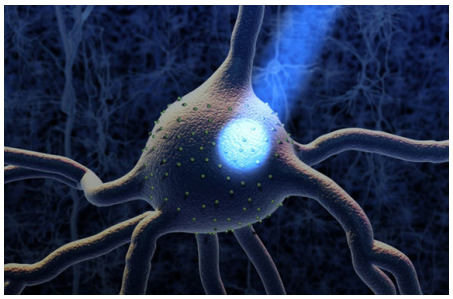
BLOOD SUGAR AND THE BRAIN:

Discovering New Treatments for Diabetes



When a scientist shines a light on neurons that have been rendered light-sensitive — a technique called optogenetics — they can observe the brain's electrical signaling and understand how it powerfully influences glucose levels.

DIABETES, elevated blood sugar that peaks and ebbs, is a global health epidemic responsible for approximately 1.5 million deaths a year. In 2013, an estimated 382 million people or 8.3 percent of the world's population suffered from diabetes and its complications, which include serious medical problems like heart disease, stroke, increased risk of infection, and kidney and eye problems.

Diabetes is not only a fatal and disabling condition for patients, but also expensive and challenging to manage. Current estimates suggest that diabetes and its complications cost global health systems nearly $550 billion annually. And with diabetes affecting as much as 10 percent of the world's population in 2035 — 592 million patients — there is an urgent need to address the societal and human toll of this disease.

UW Medicine intends to help control diabetes through an exciting new discovery. In the laboratory of Michael Schwartz, M.D., a leading faculty member at the UW Medicine Diabetes and Obesity Center of Excellence, scientists have learned that the brain plays a central role in regulating blood sugar, a process that may provide a new, untapped target for managing the disease. We invite you to learn more about this discovery and explore opportunities to join UW Medicine in its effort to alleviate the world's rising diabetes epidemic.

Diabetes-related data from the International Diabetes Federation

Discoveries: From Insulin to the Brain

The discovery of insulin some 90 years ago revolutionized our understanding of how diabetes occurs and provided an immensely valuable tool in controlling blood sugar or glucose. Scientists later recognized that other mechanisms contribute significantly to blood glucose control, but assumed that these mechanisms could not be regulated. As a result, the focus of diabetes research and care shifted almost exclusively to insulin. Today, almost all treatments for diabetes seek to either increase insulin levels or increase the body's sensitivity to insulin.

Only recently have scientists begun to explore diabetes from a biological "systems" approach, one in which insulin is part of a larger, complex and highly integrated process. Thanks to discoveries made in the Schwartz laboratory, scientists have demonstrated that normal glucose regulation involves a partnership between the pancreas and the brain's hypothalamus, and that impairment of both organs likely contributes to the development of diabetes. This discovery has the potential to transform diabetes diagnosis and care by identifying new treatment targets that are specifically focused on the brain.

Optogenetics: A Light Switch for Diabetes

Dr. Schwartz's team is using optogenetics, a new technology that allows scientists to control neuron activity with light. In this way, they can identify which areas of the brain are responsible for blood sugar regulation. They take the following steps.

- Researchers start with a harmless virus that contains the DNA for a protein that is light-sensitive.

- The virus enables light-sensitive proteins to be made in the neurons of genetically engineered mice.
- Exposing the mouse's light-sensitive neurons to light allows researchers to identify areas of the brain responsible for blood sugar regulation, and to turn these neurons "on" or "off."
- Scientists then measure how changes in neuron activity affect mouse metabolism and behavior.

In an exciting development, Schwartz's team has identified one neural circuit that appears to elevate blood sugar and does so in a way that resembles the process in patients with diabetes. In the near future, they intend to determine whether inhibiting this neural circuit can reverse elevated blood sugar in diabetic mice. Over the next several years, the Schwartz lab expects to map this circuit to assess its role in the development of diabetes, potentially locating circuits that could be targeted for new diabetes medications.

Opportunities to Make a Difference

This path-breaking research has the potential to transform our understanding and management of diabetes, revealing:

- How the brain controls blood sugar and how this system integrates with the pancreas, insulin and other hormones;
- Whether altered brain activity contributes to elevated blood sugar in people with diabetes; and
- Whether specific neurocircuits might be targets for diabetes treatment, potentially leading to new, more effective therapeutics.

In order to advance this ambitious mission, the Schwartz laboratory needs visionary partners to support the next phase of research. Your philanthropic support can help in the following ways.

Provide laboratory support for optogenetics **$50,000 to $100,000**
The Schwartz Lab needs to extend its current research model to continue to illuminate new circuits and pathways responsible for metabolism control. Gifts will expand promising, multidisciplinary research that may one day lead to new drugs that control diabetes.

Hire a junior scientist **$100,000**
Funding is needed to hire and support the operational costs of adding a junior scientist to the team. This person will process study data and identify neurotransmitters responsible for blood sugar regulation.

General laboratory support **Gifts at all levels**
Gifts of any amount will help advance the Schwartz lab's research.

Join Us

To learn how you can support UW Medicine's critical research in diabetes, please contact Jennifer Schmitt, director for philanthropy, at bumby@uw.edu or 206.616.3052.

Key Faculty

Michael Schwartz, M.D.
UW Professor of Medicine, Division of Metabolism, Endocrinology and Nutrition
Robert H. Williams Endowed Chair in Medicine
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Dr. Michael Schwartz investigates brain mechanisms governing energy balance and glucose metabolism and how obesity and diabetes result from impairment of these brain systems. He has been honored with the Naomi Berrie Award for Outstanding Achievement in Diabetes Research from Columbia University and the Solomon A. Berson Lectureship from the American Physiological Society. Dr. Schwartz also serves as an editorial board member for five medical journals.