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Thioredoxin System Regulates Vacuolar H^+-ATPase in *Dictyostelium discoideum*

Sun-Young Jeong*, Chang-Hoon Choi, and Sa-Ouk Kang

Laboratory of Biophysics, School of Biological Sciences, and Institute of Microbiology, Seoul National University

The thioredoxin system, consisting of thioredoxin, thioredoxin reductase and NADPH, has been well-known to be critical for the redox regulation of protein function and signaling. It has been known that three thioredoxins constitute multiple gene family and their expressions are developmentally regulated in *Dictyostelium discoideum.* To investigate a role of the thioredoxin system in *D. discoideum,* we generated mutant strains that underexpress or overexpress thioredoxin reductase (Trr). Trr-underexpressing cells showed defects on growth and development. Trr-overexpressing cells formed very tiny plaques on a bacterial lawn and had a lower uptake rate of bacteria. When developed in the dark, Trr-overexpressing cells exhibited a slugger phenotype, defined by a prolonged migrating slug stage. Like other slugger mutants, they were hypersensitive to ammonia, which has been known to inhibit culmination by raising the pH of intracellular acidic compartments. Interestingly, activity of vacuolar H^+-ATPase, which functions to acidify intracellular compartments, decreased in Trr-overexpressing cells. Moreover, biochemical studies confirmed the thioredoxin system was able to directly reduce oxidized subunit A, the catalytic subunit of vacuolar H^+-ATPase. Taken together, these results suggest that *Dictyostelium* thioredoxin system plays a role in the regulation of phagocytosis and culmination, possibly through modulation of vacuolar H^+-ATPase.