Glycosylphosphatidylinositol-Anchored Proteins Coordinate Lipid Metabolism Between Large and Small Adipocytes

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In response to palmitate, the anti-diabetic sulfonylurea drug glimepiride, phosphoinositoglycans or H₂O₂ the release of small vesicles (adiposomes) harbouring the glycosylphosphatidylinositol-anchored and cAMP-degrading phosphodiesterase, Gce1, and AMP-degrading 5’-nucleotidase, CD73, from primary epididymal rat adipocytes and its subsequent translocation to cytoplasmic lipid droplets (LD) and accompanying lipolysis inhibition as well as lipogenesis stimulation upon their exposure to the adiposomes have been reported. This study demonstrates that large compared to small adipocytes are more efficient in releasing Gce1 and CD73 into adiposomes but less efficient in translocating Gce1 and CD73 to LD. Furthermore, both maximal lipolysis inhibition and lipogenesis stimulation by palmitate, glimepiride, phosphoinositoglycans or H₂O₂ were observed with mixed populations of small and large adipocytes (1:1 to 1:2) rather than with either small or large adipocytes. In contrast, insulin was most effective in adipocytes of uniform small size. Both lipolysis inhibition and lipogenesis stimulation by palmitate, glimepiride and H₂O₂, but not by insulin, were dependent on the release of Gce1- and CD73-harbouring adiposomes with surface-exposed phosphatidylserine into the incubation medium. Importantly, both lipolysis inhibition and lipogenesis stimulation by palmitate, glimepiride, phosphoinositoglycans and H₂O₂, but not by insulin, in native epididymal adipose tissues from young, but not old, rats were impaired by interference with adiposome function. Together the data argue for the coordinated inhibition of lipolysis and stimulation of lipogenesis in rat adipose tissue via the release of adiposome-associated and glycosylphosphatidylinositol-anchored Gce1 and CD73 from large “donor” adipocytes and their subsequent translocation to the LD of neighbouring small “acceptor” adipocytes in response to certain anti-lipolytic stimuli, such as palmitate, glimepiride and H₂O₂. The differential efficacies between small and large adipocytes from young and old rats argue for the pathophysiological relevance of this information transfer for the coordination of lipid metabolism by adiposomes.