

Trapping Diabetes

Learning What Makes the Beta Cell Tick

Below: Kathy Zawalich; right: lab assistant Greg Tesz; background: Islets of Langerhans, clusters of pancreatic cells which secrete insulin into the blood stream, regulating blood glucose level (magnification 100x)



Imbedded at the end of a corridor in the basement of the Yale School of Nursing, Room 106, or what is commonly referred to as the “Zawalich Lab,” is not the easiest place to find. The lab’s outer appearance gives no indication that some of the most important biochemical research in diabetes occurs within its walls.

The Zawalich team, made up of Dr. Walter Zawalich, his wife Kathy Zawalich, and their lab assistant Greg Tesz, is trying to understand how the beta cell regulates the secretion of insulin. Understanding how the beta cell, the body’s sole supplier of insulin, functions is important for several reasons. In the most common form of diabetes, referred to as type 2 diabetes, it fails or decompensates; in type 1 diabetes it is singled out of the islets of Langerhans for immune-mediated destruction. “The question that has always fascinated us is what makes the beta cell so unique, and why is it singled out for destruction?” explains Dr. Zawalich. He speculates that perhaps the same processes that regulate insulin secretion

and cause the beta cell to respond so well also play a role in targeting by the immune system. “With a more comprehensive understanding of the basic physiology of the beta cell we can understand its pathophysiology in type 2 diabetes and why it is destroyed in type 1 diabetes,” he says.

In May 2003, the Zawalich Lab was awarded a grant from the National Institutes of Health. This competing continuation grant, funded for the past 13 years, will be extended for 4 additional years. The proposed studies explore how the over expression or under expression of key proteins in the islets of Langerhans regulate insulin secretion. It is anticipated that these studies will facilitate the design of surrogate beta

under the Microscope:



cells for genetic engineering studies to replace those lost in type 1 diabetes and establish how these proteins contribute to the changes that occur in type 2 diabetes. Dr. Zawalich explains that, “Understanding the factors that control insulin secretion release becomes important in trying to reverse this situation.”

In the studies proposed, several forms of the enzyme phospholipase C and protein kinase C, will be overexpressed in the beta cell by inserting extra copies of the gene that encodes for the protein. If these proteins control the release of insulin, the prediction is that the beta cell altered in this fashion should release more insulin when stimulated. “These studies are also important if, as has been proposed by others, we want to genetically engineer undifferentiated stem cells to become beta cells that can be transplanted,” says Dr. Zawalich. “We have to know what proteins are essential and have to be expressed in these cells to make them synthesize and secrete insulin.” Another aim of the grant is to try and knock out

selected beta cell proteins or receptors and determine how the secretion of insulin has been changed. The long term goal of all the studies is a more complete understanding of the biochemical pathways that control insulin secretion, how they maintain euglycemia and their involvement in the pathogenesis of diabetes.

One may not readily think of cutting edge biochemical research taking place at a nursing school, but to Dr. Zawalich the affiliation with YSN makes perfect sense. He explains that the work of his team often informs and is in turn informed by the scholarship of other YSN faculty. “The work of Professors Margaret Grey, Gail D’Eramo Melkus and other faculty has helped build a strong foundation of diabetes research at YSN,” he says. “Our efforts are often complementary, and our work in the lab informs the curriculum for masters and doctoral level students.” Dr. Zawalich is also quick to credit his colleagues at the Yale Medical Center for their ongoing support. “We’ve been extremely fortunate to have a large number of collaborators outside YSN who have contributed to our work,”



Above: Dr. Walter Zawalich (right) and Greg Tesz in the “Zawalich Lab”

he says. In particular, he credits Drs. William Philbrick and John Sterpka at the Yale Medical School for helping to guide the Zawalich Lab into the area of regulating protein expression by manipulating genes.

“Science evolves incredibly fast, especially in the area of biochemical research,” says Dr. Zawalich. “In order to stay on the cutting edge we must make full use of our colleagues’ considerable expertise. Partnering with fellow researchers throughout Yale has been an extremely rewarding experience for us.”

Collaboration with colleagues throughout Yale has also enhanced the education experience for Dr. Zawalich’s students. A number of his colleagues have been invited to discuss their work as part of his Biomedical Sciences class. Guest speakers have included some of Yale’s most prominent researchers, such as Dennis Cooper, Barbara Gulanski and Fred Gorelick, who have engaged ysn students on topics ranging from oncology, endocrinology, osteoporosis and cystic fibrosis. According to Dr. Zawalich, colleagues who have had a chance to interact with ysn students have told him that they are among the most enthusiastic learners and critical thinkers. “Our students’ keen interest in a variety of subjects creates an environment that encourages a free exchange of ideas and makes the lecture experience a rewarding one for the guest speakers,” he says.

A significant number of Dr. Zawalich’s colleagues from the Yale Medical Center have been repeat guests in his class. The class discussions are often the beginning to lasting relationships between ysn students and top experts in medical science at Yale. According to Dr. Zawalich, these relationships provide an important resource for ysn students during their years at Yale and in their later professional

development. “Ultimately, these interactions extend the reach of the nursing school,” he says. “They make the entire realm of health care science at Yale part of the ysn experience.”

Considering Dr. Zawalich’s accomplishments, it is hard to believe that he almost failed out of his biochemistry class as a student at the University of Massachusetts. “The great irony is that all the pathways I was reluctant to learn as a student I have since made my life’s work,” he says. “I credit my faculty mentors who peaked my curiosity, gave me room to grow and allowed me to make mistakes with giving me the tools necessary to pursue this work.” Dr. Zawalich often shares this story with his students during their first year at ysn. “I hope my experience demonstrates to them that it is okay to struggle with the subject matter and to make mistakes as long as one is willing to remain curious, enthusiastic, and dedicated to their work.”

According to Dr. Zawalich, students who come to ysn with little or no background in biochemistry undergo a remarkable transformation in just a few short months. “This speaks to the high caliber of students who choose to study nursing at Yale,” he says.

When asked what it is like to ride what Walter Zawalich calls “the hills and valleys of science” together with their spouse, the Zawalichs admit that the journey has been marked by “detours, important crossroads and interesting side trips.”

“Walter is so passionate about his work that it often goes home with him,” confides Kathy. She jokes that “Because we go home together, invariably I end up taking my work home with me as well.” All jokes aside, however, Walter and Kathy are quick to credit each other for their continued success. After 35 years of marriage and 15 years of working together, the Zawalichs still make a terrific team! 🏆