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Development of galectin-12 siRNA to defeat metabolic disorders

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Metabolic diseases, such as obesity and diabetes cause multitudinous health problems. Drugs used to treat obesity show limited efficacy (around 5-7% weight loss) and cause some significant side effects. Therefore, new drugs with novel biological mechanisms may improve the efficacy and safety of the treatments. Galectin-12 is preferentially expressed by adipocytes and negatively regulates lipolysis in mice. Galectin-12 knock-out mice had a significant reduction in adiposity, with ~40% reduction in whole-body lipid content, reduced adipocyte size, and ameliorated insulin resistance. Due to the anti-obesity potential of galectin-12, we designed and modified galectin-12 siRNA as a new therapeutic tool to metabolic diseases. One of the designed galectin-12 siRNA, ITRI-3, inhibits the expression of endogenous galectin-12 in adipocytes efficiently in vitro, and knock-down galectin-12 mRNA in adipose tissue (13 mg/kg;~ 60% knock down) in vivo. We further tested the efficacy of ITRI-3 in a diet-induced obesity (DIO) mouse model. It shows that ITRI-3 inhibits 50% of endogenous galectin-12 expression, reduces adipocyte size and also increases lipolysis of adipose tissue with 9 mg/kg dosage after 42 day treatment. Although in a long term experiment (88 days), no significant body weight loss was observed, these findings revealed the potential of ITRI-3 for treatment of human metabolic disorders. Application of ITRI-3 to reduce spot fat in mouse model is under investigation.

Biography

Yan-Ju Lin completed his Master's degree in National Cheng-Kung University, Taiwan. He joined Industrial Technology Research Institute as a researcher in 2004. His research is focused on transcriptome analysis and RNA technology development. He owned a patent on antisense oligonucleotide-related applications issued by the United States Patent and Trademark Office.

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