

## MELANOCORTIN SIGNALLING IN FAT CELLS

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Melanocortin peptides and their receptors have long been known to affect the central control of food intake and body weight, thus playing a critical role in the development of obesity [1].

The melanocortin 5 receptor (MC5R) has been directly linked with lipid metabolism in peripheral tissues: MC5R deletion in mouse generates defects in sebaceous gland secretion [1] and MC5R stimulation increases fatty acid oxidation in muscle cells [2].

In this study, we tackled the role of MC5R in lipolysis and adipocyte function using the well established model of differentiated mouse 3T3-L1 adipocytes. Cell-signalling based experiments were performed after adipocyte treatment with alpha-melanocyte-stimulating hormone (alpha-MSH) and compared with the MC5R specific activation previously described in HEK293 [3] and HeLa cells stably transfected with MC5R-GFP.

Adipocyte response to alpha-MSH resulted in a loss of cytoplasmatic lipid content and release of glycerol into the cell medium by an ERK1/2 dependent mechanism. Moreover, downstream of ERK1/2, alpha-MSH induces p90RSK and CREB phosphorylation and c-Fos expression. The correlation between alpha-MSH action in 3T3-L1 adipocytes and the specific signalling pathways underlying MC5R activation, strongly suggests that lipolysis is mediated by this receptor.

[1] Cone RD (2006) *Endocr Rev* 27(7):736-49

[2] An et al (2007) *J Biol Chem* 282(5):2862-70

[3] Rodrigues et al (2009) *Mol Cell Endocrinol* 303:74-81