AMP-activated protein kinase in diabetes

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Insulin resistance to stimulated glucose uptake and storage in skeletal muscle is a hallmark of Type 2 Diabetes (T2D). Muscle adaptations to exercise enhance sensitivity to insulin promoting glucose storage and combustion of fat in the post exercise recovery periods. To a large extent, such adaptations are preserved in the insulin resistant muscle of T2D patients. In this view physical activity become an attractive choice in the battle against insulin resistance. AMP-activated protein kinase (AMPK), an energy/fuel sensor of the cell, has been suggested to be a potential mechanistic link between exercise adaptations and insulin sensitivity in skeletal muscle. In the most T2D cohorts studied, AMPK related signaling elements in skeletal muscle seem well maintained and functional. Thus, the AMPK signaling pathway seems to be a fully functional site for treatment whether being though exercise or pharmacological drugs. Our newest observations are on the AMPK system and its regulation by exercise in the healthy and insulin resistant skeletal muscle. Mechanistically studies in rodents on the role of AMPK in skeletal muscle have been challenged by pharmacological regulators of AMPK with seemingly limited or unspecific bioactivity in mature muscle and by transgenic approaches which might have been biased by remnant AMPK activities. Recently, we have ben investigating the role of muscle AMPK by the use of muscle specific $\alpha 1$ and $\alpha 2$ AMPK double knockout mice. Our latest observations suggest that AMPK has the potential to increase insulin action through regulation of the GTPase-activating protein; TBC1D4. This interplay between insulin signaling and AMPK points to an important role of AMPK in post exercise insulin sensitivity.