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Lisofylline in Combination with Exendin-4 Reverses Diabetes in a Type 1 Model

LSF and GLP-1 treatment also improved islet cell viability and normalized insulin secretion

SAN DIEGO (June 13, 2005) – The combination of Lisofylline (LSF) and Exendin-4, a glucagon-like peptide-1 (GLP-1), reversed diabetes in a type 1 mouse model, according to results of a study presented at the American Diabetes Association (ADA) annual meeting. The same study also showed that the two drugs, when administered concomitantly, enhanced islet cell function and reduced islet cell death.

“The results of this study are very encouraging and demonstrate that it may be possible to regenerate beta cells with the combination of an immune modulator, such as LSF, and a GLP-1 agonist. These results are also consistent with previous findings that indicate Lisofylline has positive effects on insulin production and islet cell health,” said Jerry L. Nadler, M.D., Chief of Endocrinology and Metabolism at the University of Virginia whose group presented the results at the ADA’s Session on Beta-Cell Preservation. “If results of human studies with the LSF/Exendin-4 combination prove as successful, the treatment of type 1 diabetes and latent autoimmune diabetes of adults could be altered significantly.”

LSF is a synthetic small molecule with novel anti-inflammatory properties that block autoimmune damage to insulin producing cells. GLP-1s, such as Exendin-4, stimulate pancreatic beta cell growth. However, the autoimmune process in people with type 1 diabetes rapidly destroys the beta cells, preventing GLP-1 action. The addition of an immune modulator such as LSF should provide a novel approach to restore beta cell function without the use of toxic immunosuppressive medications.

In the study, non-obese diabetic (NOD) mice, a well established model of type 1 diabetes, were treated for 28 days with the combination of LSF/Exendin-4. The treatment completely reversed diabetes as evidenced by restored glucose homeostasis. Additionally, there was evidence of new cell growth in the area of the islet cells in the mice given the combined therapy. NOD mice treated similarly with saline or Exendin-4 alone experienced no improvement in the diabetic condition. As part of the same study, isolated mouse pancreatic islets exposed to inflammatory cytokines and treated with the LSF/Exendin-4 combination experienced a 2.5 fold increase in metabolism and a 40% decrease in apoptosis (cell death) than controls.

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“The blood sugar levels remained normal even after withdrawal of both drugs, suggesting that the combination of LSF and Exendin-4 led to beta cell regeneration,” said Zandong Yang, M.D., Associate Professor of Medicine at the University of Virginia.

The study was conducted by Jeffrey Carter, B.S.; Meng Chen, M.D., Ph.D.; Kellie Smith, B.S.; Jerry L. Nadler, M.D.; and, Zandong Yang, M.D. of the University of Virginia and funded by local donor support.

Lisofylline has demonstrated that it can effectively prevent type 1 diabetes in preclinical models. LSF has shown to improve cellular mitochondrial function and to block interleukin 12 (IL-12) signaling and STAT-4 activation in target cells and tissues. IL-12 and STAT 4 activation are important pathways linked to inflammation and autoimmune damage to insulin producing cells. Therefore LSF, and the next generation of orally bioavailable immune modulators with a similar spectrum of action, offer the promise of providing a new therapeutic approach to prevent or reverse type 1 diabetes.

GLP-1 is a hormone that has generated significant attention in the diabetes community because it has multiple gluco-regulatory effects in the body. Several GLP-1 agonists are currently in clinical development for the treatment of diabetes and one product was recently approved as an adjunctive therapy to improve glycemic control in the treatment of type 2 diabetes.

Lisofylline and related compounds are being commercialized into therapies for diabetes and related complications by DiaKine Therapeutics, Inc. Dr. Nadler is the co-founder and current Chairman and Chief Science Officer of DiaKine Therapeutics.

According to the ADA, more than 18 million Americans have diabetes, a group of serious diseases characterized by high blood glucose levels that result from defects in the body's ability to produce and/or use insulin. Diabetes can lead to severely debilitating or fatal complications, such as heart disease, blindness, kidney disease and amputations. It is the fifth leading cause of death by disease in the U.S.

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