Obesity treatment targets acetyl-CoA carboxylase (ACC) enzyme

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Obesity and diabetes treatment using enzyme that inhibits Acetyl-coenzyme A carboxylases: Acetyl-coenzyme A carboxylases (ACCs) are central to the fatty acid metabolism and are therefore promising targets for the development of therapeutic agents against obesity, diabetes, and other symptoms of the metabolic syndrome. ACC is a large, multi-domain enzyme in most eukaryotes. The activity of the enzyme is controlled by small molecule modulators at the transcriptional level. Two distinct classes of compounds, as illustrated by haloxyfop (FOPs) and tepraloxydim (DIMs), are potent inhibitors of ACCs from sensitive plants and are in wide use as herbicides.

Treatment for obesity and diabetes treatment using enzyme: This technology determines the crystal structure of the carboxyltransferase (CT) domain of yeast ACC in complex with tepraloxydim, and reveals a novel molecular mechanism of inhibiting the CT activity. This finding might be used to design and develop new and potent inhibitors against human ACCs.

Applications: • This technology can be used to design and develop novel ACC inhibitors to prevent or treat obesity, type II diabetes, metabolic syndrome, atherosclerosis and cardiovascular diseases in humans. • The growth in the prevalence of obesity in the United States represents a key driver for the anti-obesity prescription market. Over the past 25 years, the prevalence of adult obesity in the United States has more than doubled from 14.4 percent to 30.5 percent of the population and so the development of novel ACC inhibitors may alleviate the health issues resulting from obesity.

Advantages: • This technology reveals that tepraloxydim has a novel molecular mechanism of inhibiting CT domain. • This finding can be used to design and develop new and potent inhibitors against human ACCs. • This invention provides a molecular basis for DIM compounds’ distinct sensitivity to some of the resistance mutations in contrast to FOP inhibitors

Patent Status: Patent Pending

Licensing Status: Available for Licensing and Sponsored Research Support

Publications: A different mechanism for the inhibition of the carboxyltransferase domain of acetyl-coenzyme A carboxylase by tepraloxydim Xiang, S; Callaghan, M; Watson, Keith; Tong, L; PNAS December 8, 2009 vol. 106 no. 49 20723-20727

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