Therapeutic and diagnostic applications of an autoantigen (IGRP) in type I diabetes

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IP Status:

Patent pending; available for licensing.

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Background

Dr. John Hutton of the University of Colorado has identified a new autoantigen that interacts with pathogenic T-cells, which are important in the development and progression of Type I (or juvenile) diabetes in humans. This autoimmune disease occurs through T-cell mediated destruction of insulin-producing cells of the pancreas. Juvenile (or type I) diabetes is the most severe form of diabetes because it results in complete loss of insulin production due to the eradication of B-cells in the pancreas. Insulin is necessary to regulate the concentration of sugar in the blood; its prolonged absence results in death. Long term complications from medically managed diabetes include retinopathy, coronary heart disease, nephropathy, impaired circulation in the lower limbs, and neuropathy. Type I diabetes is classified as an autoimmune disease because B-cells are destroyed through a T-cell mediated pathway. Scientists are unsure exactly what triggers this autoimmune response, but they have identified several autoantigens that are targeted by T-cells. These autoantigens are derived from islet cells, insulin, glutamate decarboxylase, protein tyrosine phosphatase (a and b) and glucose-6-phosphatase related protein (IGRP).

- **More than 1 million Americans have been diagnosed with Type I diabetes**
- **30,000 new diagnoses are made each year in the US**
- **5-10% of diabetics have Type I disease**
- **Worldwide, there are 10-11 million Type I patients**
- **Worldwide, diabetes diagnoses are projected to grow 46% to 221 million in 2010**
- **Worldwide, this means 11-22 million Type I disease by 2010**
- **Better Type I disease management equates to longer lifespan, genetic perpetuation and growing disease prevalence relative to Type II adult onset diabetes**

The total cost of all forms of diabetes in the US was estimated to be $132 billion. This total included $92 billion in direct medical expenditures and $40 billion for indirect expenditures (this figure is believed to be an underestimate because pain and suffering cannot be accurately measured.). Of the direct costs, a majority went towards the treatment of chronic complications attributable to diabetes ($24.6 billion) and greater prevalence of other medical conditions ($44.1 billion). Only $23.2 billion of the $132 billion was actually spent to treat diabetes. Per capita medical expenditures illustrate the magnitude this disease impacts its sufferers. In 2002, medical expenditures for a patient with diabetes totaled $13,243 while the average cost of medical treatment for non-diabetic individuals was $2,560.

Type I diabetes is an attractive developmental target because no FDA approved diagnostic or therapeutic exists. This chronic disease begins in early life with the average age of diagnosis of approximately 7 years old (peak age of diagnosis in US is 14) and patients require constant attention throughout their lives. Current treatment regimens involve daily injections or continuous infusion of insulin, which is very difficult to manage because many other factors (diet, stress, growth, physical activity, and hormonal changes) adversely affect a person's blood sugar control. Insulin does not cure diabetes, nor does it prevent the eventual complications listed above. Because the current therapy is time consuming, painful, ineffective, and difficult to manage, finding a more effective treatment or even a cure would provide an ample revenue stream because current treatment costs are so high, equating to huge premiums for companies offering effective treatment.

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This discovery has several potentially profitable commercial applications in diagnostics and therapeutics. The University of Colorado has pending patent protection for both diagnostic and therapeutic applications.

Therapeutic Applications

The identified autoantigen has potential to be used therapeutically as an immunotolerogen. Pathogenic populations of T-cells that recognize the autoantigen have receptors for that specific autoantigen. The autoantigen or structurally similar derivatives can be used to attenuate the activity of the specifically autopathogenic T-cell population. The therapeutic ultimately slows the severity or halts progression of disease by preventing T-cell activation, proliferation and promulgation of the destructive autoimmune response. Essentially, since development of Type I diabetes is a process that takes months, this exciting technology promotes detection of autoantigens in the blood of children before the complete destruction of insulin producing pancreatic islet cells occurs. Intervention with autoantigen versions that bind the T-cell receptor but do not activate its destructive cycle would thereby prevent onset of exogenous insulin dependency.

Diagnostic Applications

Diagnostic applications could demonstrate the onset of autoimmune pathology via detection of autoantigens correlated with disease, detection of autoreactive T-cells and autoantibodies, as well as monitor the effectiveness of therapeutic interventions, among various other immune-assays.

Partnering

We are seeking a partner with both clinical development and drug delivery/formulation capabilities. The delivery, distribution, pharmacokinetics, pharmacodynamics of these compounds are as important therapeutically as the bioactivity. A partner with the proper developmental capabilities and complementary delivery technology will be able to expedite transition of these compounds into the clinic.

Key Publications:

Proc Natl Acad Sci U S A. 2003 Jul 22;100(15):8626-8. Epub 2003 Jul 14.
J Biol Chem. 2001 Jul 6;276(27):25197-207. Epub 2001 Apr 10.

Patent Application:

"Use Of Islet Glucose-6-Phosphatase Related Protein As A Diagnostic Tool And Therapeutic Target For Autoimmune Diabetes," 9/20/2004.