Glutathione Peroxidase 4, a Unique Antioxidant Enzyme, Plays a Role in Protecting Ocular Surface Mucosal Epithelia

Yoko Ogawa
Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan; yoko@z7.keio.jp

Cytoprotection is a process in which chemical substances give cells abilities to protect themselves against hazard injuries such as oxidative stress, hypoxia, and inflammation. Therefore, cytoprotection is important for cell survival and maturation. Glutathione peroxidase 4 (GPx4) is a unique antioxidant enzyme that can reduce phospholipid hydroperoxide in mammalian cells. GPx4 plays multiple roles in neuroprotection, necessary for survival and maturation of photoreceptors, and is also known as a key regulator for a newly discovered type of cell death such as ferroptosis in cancer cells.

Sakai et al. show an interesting study on how GPx4 in conjunctival epithelial cells maintains redox homeostasis and protects cells from cytotoxicity caused by oxidative stress. The authors took several approaches in comprehensively evaluating roles of GPx4 in human conjunctival epithelial cells. They have shown that GPx4 plays an integral part in (1) maintaining oxidative homeostasis under physiological condition, (2) regulating ROS production, (3) epithelial cell growth, and (4) the defense against oxidative stress in the conjunctival epithelial cells. In addition, they have demonstrated that loss of GPx4 leads to conjunctival epithelial cell death in vitro. Their molecular approaches have revealed these important things at the cellular level.

Lipid hydroperoxides activate lipoxygenase and cyclooxygenase, participate in inflammation, and act as signal molecules for apoptotic cell death and receptor-mediated signal transduction. Sakai’s future work can develop a new therapeutic intervention for ocular surface diseases, including dry eye disease, allergic diseases, and age-related ocular surface diseases.

References