PVIII-28: Connecting glucose signalling to ubiquitin-dependent transporter endocytosis: Arrestin the culprit!

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Endocytosis promotes regulated removal of transporters or receptors in response to environmental cues, allowing dynamic control of plasma membrane composition. Precursor experiments in yeast described ammonium or glucose-induced down-regulation of aminoacid or sugar transporters, respectively. Transporters endocytosis requires their ubiquitylation by the Nedd4-like E3, Rsp5. Because the ubiquitylation of a given transporter occurs only in response to its cognate signal, this raises the question of how substrate specificity is achieved, and how it is regulated dynamically. Various arrestin-like "adaptor" proteins carrying PY motifs, enabling their interaction with Rsp5 WW domains are required for ubiquitylation of specific transporters. How these arrestins promote Rsp5/substrates interaction in response to extracellular stimuli is unknown. We identified a member of the alpha-arrestin family as essential for glucose-induced ubiquitylation and endocytosis of the lactate transporter, Jen1. Interestingly, this arrestin is phosphorylated and this modification responds to glucose through the concerted action of the AMPK homologue Snf1 and PP1 phosphatase. Glucose triggers rapid dephosphorylation and ubiquitylation of this arrestin, which in turns affects its subcellular localization. Therefore, a metabolic switch on an arrestin-like protein in response to glucose appears to modulate its function as an adaptor of Rsp5 in endocytosis, connecting signalling to transporter endocytosis.