

## S37-2 **Importance of the control of fatty acid composition in the treatment of metabolic syndrome: Role of long-chain fatty acid elongase Elovl6 in energy metabolism and insulin sensitivity**

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Insulin resistance, the base disease of the metabolic syndrome, develops and deteriorates by the excessive accumulation of lipid in tissues. The decrease in the lipid accumulation is important for the improvement of insulin resistance. Recently, we observed that not only the quantitative change, but also the quality change of the tissue lipid, especially the fatty acid composition, has the important role in the regulation of insulin sensitivity. We identified a new fatty acid elongase Elovl6 as a target gene of lipid synthesis transcription factor SREBP. We also demonstrated that this enzyme specifically catalyzes the elongation of saturated and monounsaturated fatty acids with 12, 14, and 16 carbons, and an important lipogenic enzyme for the *de novo* synthesis of long chain saturated and monounsaturated fatty acids. To evaluate the physiological role of Elovl6 in vivo, we analyzed the Elovl6 KO mice. Elovl6 KO mice were resistant to diet- and obesity-induced insulin resistance despite similar hepatosteatosis and obesity. Thus, fatty acid composition controlled by Elovl6 is a new determinant for insulin sensitivity that acts independently of cellular energy balance. Inhibition of this elongase could be a new therapeutic approach for ameliorating insulin resistance, diabetes and cardiovascular risks, even in the presence of a continuing state of obesity.