Glucose is not only a nutrient, but also a signaling molecule controlling cell growth and development. Defects in glucose sensing and its metabolism are at the root of a number of metabolic disorders including diabetes, obesity, and cancer. Our research focuses on the mechanisms of glucose sensing and signaling in the yeast S. cerevisiae as a model system. We specifically investigate the role of the glucose receptor Rgt2 in sensing and responding to glucose availability. Accumulating evidence suggests that the glucose receptor generates an intracellular signal in response to glucose that promotes glucose uptake and metabolism. More recently, we have shown that this receptor is regulated at the posttranslational level in response to changes in glucose concentration. To get more insights into this observation, we assessed the cell surface expression of Rgt2 using genetic, biochemical and cell biological approaches. Several lines of evidence show that Rgt2 is endocytosed and degraded in the vacuole in glucose-starved yeast cells and that its turnover is mediated by ubiquitination. Rgt2 is mainly localized to the plasma membrane when glucose is present but targeted to the vacuole for degradation when glucose is depleted from the medium. However, Rgt2 turnover is impaired in cells lacking the Doa4 deubiquitinase and the Rsp5 ligase. Interestingly, constitutively active glucose receptor Rgt2R231K is resistant to glucose starvation-induced endocytosis. Our results suggest that cell surface expression levels of the glucose receptors are tightly associated with their ability to sense glucose.