AMPD1 is involved in the regulation of insulin sensitivity

Andreas Tandellin Tetsuaki Hirase
Keiko Toyama Jidong Cheng
Hiroko Morisaki Takayuki Morisaki

Background: Insulin resistance is a key factor in the pathogenic mechanisms of diabetes. We have reported that the deficiency of AMPD1, an isoform of AMP catalyzing enzyme AMP deaminase which is preferentially expressed in skeletal muscles, attenuates insulin resistance induced by high fat diet challenge. In this study, we further studied signaling pathways that play roles in AMPD1-dependent regulation of insulin sensitivity.

Methods and Results: AMPD1-deficient mice and control C57BL6 wild type mice were fed with a high fat diet to induce glucose tolerance. Body weight and adiposity showed no significant differences between wild type and AMPD1-deficient mice. Glucose tolerance and insulin tolerance were augmented after high fat diet challenge in AMPD1-deficient mice compared to wild type mice. Insulin-dependent activation of Akt and p70S6 kinase in skeletal muscles was attenuated after high fat challenge compared to mice fed with normal chow diet in wild type mice, which was partially reversed by AMPD1 deficiency. The expression levels of mTOR complex components were increased by AMPD1 deficiency after high fat diet challenge. mRNA expression of PGC1α and PGC1β, downstream targets of p70S6 kinase, in skeletal muscles was upregulated by AMPD1 deficiency after high fat diet challenge.

Discussion: These data suggest that insulin resistance induced by high fat challenge is attenuated in AMPD1-deficient mice compared to wild type mice. Inactivation of Akt and p70S6 kinase in the setting of high fat diet challenge was attenuated by AMPD1 deficiency, probably due to increased expression levels of mTOR complex components. Further studies focusing on the roles of AMPD1 in mTOR activation that may contribute to the regulation of glucose metabolism is on going.

Department of Bioscience and Genetics, National Cerebral and Cardiovascular Center Research Institute