A New Nutritional Effector of Autophagy in the Yeast *Saccharomyces cerevisiae*

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Introduction: Autophagy is a conserved process that recycles cellular contents to promote survival during nutrient depletion. The genes and regulatory mechanisms of this pathway were first discovered in the budding yeast *Saccharomyces cerevisiae* and subsequently confirmed in higher eukaryotes. Although nitrogen starvation is the canonical inducer of autophagy, recent studies have revealed the important roles of other nutrients.

Methods: Yeast growth medium is comprised of a nitrogen source, sugar, amino acids and nucleotides, and a complex mixture of salts, vitamins, and trace elements (yeast nitrogen base, YNB). We systematically analyzed individual components of YNB using Rosella, a quantitative biosensor composed of pH stable red fluorescent protein (DsRed.T3) and pH sensitive green fluorescent protein (super-ecliptic pHluorin). Autophagy is quantified as the ratio of red to green fluorescence.

Results: Our comprehensive analysis revealed that potassium is a unique and potent inducer of autophagy. Peak response to potassium is one-third of that induced by nitrogen. We validated our findings using the GFP-Atg8 reporter, a complementary and established method. A targeted screen of ion channels revealed a new role of the Hal4 regulatory kinase in nitrogen and potassium dependent autophagy.

Conclusions: These systematic studies highlight the importance of potassium ions in the regulation of autophagy. In humans, ion homeostasis is important for many fundamental physiological processes such as muscle contraction, heart function, and memory. Similarly, autophagy is implicated in cell differentiation, embryonic development, and aging. Therefore, a thorough understanding of the regulatory mechanisms by which ions affect autophagy is crucial to develop therapeutic interventions.