PCI-07

Role of mitochondrial phosphatase PGAM5 in inflammation

Kohsuke Takeda

Division of Cell Regulation, Graduate School of Biomedical Sciences, Nagasaki University, and PRESTO, JST, Japan

Abstract

Mitochondria serve not only as the ‘powerhouses’ that produce ATP through the process of oxidative phosphorylation but also as the signaling platforms for cell survival/death and antiviral immunity. Mitochondrial dysfunctions thus disrupt cellular homeostasis, leading to various human diseases, such as neurodegenerative diseases, metabolic diseases, cancers and immunocompromised disorders. We have been focusing on phosphoglycerate mutase family member 5 (PGAM5) as a signaling intermediate that responds to mitochondrial dysfunctions. PGAM5 lacks phosphoglycerate mutase activity but instead acts as an atypical serine/threonine-specific protein phosphatase. Its Drosophila ortholog protects neurons from heat shock-induced apoptosis, whereas PGAM5 has recently been reported to be involved in necrosis induction. We recently found that PGAM5 is localized to the inner mitochondrial membrane through its N-terminal transmembrane domain and is cleaved within the transmembrane domain upon loss of mitochondrial membrane potential, although the physiological meaning of the cleavage remains to be understood. Consistent with accumulating evidence indicating the involvement of mitochondria in the regulation of NLRP3 inflammasome, we found that PGAM5 is involved in the activation of NLRP3 inflammasome. In this symposium, I would like to discuss the possible roles of PGAM5 as an intermediate that links mitochondrial functions with inflammation.