

P018 Disruption of PKA anchoring in adipose tissue using animal models

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The specificity of protein kinase A (PKA) is regulated by A-kinase anchoring proteins (AKAPs) that target PKA to specific subcellular compartments and a subset of potential substrates. In adipocytes, PKA plays a role in catecholamine-induced lipolysis where it phosphorylates hormone sensitive lipase (HSL) and perilipin. The major role of perilipin is to regulate lipolysis by protecting the intracellular lipid droplets from neutral lipases under basal conditions. In response to lipolytic stimuli, perilipin becomes phosphorylated and recruits HSL to the surface of the lipid droplet. HSL can then hydrolyse stored triacylglycerol to fatty acids and glycerol. Previous results have revealed that mice lacking RII β of PKA have reduced deposits of white fat, upregulated levels of RI α and uncoupling protein 1 (UCP1) and therefore increased basal lipolytic rate. Transgenic mice overexpressing the transcription factor FOXC2 have similar phenotype with increased levels of RI α and UCP1. To examine the importance of compartmentalized signaling in adipose tissue, PKA anchoring was disrupted in cell lines and in transgenic mice by expressing the soluble PKA-binding peptide Ht31. Preliminary results show that Ht31-tg mice have unchanged levels of PKA, increased levels of UCP1 and decreased levels of perilipin phosphorylation.