Proinsulin C-peptide Induces Phosphorylation of Mitogen-Activated Protein Kinases (MAPK) in Swiss 3 T 3 and 3 T 3 -F442A Cells.

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C-peptide, a cleavage product of proinsulin, had been considered to have no biological activity. However, several recent studies indicate that C-peptide is a biologically active peptide, which increases glucose uptake in skeletal muscle, decreases glomerular hyperfiltration, improves autonomic nerve function and microcirculation in insulin-dependent diabetic patients and its animal models. Despite these findings, however, the molecular and cellular mechanisms of the actions of C-peptide have been poorly elucidated. In the present study, I examined the effect of C-peptide on the activation of the mitogen-activated protein kinases (MAPK) cascade in various cell lines by measuring phosphorylation of MAPK. I found that human C-peptide enhanced phosphorylation of MAPK in fibroblast cell lines, Swiss 3 T 3 and 3 T 3 -F442A cells, but not in 3 T 3 -L 1 cells. In Swiss 3 T 3 cells, C-peptide induced phosphorylation of MAPK in a time- and concentration-dependent manner, showing maximal response at 1 min and at 1 nM C-peptide. Pretreatment of the cells with pertussis toxin abolished the stimulatory effect of C-peptide. My results indicate that C-peptide activates the MAPK cascade in some types of cell, probably through a putative G-protein-coupled receptor for C-peptide.

The relationship between uncoupling proteins and obesity-resistance in mice.

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Uncoupling protein 1 (UCP- 1) is exclusively expressed in brown adipose tissue (BAT) and located in inner mitochondrial membrane. UCP- 1 functions as an uncoupler of mitochondrial respiration and liberates energy as heat. Genetic ablation of BAT by modifying UCP- 1 gene develops obesity in mice. Therefore, UCP- 1 exerts as a key molecule not only the thermogenic function of BAT but also energy expenditure regulation in whole animals. Recently, novel members of the UCP family, UCP- 2 and UCP-3, have been