A NOVEL PEPTIDE INVOLVED IN ENERGY HOMEOSTASIS

ABSTRACT

The expression of a mRNA encoding a putative 76 amino acid, secreted protein ('Swirl') was found to negatively correlate with fasting triglyceride and cholesterol levels. A recombinant adenovirus was used to increase the expression of Swirl mRNA in two mouse models of obesity, KK-Ay and Lepob/Lepob mice. Over-expression of Swirl by adenovirus injection significantly, and reproducibly, reduced fasting triglyceride and cholesterol levels in both models. In addition, transgenic mice strains were made that over express Swirl protein. The expression of a key gene involved in lipogenesis (fatty acid synthase) and FAS protein levels were reduced by SWIR1 adenoviral treatment in Lepob/Lepob mice. Full-length SWIR1 peptide, or peptide derivatives, homologues, analogues, or mimetics thereof, delivered by oral intake, injection, subcutaneous patch, or intranasal routes, could be used as therapeutic or diagnostic agents for hypercholesterolemia, hypertriglyceridemia, insulin resistance, obesity, diabetes, and/or energy imbalance.

Figure 6B