Two experiments suggest new direction for diabetes

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By Maggie Fox, Health and Science Editor

WASHINGTON (Reuters) - Two experimental treatments suggest new directions for treating diabetes, both using compounds already made by the body, researchers in the United States reported on Monday.

One of the two studies suggests that some current treatments for autoimmune diseases such as the bowel-cramping Crohn's disease may be taking the wrong approach and doing active harm in some patients.

The two reports, published in the Proceedings of the National Academy of Sciences, each aim to correct some of the things that go wrong to cause type-1 diabetes, which is caused when immune cells mistakenly destroy the cells in the pancreas that make insulin.

The International Diabetes Federation estimates that 230 million people globally have diabetes, and about 10 percent of these have type 1. Patients are usually diagnosed at a young age and must carefully measure blood sugar levels and take insulin for life. There is no cure.

Dr. Denise Faustman and colleagues at Massachusetts General Hospital and Harvard Medical School in Boston tested a cheap generic drug used to prevent tuberculosis, called bacillus Calmette-Guerin or BCG.

Faustman said BCG temporarily elevates levels of an immune system protein called tumor necrosis factor or TNF. Earlier studies had shown that raising TNF in mice can cure them of a condition resembling human diabetes.

"If you are a mouse, we have got you covered. But the ultimate goal is people," Faustman said.

'BAD' T-CELLS

Her team showed that people with type-1 diabetes have certain numbers of abnormal immune system cells called T-cells. These attack and destroy the pancreatic tissues that normally make insulin.

The tests on blood from 675 people with diabetes and 512 healthy people showed the diabetics had some CD8 "killer" T-cells that could be killed by either TNF or BCG.

"Good" T-cells were not killed by the treatment, they wrote.

The same team is now testing BCG at very low doses in a Phase I clinical safety trial in a few human volunteers.

"Now we have these T-cell markers from blood ... so we can know within weeks if we are getting rid of the bad T-cells," Faustman said.

She said her study suggests that anti-TNF therapies such as etanercept, sold by Wyeth and Amgen under the brand name Enbrel, and Johnson & Johnson's Remicade may actually cause new autoimmune diseases in some patients with Crohn's and rheumatoid arthritis.

A second team, at the University of Texas Southwestern Medical Center in Dallas, took a different tack, using a hormone called leptin.

Leptin, only discovered in 1994, is made by fat cells but people with type-1 diabetes often have abnormally low levels of leptin.

Roger Unger of UTSW and colleagues used gene therapy to treat mice with damaged pancreases that made no insulin at all and were dying. They used a virus to carry in genes for leptin, which in turn caused their livers to pump out huge levels of the hormone.

"Within two weeks they were completely normal," Unger said in a telephone interview. "This was totally unexpected."

Unger believes the leptin changed the function of another hormone called insulin-like growth factor 1 or IGF1, making it act more like insulin to regulate blood sugar levels.

It may also suppress the unhealthy effects of another compound called glucagon, which is produced excessively in diabetes, he said.

The gene therapy approach would be too risky in people so Unger plans to inject diabetic mice with leptin to see if this works in the same way.