

Moderate expression of SEC16 increases protein secretion by *Saccharomyces cerevisiae* - DTU Orbit (09/11/2017)

Moderate expression of SEC16 increases protein secretion by *Saccharomyces cerevisiae*

The yeast *Saccharomyces cerevisiae* is widely used to produce biopharmaceutical proteins. However, the limited capacity of the secretory pathway may reduce its productivity. Here, we increased the secretion of a heterologous α -amylase, a model protein used for studying the protein secretory pathway in yeast, by moderately overexpressing SEC16, which is involved in protein translocation from the endoplasmic reticulum to the Golgi apparatus. The moderate overexpression of SEC16 increased α -amylase secretion by generating more endoplasmic reticulum exit sites. The production of reactive oxygen species resulting from the heterologous α -amylase production was reduced. A genome-wide expression analysis indicated decreased endoplasmic reticulum stress in the strain that moderately overexpressed SEC16, which was consistent with a decreased volume of the endoplasmic reticulum. Additionally, fewer mitochondria were observed. Finally, the moderate overexpression of SEC16 was shown to improve the secretion of two other recombinant proteins, *Trichoderma reesei* endoglucanase I and *Rhizopus oryzae* glucan-1,4- α -glucosidase, indicating that this mechanism is of general relevance.

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