Ativação da AMPK inibe a ACC1 e ACC2 – acetil coenzima A carboxilase

Regulation of fatty acid synthesis and oxidation by the AMP-activated protein kinase.

Hardie DG[1], Pan DA.
Biochem Soc Trans. 2002 Nov;30(Pt 6):1064-70.

Author information

- [1]Division of Molecular Physiology, School of Life Sciences, Dundee University, UK. d.g.hardie@dundee.ac.uk

Abstract

The AMP-activated protein kinase (AMPK) is a sensor of cellular energy charge and a 'metabolic master switch'. When activated by ATP depletion, it switches off ATP-consuming processes, while switching on catabolic pathways that generate ATP. AMPK exists as heterotrimeric complexes comprising catalytic alpha subunits and regulatory beta and gamma subunits, each of which occurs as multiple isoforms. Rising AMP and falling ATP, brought about by various types of cellular stress (including exercise in skeletal muscle), stimulate the system in an ultrasensitive manner. Acetyl-CoA carboxylase (ACC) exists in mammals as two isoforms, termed ACC-1 and ACC-2 (also known as ACC-alpha and ACC-beta). AMPK phosphorylates and inactivates both isoforms at the equivalent site. Knockout mice, and other approaches, suggest that the malonyl-CoA produced by ACC-2 is exclusively involved in regulation of fatty acid oxidation, whereas that produced by ACC-1 is utilized in fatty acid synthesis. Activation of AMPK by cellular stress or exercise therefore switches on fatty acid oxidation (via phosphorylation of ACC-2) while switching off fatty acid synthesis (via phosphorylation of ACC-1). The Drosophila melanogaster genome contains single genes encoding homologues of the alpha, beta and gamma subunits of AMPK (DmAMPK) and of ACC (DmACC). Studies in a Drosophila embryonal cell line show that DmAMPK is activated by stresses that cause ATP depletion (oligomycin, hypoxia or glucose deprivation) and that this is associated with phosphorylation of the site on DmACC equivalent to the AMPK sites on mammalian ACC-1 and ACC-2. This is abolished when expression of DmAMPK is ablated using an RNA interference approach, proving that DmAMPK is necessary for phosphorylation of DmACC in response to ATP depletion.

PMID:
12440973