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PROTEIN DEGRADATION

Ribophagy: selective ribosome 'eating'

> …ribosome degradation relies on both selective and non-selective autophagy processes.

Protein degradation by autophagy in yeast involves the sequestering of organelles and other macromolecular complexes within membrane vesicles, which are subsequently delivered to the vacuole where the cargo is degraded. Autophagy can occur through a basal, non-selective 'bulk' process or can involve an organelle-specific pathway. However, little is known about what determines the selectivity of autophagy pathways and how they are regulated.

Under nutrient-rich conditions, large amounts of ribosomal subunits are assembled, which raises the possibility for the need to remove excess ribosomes in response to changing environmental circumstances. To examine whether ribosomes are degraded by autophagy following starvation, Kraft *et al.* tagged proteins of the large and small ribosomal subunits with green fluorescent protein (GFP) and observed the accumulation of GFP in the vacuole. This relocalization required components of the basal, non-selective autophagy machinery but was independent of the selective cytoplasm-to-vacuole autophagic pathway. The ribosomal proteins have increased turnover kinetics compared with other cytoplasmic proteins, suggesting that ribosome degradation involves a new selective autophagy pathway, which the authors termed 'ribophagy'. Given that both ribosomal and cytoplasmic protein accumulation in the vacuole was abolished in cells that lacked the basal autophagy machinery, the authors concluded that ribosome degradation relies on both selective and non-selective autophagy processes.

Next, Kraft *et al.* screened a collection of starvation-sensitive mutants for defects in vacuolar accumulation of GFP-tagged ribosomal proteins and identified the ubiquitin protease Ubp3 and its co-factor Bre5. *ubp3*Δ and *bre5*Δ mutant cells accumulate proteins of the 60S large ribosomal subunit (but not of the 40S small ribosomal subunit) following starvation, while retaining functional nutrient sensing and general trafficking and autophagy pathways. This implies that ribophagy is a specific process that is not caused by a deficiency in basal autophagy, and that proteins of the large and small ribosomal subunit may require different selective degradation machineries. Also, even though *ubp3*Δ and *bre5*Δ mutant cells died following prolonged nutrient starvation and were sensitive to rapamycin (which inhibits the nutrient-sensing regulator Tor), the physiological relevance of the ribophagy pathway warrants further investigation.

A catalytically inactive Ubp3 mutant was unable to rescue the ribophagy defect, which suggests that the de-ubiquitylation activity of Ubp3 is essential. Moreover, *ubp3*Δ mutant cells were enriched in ubiquitylated ribosomal proteins, implying a deubiquitylation event in the regulation of ribophagy. However, it remains unclear which E3 ligases and ubiquitylated substrates are involved in regulating this mechanism of selective ribosome degradation.

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ORIGINAL RESEARCH PAPER Kraft, C. *et al.* Mature ribosomes are selectively degraded upon starvation by an autophagy pathway requiring the Ubp3/Bre5p ubiquitin protease. *Nature Cell Biol.* 6 April 2008 (doi:10.1038/ncb1723)
FURTHER READING Klionsky, D. J. Autophagy: from phenomenology to molecular understanding in less than a decade. *Nature Rev. Mol. Cell Biol.* **8**, 931–937 (2007)