Targeting diabetes: New agents track onset of disease

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Ron Lynch analyzes images of beta cells delineated by indicator molecules attached to the cell surfaces.(Photo by Beatriz Verdugo/UANews)

(PhysOrg.com) -- University of Arizona researchers have received a prestigious grant to develop indicator molecules to track the onset of diabetes in patients before the disease develops – potentially paving the way to developing treatments.

Several potential treatments have been proposed to prevent or postpone the development of diabetes. But currently there is no way to monitor whether the treatments are effective to delay its onset.

Now, researchers at the University of Arizona are working to develop a method of determining at an early stage whether a person is developing diabetes and to track the effects of potential treatments.

Ronald Lynch, professor of physiology at the UA's department of physiology; Sean Limesand, associate professor of animal science at the UA's department of animal sciences; and Josef Vagner, an associate research professor at the UA's BIO5 Institute, together received a $500,000 grant from the Juvenile Diabetes Research Foundation to develop an accurate way to target imaging contrast agents – molecules that can be viewed through a scanner – to beta cells in the human pancreas.

The research could provide a much-needed method of monitoring pre-diabetic patients to determine whether new therapies to curb development of the disease are effective.

Type 1 diabetes, often referred to as juvenile diabetes because of the large proportion of people who develop it at a young age, occurs when the body's immune system malfunctions, eliminating normal beta cells from the pancreas.

Beta cells are needed to secrete insulin, a protein that instigates removal of glucose from the bloodstream. Without beta cells to secrete insulin, glucose levels in the bloodstream become too high, presenting dangerous health consequences that will lead to death if untreated.

Thus, type 1 diabetics must constantly monitor their blood glucose levels and periodically inject calculated amounts of insulin to stay alive.

"One of the biggest problems in diabetes research is how to monitor the health of beta cells," said Lynch. "With current methods, patients have to lose about 90 percent of their beta cells before they are diagnosed as diabetic."

While diabetes is incurable, several potential treatment methods exist to try to slow down or reverse the loss of beta cells. But with no way to

detect and monitor changes in the population of beta cells in a patient, the success or failure of a specific treatment has been difficult to assess.

Now, that could change.

Lynch, Limesand and Vagner are developing a way to reliably, non-invasively track changes in beta cell populations.

"Beta cells come in groups and these groups are small," said Lynch. "In fact they're so small that most of the imaging devices that are used on people can't see them. Our approach is to develop chemicals that will target specifically to these beta cells, while carrying along a marker that can be imaged, so now we can measure how many beta cells a patient retains."

The marker is an indicator molecule that, once injected into a patient becomes attached to the exterior of the beta cells in the pancreas. The indicator molecules can be seen via a PET scan, a common method for human imaging that allows researchers to visualize and count the beta cells to which the molecules are attached.

Theoretically, if a patient repeats the scan periodically, doctors will be able to track changes in the patient's beta cell population and adjust treatments accordingly.

Previous research has targeted indicator molecules onto the surface of cells by attaching them to signal molecules called ligands. The ligands fit corresponding receptors on the cell surfaces like keys in locks.

The problem is that different types of cells often have some of the same receptors, so the signal molecules might bind to the target cells but they could just as easily bind to other types of cells as well. With no differentiation, researchers and doctors have no way to tell the

difference in cell type and could get an incorrect count of the beta cell population.

The UA researchers may have solved this problem.

"Because the beta cells make up such a small amount of tissue in the abdomen, it is important that the molecules don't bind to cells in the liver or the intestine. These organs are much larger, and because they sit near the pancreas they would mask the signal from the beta cells," said Lynch.

"The ligand needs to bind only to the beta cells. We've developed technology that allows for that type of specificity."

Specificity can be achieved by linking together a combination of different ligands to create a ligand chain that will bind only to beta cells that have the exact combination of corresponding receptors, which no other type of cell in the abdomen will have.

"We call this molecular bar-coding," said Lynch. "You have all these lines in a barcode: some are thicker, some are thinner, but the overall barcode tells you what you need to know. Each cell has a lot of different receptors on its surface, and if you pick one type of receptor then it might also be on another cell and give you the wrong information. But if you find the right combination of different receptors then that information is a cell's barcode. We're trying to find out what barcode specifies a beta cell."

"This technology is very useful because as we start to build that barcode we will obtain specific and novel information about the beta cell."

Using the UA researchers' method, researchers and doctors may be able to determine if and when patients with family history of diabetes begin

to lose beta cell mass – precious knowledge that could help determine which treatments for an individual patient are helping to forestall the development of diabetes.

Provided by University of Arizona