

Jeaho Lim

Genetics GIDP

The evolutionarily conserved Target of Rapamycin kinase Complex I (TORC1) controls cell growth and metabolism in all eukaryotes, and is misregulated in numerous diseases and disorders including, cancer, obesity, diabetes, depression, and aging. Despite significant progress in mapping the TORC1 signaling network in yeast and humans, it remains unclear how cells sense nutrient levels and transmit that information to TORC1. To address this question, we mapped the TORC1 interactome in *Saccharomyces cerevisiae* after exposure to various stress and starvation stimuli. These experiments led to the identification of several novel TORC1 binding proteins which we studied in detail using knockout strains. Here, we report that a poorly studied vacuolar membrane protein, Vsb1, acts as an amino acid sensor that inhibits TORC1 via the small GTPases Gtr1/2 (the Rags in humans) during histidine starvation and in poor nutrient conditions. Our data also suggest that Vsb1 is regulated by an intermediate that accumulates during histidine synthesis, rather than by histidine itself. This likely allows the cell to determine if the cell is growing using histidine from the environment or actively producing the amino acid during growth in a low nutrient environment.