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Protection Against Diet-Induced Obesity and Insulin Resistance

Type 2 diabetes (T2DM) and the metabolic syndrome, often associated with visceral obesity, have reached an epidemic in the US. Insulin resistance, or reduced response to insulin, is the hallmark of T2DM. Insulin resistance is also an important step in the pathogenesis of non-alcoholic steatohepatitis (NASH), a liver disease that is characterized by increased fat production and inflammation in liver, and a precursor of liver cirrhosis. NASH is predicted to become the new epidemic in parallel to the increase in obesity. Because obesity, T2DM and NASH are associated with insulin resistance, it is imperative to understand its underlying mechanisms in order to develop preventive measures against these diseases.

Impaired insulin clearance in liver plays a key role in the pathogenesis of insulin resistance. When insulin is not adequately removed from blood, hyperinsulinemia develops. This elevates triglyceride formation and output from the liver and leads to compensatory increase in insulin secretion from pancreatic b-cells. In response to insulin secretion, the white adipose tissue expands to take up excess triglyceride for storage. In this manner, visceral obesity develops.

Dr. S.M. Najjar has identified a liver protein, which mediates insulin removal to promote insulin response. Inactivation and deletion of this protein impairs insulin clearance and causes insulin resistance and obesity. Its content is markedly reduced in the liver of obese humans and rodents, and in response to high-fat intake. Conversely, its induction in liver protects against diet-induced insulin resistance and obesity. This novel firm mechanistic link between the newly identified liver protein, impaired insulin clearance, visceral obesity, and NASH identifies this protein as a potential therapeutic target.

The University of Toledo is seeking a pharmaceutical company interested in exploiting this target to prevent the spread of obesity and related metabolic and cardiovascular abnormalities.

Applications:

1. Marker of insulin resistance for use in preventing the spread of obesity related metabolic and cardiovascular abnormalities
2. Diagnosis and treatment of impaired insulin clearance, visceral obesity, and NASH

This invention is patent pending

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