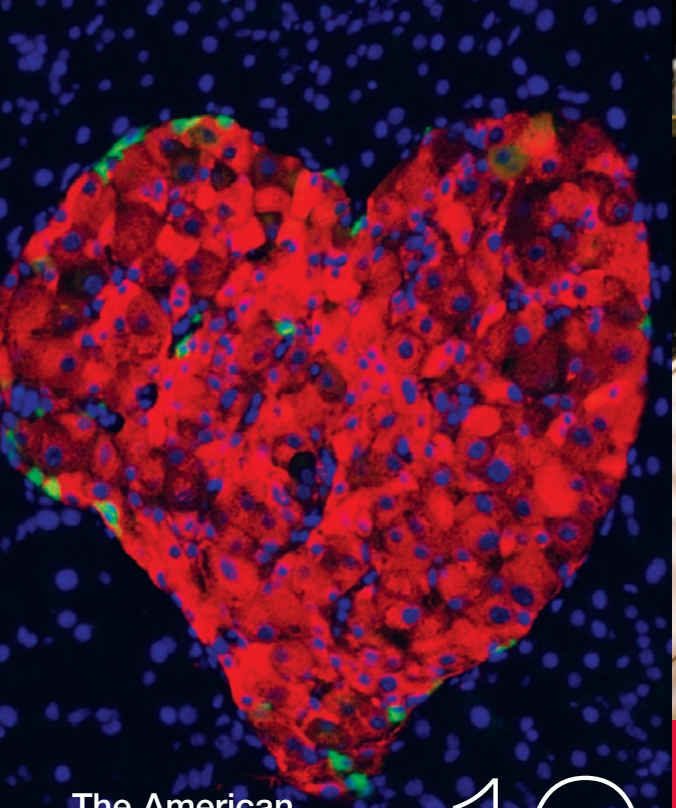
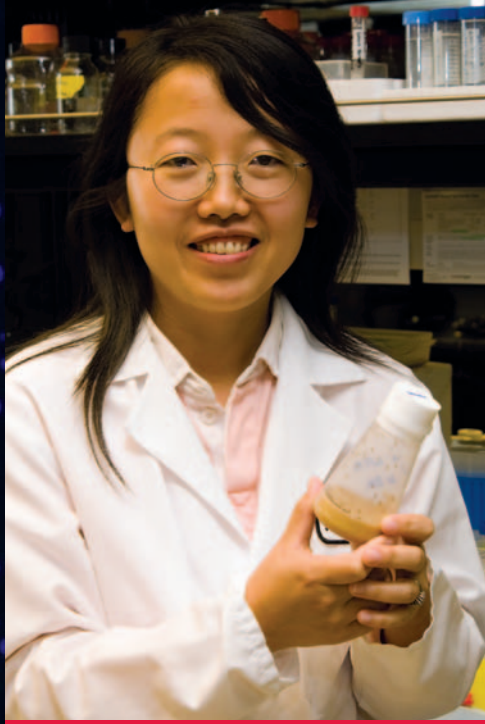




The American Diabetes Association Research Foundation's

10 Breakthrough Highlights

American Diabetes Association®

ResearchFoundation

Science. Progress. Hope.

1

"Friendly" bacteria protects mice against type 1 diabetes

Li Wen, MD, PhD
Yale University
Research Award: $295,000

Spontaneously type 1 diabetic NOD (non-obese diabetic) mice living in a germ-free environment and lacking normal gut bacteria develop severe diabetes. However, when the same type of mice is raised in a normal environment, and its intestines contain normal bacteria, this type of mice is protected from developing diabetes. These findings support the "hygiene hypothesis," which suggests that a lack of exposure to common bacteria and viruses may cause an increased risk of immune system disorders.

2

Leptin signaling in the brain influences obesity and type 2 development

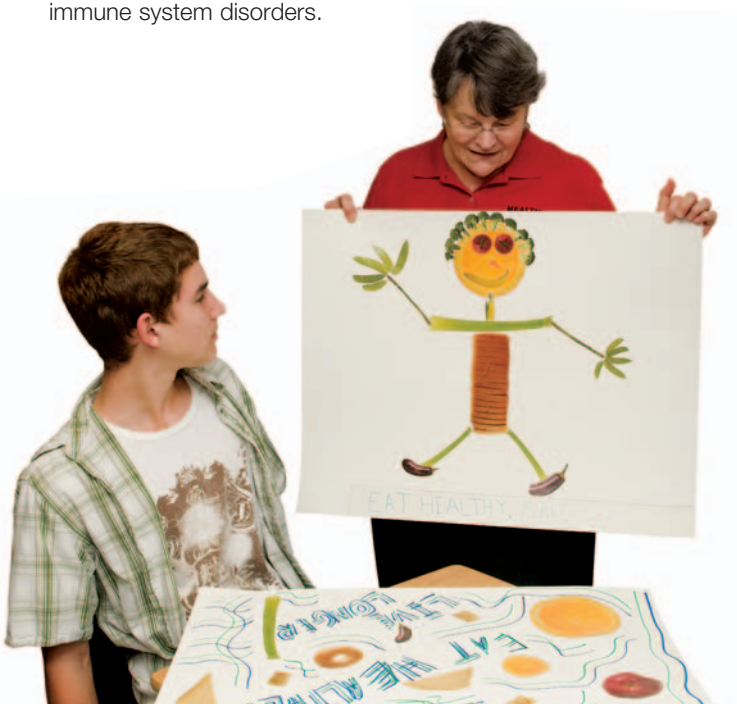
Beth Israel Deaconess:
Christian Bjorbaek, PhD
Anthony N. Hollenberg, MD
Young-Bum Kim, PhD
Joel Keith Elmquist, DVM, PhD

University of Texas Southwestern:
Joel Keith Elmquist, DVM, PhD

The Richard & Susan Smith Family Foundation Pinnacle Program Project Award: $3,912,498

Funded by Richard & Susan Smith Family Foundation

Specific nerve cell groups in the brain sense the fat hormone leptin and influence development of obesity and type 2 diabetes. Leptin plays a key role in regulating energy intake/expenditure, thereby affecting appetite and metabolism. Restoration of leptin signaling in key nerve cell groups in the brain can prevent type 2 diabetes in a mice; reestablishment of leptin signaling may also improve islet function; leptin signaling pathways influence systemic glucose regulation; and regulation of food intake is also controlled by these pathways. New therapies targeted to these pathways may prove beneficial in preventing or treating obesity and type 2 diabetes.

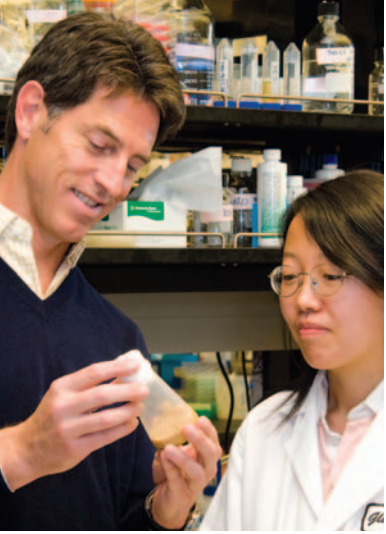


3

Fetuin-A levels may act as a predictor of diabetes in older people

Joachim Ix, MD
University of California at San Diego
ADA-ASP Innovation Award in Geriatric-Endocrinology: $150,000

Fetuin-A is a liver-produced protein that, when released into the bloodstream, can inhibit the actions of insulin, leading to increased glucose levels and development of type 2 diabetes. Higher serum levels of fetuin-A have been identified in the elderly population. It appears that at least a part of this association is linked to the extent of abdominal fat. Therapeutic strategies to



reduce serum levels of fetuin-A may prove useful in prevention of type 2 diabetes.

4

Zinc transporter 8 (ZnT8) is useful to diagnose and monitor progression of type 1 diabetes

John Hutton, PhD
University of Colorado Health Sciences Center
Research Award: $180,000
Funded by Valerie & Peter Kompaniez

The first diabetes auto-antigen (a substance that can induce an autoimmune response) to be discovered in 10 years, ZnT8, was recently identified. ZnT8 is localized to the beta cell and stimulates the production of auto-antibodies involved in the progression to type 1 diabetes. The additional detection of ZnT8 auto-antibodies may better help diagnose and follow the progression of the disease, and also generate new therapies to prevent or delay onset of type 1 diabetes.

5

A virtual NOD mouse model helps advance understanding of type 1 diabetes

Entelos Diabetes Research Center:
Matthias Von Herrath, MD
Kevan Herold, MD
Co-supported Research Award with Entellos: $500,000

In this age of virtual reality, a virtual model of the NOD mouse was recently developed. The software platform has been used to conduct in silico experiments related to the components of the autoimmune response in type 1 diabetes. This use of predictive biosimulation will help expedite the acquisition of new knowledge relevant to type 1 diabetes and will also aid in predicting what therapies may be of more benefit in the treatment and perhaps prevention of type 1 diabetes. Future development in this platform will be aimed at developing virtual human patients with type 1 diabetes.

6

Free radical regulation in brain may play a role in weight control and appetite

Sabrina Diano, PhD
Yale University
Research Award: $300,000

The brain actually utilizes fat as fuel. This process involves the generation of free radical molecules that contribute to aging and neurodegeneration. Appetite control may be directly regulated by these free radicals, and interference with free radicals could affect the feeling of fullness. Free radicals are maximally produced when brain cells that promote fullness are active, perhaps contributing to a decrease in maximum lifespan. This suggests that oral supplementation with antioxidants may prove useful in appetite control.

7

Re-educating the immune system may prevent and cure type 1 diabetes

Mark Rigby, MD, PhD
Emory University
Junior Faculty Award: $444,000
Funded in Part by Kent and Ann Seeley

Drugs known as co-stimulation blockers (CoBs) may induce immune tolerance in type 1 diabetes. CoBs slow disease-causing T cells in diabetic mice, while allowing expansion of functional regulatory T cells. This combination produces short- and long-term diabetes protection. In the future, CoBs could be used as treatment to delay or prevent the onset of diabetes. CoBs could also provide therapy to individuals who already have diabetes by accepting curative islet cell transplants without the need for life-long immune suppressive medicines.

8

Immune system "educator cells" help prevent autoimmunity

James Gardner
University of California at San Francisco
Clinical Scholars Award: $30,000

A novel population of cells that may be important in preventing type 1 diabetes has been recently identified. A unique gene called Auto Immune Regulator (Aire) directs a group of specialized educator cells, usually found in the thymus gland, to teach developing T cells how to identify and attack invaders to the body (and not attack itself), as part of the immune system defense. The newly-discovered population of educator cells—found within the lymph nodes and spleen, outside of the thymus—can directly interact with and destroy self-reactive T cells. This suggests that the educator cells may act as a back-up system to eliminate self-reacting cells that escape detection in the thymus.

9

Obesity pathway in the brain of mice is triggered by overeating

Dongsheng Cai, MD, PhD
University of Wisconsin at Madison
Junior Faculty Award: $413,811

Excessive calories can trigger a normally inactive inflammatory pathway in the brain of mice, possibly contributing to development of obesity and type 2 diabetes. This pathway, also known to cause inflammation in other body tissues in the presence of excess caloric intake, can cause changes in the brain, such as resistance to both insulin and leptin. If a similar pathway is active in humans, it could be targeted to counter the effects of overeating, obesity and their complications.

10

Inflammation is the key to insulin resistance in gestational diabetes

Jacob Friedman, PhD
University of Colorado Health Sciences Center
Mentor-based Postdoctoral Fellowship Award: $180,000

Insulin resistance in women with gestational diabetes appears to be increased by inflammation. Gestational diabetes also increases the risk of a type 2 diabetes diagnosis after pregnancy. A pro-inflammatory compound, TNFalpha, appears to be the primary cause of this increased inflammation. Strategies to decrease inflammation in gestational diabetes may have immediate and long-term benefits.

Dear Friends,

When will we find a cure? My wife, Laurie, and I hear this profound question asked at every diabetes-related event we attend. It is the same question we had 25 years ago when our then-2-year old daughter, Becca, was diagnosed with type 1. When indeed?

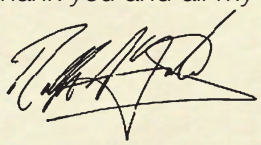
I have heard countless researchers struggle to reply to this question, but I finally found my own way to answer this pressing problem that weighs on people with diabetes and those who love them. I found my own definition of "cure." To some, a cure is a world without insulin. To others, it is life without testing or shots. Becca's expectation today of a full life in front of her is my definition of a "cure."

Twenty-five years ago, we struggled to contemplate Becca's impending complications and a severely shortened lifespan. Today, she is happy, independent, and without diabetic complications with the help of devices and medications that were not previously available.

Although our ultimate goal at the American Diabetes Association (ADA) Research Foundation is to fund and find a cure for diabetes altogether, we appreciate daily the substantial, life-altering strides that we have already made thanks to the research you help support.

In this brochure, you may read about some of the ADA Research Foundation's top scientists and their groundbreaking ideas. These research projects are the immediate outcomes of the ADA's search for your definition of cure, whatever it may be. Here, at the ADA Research Foundation, we fund science, and with it, we fund hope.

Thank you and all my best,



Ralph Yates, DO
Chair, Research Foundation

American Diabetes Association®

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Research Foundation
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The ADA Research Foundation *and its investment partners have witnessed progress in better therapies for treating diabetes. Each breakthrough fuels our belief in success and gives us hope that we will one day find a cure for diabetes. With your financial support, we have helped and will continue to help our loved ones live better lives.*

If you would like expanded information on these discoveries or how to find a specific project or researcher, please contact 1-888-700-7029 or email Elly Brtva, Managing Director of Research Foundation at ebrtva@diabetes.org