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The Role of KCNMA1 on Insulin Signaling in Mature Adipocytes

Makoto Nishizuka

Nagoya City University

Summary

Potassium channel, calcium activated large conductance subfamily M alpha, member 1 (KCNMA1) has the ability to integrate changes in intracellular calcium and membrane potential and plays significant roles in various physiological functions such as the regulation of smooth muscle tone, neurotransmitter release and neuronal excitability. Some reports showed that the function of BK channels in vascular smooth muscle are involved in the development of hypertension, diabetes, and insulin resistance. However, little is known about the expression and physiological role of KCNMA1 in mature adipocytes.

In this study, we revealed that the expression level of *kcnma1* was drastically elevated at the late stage of adipogenesis in 3T3-L1 cells. The expression of *kcnma1* abundantly expressed in white adipose tissue (WAT) and *kcnma1* expression in WAT was decreased by a high-fat diet. Furthermore, *kcnma1* expression was decreased in hypertrophic mature 3T3-L1 adipocytes. These results suggested that KCNMA1 has an important role in the function of mature adipocytes. It is well known that mature adipocytes are highly sensitive to insulin. To examine whether KCNMA1 regulates insulin signaling in mature adipocytes, we next performed the knockdown experiments. Insulin-induced Akt phosphorylation in mature adipocytes was clearly suppressed by the reduction of *kcnma1* expression, whereas the level of total Akt did not differ between *kcnma1* knockdown and control cells. In addition, paxilline, a BK channel blocker, repressed insulin-induced Akt phosphorylation in mature adipocytes, indicating that KCNMA1 contributes to the regulation of insulin signaling in mature adipocytes. Furthermore, we showed that the expression of some potassium channels including KCNA1, KCNA5, KCNJ11 and KCNJ12 in WAT was changed by a high fat diet. These results suggested that some potassium channels in addition to KCNMA1 have an important role of regulation of obesity and insulin resistance.