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Title: Control of vesicular trafficking of the glucose transporter Ght5 by the deubiquitinating enzyme Ubp5 in Schizosaccharomyces pombe.

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Abstract:

Deubiquitination trims off covalently conjugated ubiquitin either from covalently conjugated mono- and poly-ubiquitinated substrates. This process is carried out by deubiquitinating enzymes (DUBs) working in cytoplasm and nucleus and also at different organelles. Golgi is a well-characterized protein sorting hub that sorts cargoes to the plasma membrane as well as to the vacuoles (lysosomes). Ubiquitination serves as a crucial signal for protein quality control at the Golgi apparatus. While various E3 ubiquitin ligases that conjugate ubiquitin to substrates have been studied in this context, the role of deubiquitinating enzymes (DUBs) remains relatively unexplored. Therefore, we aimed to investigate the significance of the Golgi-localized DUB Ubp5. As previously reported, we observed an interaction between Ftp105 and Ubp5, and both proteins localize at the Golgi. Disruption of this DUB complex by deleting either of the two proteins resulted in the mislocalisation of the high affinity glucose transporter Ght5 and its subsequent degradation in the vacuole. Schizosaccharomyces pombe contains eight hexose transporters through which glucose, fructose and their derivatives are transported inside the cell 1. Out of these eight transporters, Ght5 is necessary for cell survival in glucose starvation. By monitoring Ght5 localisation and protein level in different mutant backgrounds, we found the degradation of Ght5 during glucose starvation takes place via the MVB (Multivesicular body) pathway. In addition, we observed that the turnover of Ght5 becomes slower after prolonged starvation. Our study shows that the regulation of this glucose transporters in the fission yeast is reminiscent of glucose uptake in the human skeletal muscles. This knowledge will strengthen our understanding about the glucose starvation response in human cells which may be helpful to find the cure for many diseases like Diabetes and Cancer.

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