AMPK signaling and exercise

B.E. Kemp,[1] J.S. Oakhill,[1] J.W. Scott,[1] M.D. Fullerton,[1] S. Galic,[1] H.M. O'Neill[1] and G.R. Steinberg,[2] [1]St. Vincent's Institute of Medical Research and Department of Medicine, University of Melbourne, Fitzroy, VIC 3065, Australia and [2]Department of Medicine, McMaster University, Hamilton, ON L8N 3Z5, Canada.
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The adenosine monophosphate (AMP)-activated protein kinase (AMPK) regulates whole-body and cellular energy balance in response to energy demand and supply. AMPK is an αβγ heterotrimer activated by increasing ADP/AMP concentrations. AMPK activation depends on phosphorylation of the catalytic subunit Thr^{172} by the upstream kinases LKB1 or CaMKKβ. Both ADP and AMP binding to the subunit promote Thr^{172} phosphorylation by upstream kinases and protect against dephosphorylation by phosphatases. Once phosphorylated AMPK can be further activated allosterically by AMP, but given its relative cellular abundance it now seems likely that ADP plays the dominant role in regulating AMPK activity *in vivo*. AMPK inhibits fatty acid synthesis and promotes fatty acid oxidation, mitochondrial biogenesis and glucose uptake into muscle, and for these reasons has been a target for small molecule drug development for the treatment of Type 2 diabetes and cardiovascular disease. We have used several AMPK tissue specific subunit knock out and substrate Ser/Ala knock in mouse models to evaluate the role of AMPK in skeletal muscle.