researchers with a broad array of scientific and career mentoring and
- Creating systems and programs for collaboration, communication, and career advancement.

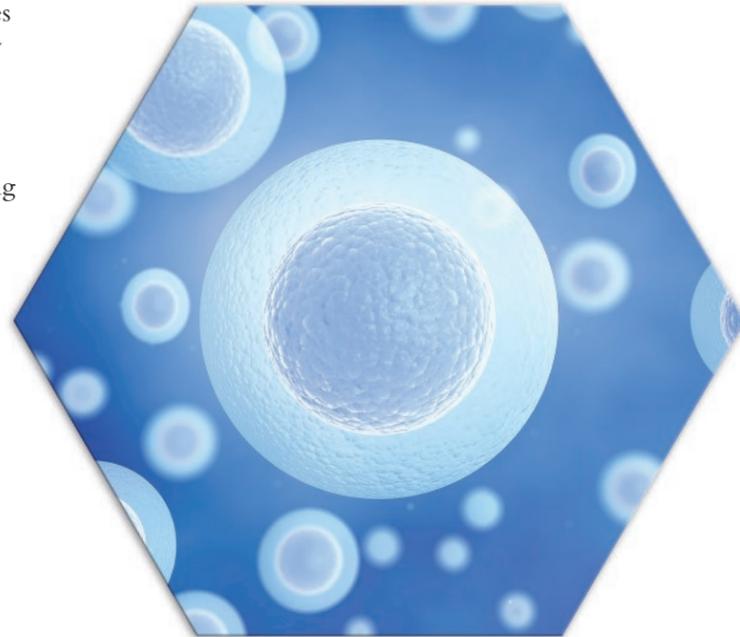
With more than \$35 million in generous gifts from individuals, foundations and corporations, including Pathway corporate sponsors Sanofi, Novo Nordisk, AstraZeneca and the Eli Lilly and Company Foundation, the American Diabetes Association is making significant progress toward accelerating diabetes research.

Three types of Pathway grants support early-career investigators and those established in other fields:

- **Pathway Initiator** — For scientists currently in training through their transition to independence
- **Pathway Accelerator** — For scientists early in their independent careers
- **Pathway Visionary** — For established scientists with a track record of success in another field of study who wish to apply their expertise and novel approaches to diabetes research

*“Diabetes research still needs its champions to find new treatments and treatment strategies for patients into the next decade. We look forward to seeing where the research leads us.”*

— Todd Hobbs, Chief Medical Officer,  
Novo Nordisk Inc.



*“Sanofi shares a mutual goal with these researchers in our commitment to discover and deliver innovative solutions to improve diabetes management. We look forward to seeing their scientific contributions.”*

— Andrew Purcell, Vice President and  
Head of U.S. Diabetes, Sanofi US

*Pathway provides crucial support to individuals exploring innovative ideas and transformational approaches to Stop Diabetes®.*

## Highlights from 2015

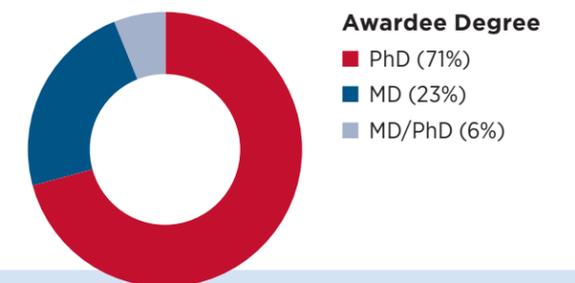
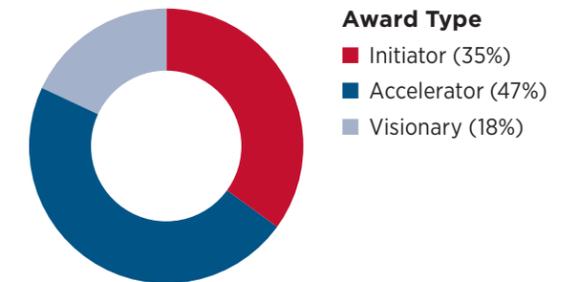
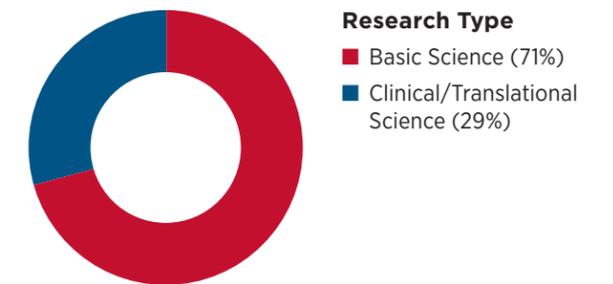
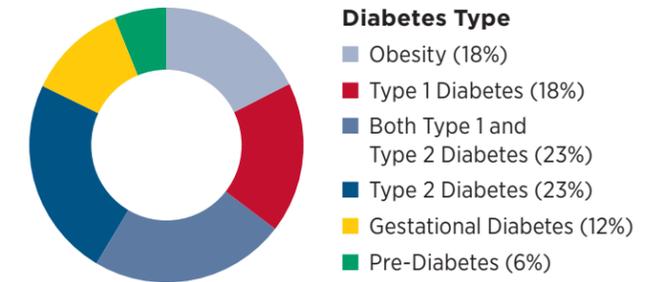
- ▶ Six new Pathway scientists initiated their projects in January 2015, joining the five selected in 2014.
- ▶ Pathway scientists were extraordinarily productive; collectively they published nine papers during the second year of the program and gave more than 70 presentations on their Pathway research findings.
- ▶ Two Pathway scientists were promoted in their academic careers.
- ▶ Two patent applications have been submitted by Pathway scientists over the last two years.
- ▶ Pathway scientists presented their work to the Mentor Advisory Group, Association leadership, and Pathway sponsors and donors at the second annual Pathway Symposium in Boston, Massachusetts.
- ▶ In early 2016, the third class of six new Pathway scientists was named.

## The Pathway Portfolio

The Pathway program comprises a strong and balanced research portfolio, representing the full breadth of diabetes research topics and achieving key program objectives.

Highlights of the Pathway portfolio include:

- Investments across diabetes types and diabetes-related disease states, focusing on all people affected by diabetes and its complications
- Collaborative, multi-disciplinary approaches with investigators combining efforts to accelerate progress
- Early career researchers and experienced investigators from other fields, all bringing fresh perspectives to diabetes research



# 37

**Average age of first-year Pathway Initiator and Accelerator Awardees**

Compared to 42 for first NIH research project (R01) grant awardees and 51 for NIH R01 awardees overall

## Key Accomplishments by Pathway Scientists in 2015

The eleven Pathway scientists who were funded during the 2015 calendar year contributed impressively to the diabetes field and advanced in their careers as diabetes experts.

### Rapidly Expanding the Knowledge Base

All still very early in their funding, the Pathway scientists published a combined nine manuscripts in peer-reviewed academic journals in 2015. In addition, they gave more than 40 poster and oral presentations and 32 invited lectures. This level of productivity and the rapid dissemination of results to the research community served to accelerate progress in the field.

### Selected Publications

Dennis MD, Kimball SR, Fort PE, Jefferson LS. Regulated in development and DNA damage 1 is necessary for hyperglycemia-induced vascular endothelial growth factor expression in the retina of diabetic rodents. *Journal of Biological Chemistry*. 2015 Feb 6;290(6):3865-74.

Peti W, Page R. Perspective: Strategies to make protein serine/threonine (PP1, calcineurin) and tyrosine phosphatases (PTP1B) druggable: Achieving specificity by targeting substrate and regulatory protein interaction sites. *Bioorganic & Medicinal Chemistry*. 2015 Jun 15;23(12):2781-5.

Yu J, Zhang Y, Ye Y, DiSanto R, Sun W, Ranson D, Ligler FS, Buse JB, Gu Z. Microneedle-array patches loaded with hypoxia-sensitive vesicles provide fast glucose-responsive insulin delivery. *Proceedings of the National Academy of Sciences U.S.A. (PNAS)*. 2015 Jul 7;112:8260-5.

Di J, Yu J, Ye Y, Ranson D, Jindal A, Gu Z. Engineering synthetic insulin-secreting cells using hyaluronic acid microgels integrated with glucose-responsive nanoparticles. *Cellular and Molecular Bioengineering*. 2015 Sep 3;8(3):445-54.

Riera CE, Dillin A. Tipping the metabolic scales towards increased longevity in mammals. *Nature Cell Biology*. 2015 Mar;17(3):196-203.

### Awards and Recognition

The Pathway vetting process is stringent and selective. Only the best candidates are selected for these awards. In addition to Association recognition, Pathway awardees also received significant recognition from other sources in 2015.

Michael Dennis, PhD, was awarded the *Frontiers in Eye and Vision Research Award* from the Penn State Hershey Eye Center.

Zhen Gu, PhD, was named to the list of “Top 35 Innovators Under 35” by *MIT Technology Review* and was recognized as a “Young Innovator in Cellular and Molecular Bioengineering” by the Biomedical Engineering Society.

### Career Advancement

Pathway endeavors to provide investigators the resources and autonomy to allow them to fully dedicate themselves to their research. Establishing stable, supportive academic positions is a critical step toward accomplishing this goal. During the 2015 calendar year, two Pathway Scientists were promoted. An Initiator Awardee was advanced to tenure track and a Visionary Awardee was promoted to full professor.

### Patents

The rapid translation of discoveries into tools and cures for people with diabetes is the central objective of the Pathway program. Protecting intellectual property is an essential step in this process. Pathway Scientists have filed two patents related to their Pathway research projects.



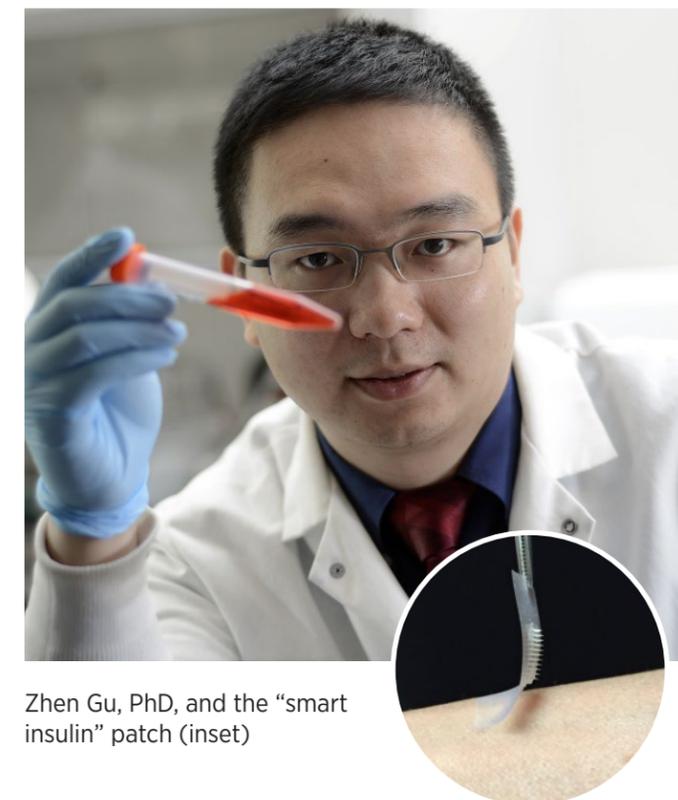
## Pathway Scientists Driving Progress

2015 awardee Zhen Gu, PhD, published a paper in *Proceedings of the National Academy of Sciences* describing the development of an innovative “smart insulin” patch that imitates the body’s beta cells by both sensing blood glucose levels and releasing insulin using a nanotechnology that leverages bioengineering, biochemistry and materials science. Dr. Gu found the patch to be effective in controlling blood glucose levels in laboratory mice over the course of several days. If it is also effective and safe in humans, this technology would be a game-changer for diabetes management.

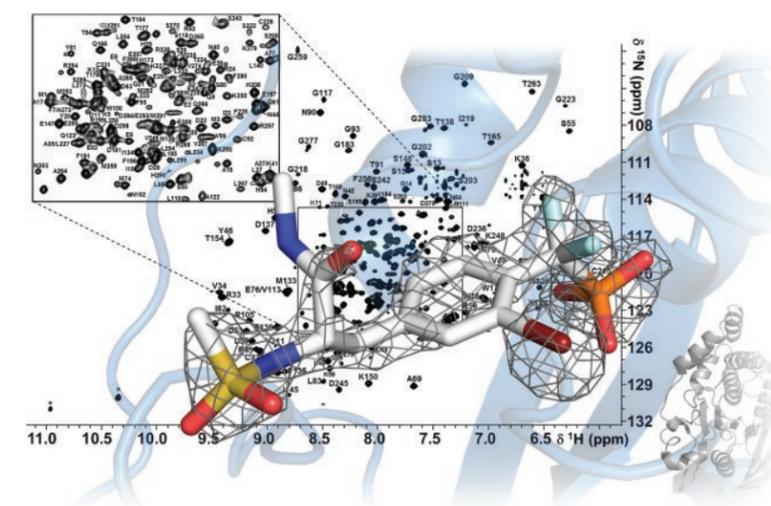
2014 awardee Wolfgang Peti, PhD, published a paper in *Bioorganic and Medicinal Chemistry* describing new insights into the atomic structure of a protein called PTP1B that regulates insulin receptor activity. Because this protein is known to be important to glucose metabolism, many previous attempts have been made to develop drugs to deactivate it, but those attempts have been unsuccessful. By using a technology called nuclear magnetic resonance (NMR) spectroscopy, Dr. Peti has been able to determine the structure of this protein in remarkable detail. In doing so, he has found that a previously disregarded part of the protein may in fact be an attractive target to inhibit the action of the protein. With this new information, scientists can begin to develop and test new drugs to interact specifically with this domain of the protein, perhaps leading to a new therapy for diabetes.

“AstraZeneca is proud to support the American Diabetes Association’s Pathway to Stop Diabetes researchers working to discover innovative treatment options and solutions to address a wide range of needs for patients living with diabetes.”

— Topher Brooke, Vice President,  
U.S. Diabetes, AstraZeneca



Zhen Gu, PhD, and the “smart insulin” patch (inset)



Model of PTP1B protein inhibition (courtesy of Wolfgang Peti, PhD)

## Announcing the 2016 Pathway Scientists

Pathway candidates were nominated from 103 institutions in 33 states. Thirty-six finalists were selected for detailed discussion at an in-person review meeting where applications were evaluated and scored by the Mentor Advisory Group. The Mentor Advisory Group recommended funding for the top six applicants who were ultimately selected as Pathway Scientists. They represent a diverse group of the highest quality scientists with bold and innovative approaches to Stop Diabetes®.

### INITIATOR AWARDS

#### Sui Wang, PhD

Harvard Medical School, Boston

#### Understanding How Diabetes Leads to Blindness

**Project Title:** *Dissection of Gene Regulatory Networks Underlying Diabetic Retinopathy*

Diabetes affects the retina, the inner layer of the eye responsible for communicating the images we see to the brain. Diabetic retinopathy is one of the most common complications of diabetes and is the leading cause of blindness among working-age adults. Currently, the only therapies for retinopathy are laser treatment and injection of drugs, which are used to slow down the progression of retinopathy, but are not able to reverse vision loss. To instead prevent diabetic retinopathy before it starts, researchers need to better understand how it develops in the first place. Dr. Wang is pursuing an innovative approach to understanding how diabetes impacts gene activity in the retina. She plans to map the gene networks involved in the initial development and progression of retinopathy. With this information, we can better identify early signs of retinopathy to begin treatment before vision loss occurs, and perhaps discover previously unknown molecules that may be candidates for the development of new drugs to preserve vision.

#### Phillip James White, PhD

Duke Molecular Physiology Institute, Duke University, Durham, North Carolina

#### Linking Diet and Metabolism to Diabetes Risk

**Project Title:** *A New Homeostatic Mechanism for Metabolic Control*

Very frequently, fatty liver and insulin resistance precede the onset of type 2 diabetes. Compounds called “branched chain amino acids” (BCAAs), which come from certain proteins in our diets, are linked to insulin resistance and the risk for developing type 2 diabetes. However, precisely how circulating BCAAs are connected to abnormal glucose and lipid metabolism is unclear. Dr. White has discovered that some of the components of the molecular network that go awry in protein metabolism and prevent BCAAs from breaking down also interact with both glucose and lipid metabolism pathways in the liver. Dr. White’s project will examine this network and how it is controlled. He hopes to further define how the molecules interact to control fat and glucose metabolism—and then to identify where new drug development efforts may be focused to treat prediabetes, fatty liver disease and type 2 diabetes.



### ACCELERATOR AWARDS

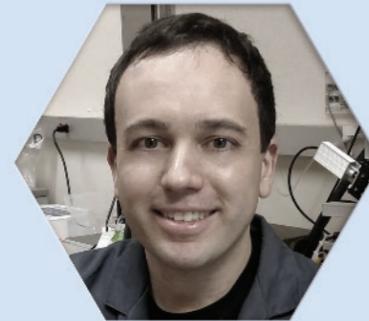
#### Daniel J. Ceradini, MD, FACS

Wyss Department of Plastic Surgery, New York University Langone Medical Center, New York

#### Uncovering a New Approach to Wound Healing in Diabetes

**Project Title:** *Therapeutically Targeting Keap1/Nrf2 Dysfunction in Diabetes*

Diabetes is the leading cause of non-healing wounds and lower extremity amputation in the U.S. Despite efforts to tightly control blood glucose in people with diabetes, poor wound healing persists as a common complication. Dr. Ceradini has discovered that high blood glucose levels associated with diabetes disrupt antioxidant networks important for tissue regeneration. His project seeks to determine whether restoring this critical antioxidant pathway to normal will reverse the impaired tissue regeneration caused by diabetes. Using innovative approaches and technologies, Dr. Ceradini will develop and test a novel therapy to restore the antioxidant protection program and determine whether it can overcome poor wound healing in diabetes.



#### Zachary A. Knight, PhD

University of California, San Francisco

#### Examining How the Brain Controls Obesity

**Project Title:** *Reinvestigation of the Arcuate Feeding Circuit*

Because the brain controls food intake, it is likely to be an important target for new therapeutics to reduce obesity. However, little is known about the specific site in the brain where environmental or dietary signals override the system that normally regulates feeding and weight maintenance. Dr. Knight’s project will use new technologies to investigate the key neurons in the brain that control food intake. If successful, this project will identify the signals that are responsible for activating the sensation of hunger, determine how the neurons motivate food consumption, and clarify how obesity leads to dysregulation of these neurons. Understanding of these networks in the brain may lead to development of new therapies to treat or prevent obesity by stimulating or inhibiting the neurons responsible for hunger and feeding behavior.

*“Diabetes treatments and solutions have advanced over the years. People with diabetes have many more options available to them, including long-acting medications and easier delivery systems.*

*None of that would have been possible without valuable research from dedicated scientists.*

*Lilly is pleased to support the American Diabetes Association and the Pathway researchers in their efforts to find future innovative solutions.”*

— Sherry Martin, MD, Vice President, Lilly Diabetes Medicines Development Unit



**Praveen Sethupathy, PhD**

University of North Carolina at Chapel Hill

**How Genetic Factors, Gut Bacteria and Diet Interact in Development of Obesity**

**Project Title:** *Systems Approach to Defining Genetic Regulation of Intestinal Physiology and Gut Microbiota in Diet-Induced Obesity*

In the human body, microorganisms outnumber human cells ten to one. These microorganisms, mostly bacteria, are influenced by both diet and genetic factors and are linked to metabolic disease. The gastrointestinal tract is home to a significant population of microorganisms and is the primary organ system responsible for absorbing nutrients from food. Obesity and diabetes are associated with changes in the microbial communities of the gut and with impaired intestinal function. Dr. Sethupathy's project seeks to identify the genetic factors that contribute the most to shaping the way our intestines respond to gut microorganisms under normal conditions and in diet-induced obesity and diabetes. These studies could lead to the identification of new therapeutic targets that may be leveraged to prevent or effectively treat obesity and diabetes.

**VISIONARY AWARD**

**Andrew Scharenberg, MD**

Seattle Children's Hospital and Seattle Children's Research Institute, Seattle

**Applying New Technology to Change Genes Involved in Type 1 Diabetes**

**Project Title:** *Regulatory T-Cell Stabilization via Gene Editing as Novel Therapy for Type 1 Diabetes*

Development of type 1 diabetes is known to involve the immune system inappropriately attacking the body's own insulin-producing beta cells. Several lines of evidence suggest that dysfunction of a type of immune cell, known as a thymic regulatory T-cell (tTreg), leads to a breakdown of normal protection from the immune system in insulin-producing beta cells. When the tTreg cells fail, the immune system begins to attack and destroy the body's own beta cells, leading to type 1 diabetes. Dr. Scharenberg is applying an innovative approach that he developed for "editing" genes to try to tackle type 1 diabetes. Using this technology, his Pathway to Stop Diabetes project aims to edit genes in tTreg cells to preserve their function and protect the beta cells from autoimmune attack, potentially preventing or reversing type 1 diabetes.



*innovation*

**The Future**

The fourth annual Pathway call for nominations opened in early 2016, with an application deadline of July 1, 2016.

Prior to the start of the American Diabetes Association's 76th Scientific Sessions in New Orleans, the Pathway scientists will assemble for the 3rd Annual Pathway Symposium, held on June 10, 2016. The invitation-only symposium includes the Mentor Advisory Group and Association leadership, as well as the individual donors and sponsors of the program. The newly-announced 2016 class of Pathway Scientists will present their research plans and progress to date. The Mentor Advisory Group will provide feedback, assess progress, and challenge traditional thinking.

Also at the Association's 76th Scientific Sessions, the Pathway Scientists who are continuing in their second or third years of funding have the opportunity to present at a special Pathway poster session on Sunday, June 12, and a Pathway oral session on Monday, June 13. These events are open to all attendees, and will allow the Pathway scientists to share their exciting results with the diabetes scientific community. Through events like these, the Pathway program provides opportunities for the Pathway Scientists to develop lasting professional and personal relationships that will enhance their research and careers in diabetes.

C. Ronald Kahn, MD, Chair, Pathway Mentor Advisory Group



## The Pathway Mentor Advisory Group

The Pathway Mentor Advisory Group comprises eminent scientists who seek in the Pathway applicants the core elements for exceptional science: rigorous thought processes, keen intellect, and capacity for innovation, creativity, and productivity. They select and mentor the Pathway Scientists throughout the duration of their awards.

**Barbara J. Anderson, PhD**

Baylor College of Medicine  
Houston

**Mark Stuart Anderson, MD**

University of California, San Francisco  
San Francisco

**Mark A. Atkinson, PhD**

The University of Florida  
Gainesville, Fla.

**Richard N. Bergman, PhD**

Cedars-Sinai Medical Center  
Los Angeles

**Morris J. Birnbaum, MD, PhD**

Pfizer, Inc.  
Cambridge, Mass.

**Charles Burant, MD, PhD**

University of Michigan Medical School  
Ann Arbor, Mich.

**John B. Buse, MD, PhD**

University of North Carolina School of  
Medicine  
Chapel Hill, N.C.

**Lawrence Chan, MD**

Baylor College of Medicine  
Houston

**Silvia Corvera, MD**

University of Massachusetts Medical School  
Worcester, Mass.

**Robert H. Eckel, MD**

University of Colorado Anschutz Medical  
Campus  
Aurora, Colo.

**Michael S. German, MD**

University of California, San Francisco  
San Francisco

**Margaret Grey, DrPH, RN, FAAN**

Yale University School of Nursing  
New Haven, Conn.

**David M. Harlan, MD**

University of Massachusetts Medical School  
Worcester, Mass.

**Barbara V. Howard, PhD**

MedStar Research Institute and  
Georgetown University  
Hyattsville, Md.

**Barbara Kahn, MD**

Beth Israel Deaconess Medical Center  
Boston

**Steven Kahn, MB, ChB**

VA Puget Sound Health Care System  
and University of Washington School of  
Medicine  
Seattle

**Martin G. Myers, MD, PhD**

University of Michigan  
Ann Arbor, Mich.

**Christopher B. Newgard, PhD**

Duke University  
Durham, N.C.

**Alvin C. Powers, MD**

Vanderbilt University School of Medicine  
Nashville, Tenn.

**Christopher J. Rhodes, PhD**

MedImmune  
Gaithersburg, Md.

**Philipp E. Scherer, PhD**

University of Texas Southwestern Medical  
Center  
Dallas

**Elizabeth R. Seaquist, MD**

University of Minnesota  
Minneapolis

**Randy J. Seeley, PhD**

University of Michigan  
Ann Arbor, Mich.

**Gerald I. Shulman, MD, PhD**

Yale University School of Medicine  
New Haven, Conn.

*“Through identifying and supporting innovative researchers, Pathway to Stop Diabetes is designed to radically transform diabetes research, setting us on the road to breakthrough discoveries to dramatically improve lives for people with diabetes.”*

— C. Ronald Kahn, MD, Chair, Pathway Mentor Advisory Group  
Joslin Diabetes Center and Harvard Medical School, Boston



“The Pathway Award is **giving me a voice** in a new field of study and allowing me to introduce **a novel angle** to the classical approaches undertaken **to study diabetes.**”



discovery

**Celine Emmanuelle Riera, PhD**  
PATHWAY INITIATOR AWARD RECIPIENT

## Pathway to Stop Diabetes Corporate Sponsors and Philanthropic Supporters

Through the tremendous generosity of four corporate sponsors and many philanthropic supporters who embrace new ways of thinking, Pathway to Stop Diabetes is accelerating the types of scientific investigations needed to discover solutions and ultimately end diabetes.

The Association extends deep appreciation for the investments that contribute toward the successes of this bold research initiative\*.

### CORPORATE SPONSORS

Visionary (\$7.5 Million Commitment)



Benefactor (\$5 Million Commitment)



### PHILANTHROPIC SUPPORTERS

#### Trailblazer (\$1 Million and above)

Pete & Linda Cummin  
Peter & Valerie\*\* Kompaniez  
Drs. Karen Talmadge & John Fiddes  
Don & Arleen Wagner  
Merck

#### Accelerator (\$100,000 - \$999,999)

Mr. & Mrs. Irvin Angel  
Alan & Elaine Armer, Trust  
Mr. & Mrs. Joseph C. Cook, Jr.  
Ginger & Jack Graham  
Mr. Douglas C. Hepper  
Louise S. Hoffman  
George & Judy Huntley  
Ann E. Juster\*\*  
Dr. Orville G. Kolterman & Mrs. Gayle Lorenzi-Kolterman  
Mr. & Mrs. James W. Quinn  
Dr. & Mrs. Robert E. Sevier  
Ralph & Laurie Yates

#### Initiator (\$10,000 - \$99,999)

Vaneeda & Robert Bennett  
Drs. David & Jane Bloomgarden  
Elly & Roger Brtva  
Steven & Eileen Cortese  
Mara Darsow & Anthony Moreau  
Richard J. Farber & Janet M. Leahy  
Vivian & Sarita Fonseca  
John Griffin & Lynn Knaupp  
Dr. & Mrs. Robert R. Henry  
Dwight Holing & Annie Notthoff  
Dr. Emily Holing & Mr. Bill Dillon  
S. Daniel & Cynthia Johnson  
Dr. David M. Kendall  
Karmeen Kulkarni  
Lebherz Family Foundation  
Wendell E. Mayes, Jr., PhD  
Dr. Dinesh Patel & Mrs. Kalpana Patel  
Nan & Robert Ratner  
Robert Singley  
Bess Weatherman

\* Contributions received through December 31, 2015

\*\* Deceased



[diabetes.org/pathway](https://diabetes.org/pathway)