Secreted target for type 2 diabetes and metabolic disease

Published date: Feb. 1, 2012

Technology description

Summary

MARKETS ADDRESSED:
Metabolic disease, a collection of disorders including type 2 diabetes, atherosclerosis, fatty liver disease, hypertension and dyslipidemia, has reached epidemic levels worldwide, with approximately 115 million affected individuals in the US, Japan, France, Germany, Italy, Spain and the UK. This number is increasing rapidly, fuelled by the rising obesity and diabetes epidemic in industrialized countries such as China. The worldwide market size of metabolic disorders was estimated at US$97.7 billion in 2008. Numerous medications are used routinely to treat patients with metabolic disease, putting them at risk for the occurrence of adverse reactions and drug-drug interactions. Biologics in development include those targeting interleukin 1 beta (Canakinumab, Novartis; XOMA A052, Xoma) and are designed to alleviate inflammatory symptoms of type 2 diabetic patients without addressing the underlying cause of disease. Thus, current options are limited and new therapeutics with minimal side effects that address the primary etiology are needed.
The secreted factor is derived from adipocytes with marked increase in dietary and genetic models of obesity. Evidence indicates that the adipokine is a key component of the adipo-hepatic communication system linking lipolysis to liver glucose production. Hotamisligil's work suggests that the secreted factor is involved in a novel mechanism of inter-organ communication regulating glucose metabolism and represents a promising target for the treatment of metabolic disease. Finally, this factor is highly elevated in human obesity and its expression levels correlate very strongly with metabolic complications and cardiovascular disease risk. Hence, this target presents a safe and effective therapeutic opportunity against type 2 diabetes with cardiovascular benefits.

Advantages

Hotamisligil's group at the Harvard School of Public Health has identified a secreted factor from adipose tissue (adipokine) that functions systemically to mediate fundamental aspects of metabolic disease. To investigate the function of this factor they developed a neutralizing polyclonal antibody and

demonstrated that specific antibody depletion of the adipokine in serum reversed the diabetic phenotype of obese mice. Antibody administration caused a significant decrease in blood glucose levels within two weeks of treatment and markedly improved glucose disposal curves compared to control animals. Obese mice with decreased serum levels of the factor also exhibited enhanced systemic insulin response as determined by insulin tolerance tests. Conversely, delivery of a recombinant form of the factor into wild type lean mice caused glucose intolerance.

Institution

Harvard University