

**P024** Translocation of cAMP-degrading enzymes to lipid droplets during inhibition of lipolysis

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The release of fatty acids and glycerol from lipid droplets (LD) of mammalian adipose cells is tightly regulated by a number of counterregulatory signals and negative feedback mechanisms. The molecular mechanisms of three anti-lipolytic agents were studied in isolated rat adipocytes. Inhibition of isoproterenol-induced lipolysis by palmitate,  $H_2O_2$  and the anti-diabetic sulfonylurea drug, glimepiride, relies on the upregulated conversion of cAMP to adenosine by the glycosylphosphatidylinositol (GPI)-anchored phosphodiesterase, Gce1, and 5'-nucleotidase, CD73, which become associated with LD, rather than on cAMP degradation by the insulin-stimulated microsomal phosphodiesterase 3B. Analysis of the steady state distribution using photoaffinity labelling and activity determination of Gce1 and CD73 as well as of their redistribution after pulse or equilibrium metabolic labelling revealed translocation of Gce1 and CD73, harbouring the intact GPI anchor, from detergent-insoluble glycolipid-enriched plasma membrane domains to the LD in response to palmitate,  $H_2O_2$  and glimepiride. Remarkably, inhibition of GPI-specific phospholipase C (GPI-PLC) blocked both agent-dependent upregulation of LD-associated cAMP-to-adenosine conversion and inhibition of lipolysis. These data suggest a novel insulin-independent anti-lipolytic mechanism in rat adipocytes which relies on the GPI-PLC-dependent translocation of (c)AMP-degrading GPI-proteins from the adipocyte cell surface to LD. The findings may shed new light on biogenesis and degradation of LD in response to physiological and pharmacological agents.