Post-translational modifications offer novel mechanisms of regulating proteins. I will present an example utilized by unicellular eukaryotes for the regulation of the ubiquitin-proteasome system, which is important for controlling the lifetime of proteins in response to intracellular and extracellular signals. A prolyl hydroxylase related to an oxygen sensor that controls the lifetime of hypoxia inducible factor 1alpha in animals modifies Skp1, a subunit of the SCF (Skp1/cullin-1/F-box protein/Rbx1) class of E3-ubiquitin ligases. Prolyl hydroxylation primes Skp1 for modification by a series of five glycosylation reactions resulting in a glycan chain that is novel for a protein residing in the nucleocytoplasmic compartment of cells. Recent studies suggest that the glycan modifies the fold of Skp1, which may explain its increased association with F-box proteins *in vitro* and in cells. Skp1 glycosylation is important for oxygen dependent morphogenesis in the social amoeba *Dictyostelium* and for optimal growth of *Toxoplasma* gondii, agent for human toxoplasmosis, in a cell culture infection model. Oxygen availability is rate limiting for Skp1 glycosylation *in vitro* and in cells, over a range that correlates with regulation of morphogenesis and growth in these protists, respectively. Inhibitors of the 26S-proteasome compensate for the effect on *Dictyostelium* morphogenesis of genetically blocking glycosylation, suggesting that this biochemical mechanism links oxygen availability to morphogenesis by pacing the turnover of critical regulatory proteins. This model suggests opportunities to control *Toxoplasma* and other pathogens that utilize this mechanism through the development of inhibitors of the enzymes that modify Skp1.