

## Department of Defense awards EVMS

# \$1 MILLION TO DEVELOP

## new approach to reversing Type 1 diabetes

### Results could have broader application to other autoimmune diseases

Imagine you are blowing up balloons in a room full of people with pins. How long would your balloons last? That's the analogy David Taylor-Fishwick, PhD, associate professor of internal medicine and director of Eastern Virginia Medical School's Cell, Molecular and Islet Biology Laboratory, often uses to describe his research to find new therapies that could ultimately lead to a functional cure for Type 1 diabetes.

Dr. Taylor-Fishwick and his team of researchers at EVMS' Strelitz Diabetes Center, have been awarded a \$1,076,250 grant by the Department of Defense (DoD) Peer Reviewed Medical Research Program to develop new ways of reversing the underlying causes of Type 1 diabetes, an autoimmune disease in which the body's immune system attacks the insulin-producing beta cells in the pancreas.

"Type 1 diabetes is unique among autoimmune disorders in that the body does not automatically replace these cells once they are destroyed," Dr. Taylor-Fishwick explains.

Current treatments, such as insulin injections, help patients maintain normal blood-sugar levels but don't prevent the serious health problems associated with diabetes such as blindness, nerve damage, heart disease and kidney failure.

Now back to the balloon analogy. "The challenge in reversing Type 1 diabetes is to regenerate the beta cells and at the same time stop the body's autoimmune attack," Dr. Taylor-Fishwick says. "We're blowing up the balloons — creating the new cells that are making insulin — but we're not going to create very many in that room if everybody is popping them with pins. The pins represent the immune system, which we believe is a key component in that negative environment."



From left to right: Jessica Weaver, PhD, postdoctoral fellow; David Taylor-Fishwick, PhD, associate professor of internal medicine and director of the Cell, Molecular and Islet Biology Laboratory; Margaret Morris, PhD, research assistant professor; Kendall Leone, research associate.

Dr. Taylor-Fishwick's research on beta-cell regeneration has focused on INGAP (Islet Neogenesis Associated Protein), branded as Exsulim, the breakthrough discovery made by Aaron I. Vinik, MD, PhD, director of research at the Strelitz Diabetes Center, and Lawrence Rosenberg, MD, PhD, of McGill University. The INGAP gene stimulates the growth of insulin-producing beta cells in the pancreas, allowing an individual to regenerate his or her own cells without the need for donated cells, which the body may reject.

Now that the center's scientists have established that they can effectively regrow beta cells, the DoD grant will fund the next phase in the team's research — finding a way to neutralize the immune system's attack.

"The main emphasis of this grant is to build on the successes that we've had," says Dr. Taylor-Fishwick. "It looks like we can make those balloons, but we need to do something to neutralize the pins, so that when the cells do grow, they enter a stable environment — a room full of balloons with no pins."

In this next stage of their research, Dr. Taylor-

Fishwick and his team will test several experimental drugs developed by Jerry Nadler, MD, chair of internal medicine and director of the EVMS Strelitz Diabetes Center. The compounds are designed to modify the autoimmune response and stabilize beta cells. The goal is to develop these compounds into an oral pill that, when used in conjunction with INGAP, may help create a combination therapy that reverses Type 1 diabetes. If successful, their findings may also prove useful in developing treatments for other autoimmune diseases such as lupus and rheumatoid arthritis.

"The Department of Defense, through its Congressionally Directed Medical Research Program, is especially interested in research to combat autoimmunity," Dr. Taylor-Fishwick says. "So part of our work is to block the process of autoimmunity that occurs in diabetes. We are using a drug called Lisofylline (LSF) and related molecules to block interleukin-12, a protein that triggers the autoimmune response. By targeting interleukin-12 signaling, we hope to redirect the immune system, but not wipe it out." □