アドバンス生命理学特論 Topics in Advanced Biological Science

IGER SEMINAR

Stress-induced dynamic regulation of mitochondrial STAT3 and its association with cyclophilin D reduce mitochondrial ROS production

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Signal Transducer and Activator of Transcription 3 (STAT3) has been tied to various physiological and pathological functions, mainly as a transcription factor that translocates to the nucleus upon tyrosine phosphorylation induced by cytokine stimulation. In addition, a small pool of STAT3 resides in the mitochondria where it serves as a sensor for various metabolic stressors including reactive oxygen species (ROS). Mitochondrially-localized STAT3 largely exerts its effects through direct or indirect regulation of the activity of the electron transport chain (ETC). It has been assumed that STAT3 amounts in the mitochondria are static. We showed that various stimuli, including oxidative stress and cytokines, triggered a signaling cascade that resulted in a rapid loss of mitochondrially-localized STAT3. Recovery of the mitochondrial pool of STAT3 over time depended upon phosphorylation of Ser727 in STAT3 and new protein synthesis. Under these conditions, mitochondrially-localized STAT3 also became competent to bind to cyclophilin D (CypD). Binding of STAT3 to CypD was mediated by the N-terminus of STAT3, which was also important for reducing mitochondrial ROS production after oxidative stress. These results outline a role for mitochondrially-localized STAT3 in sensing and responding to external stimuli.

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理学南館１階セミナー室

Seminar Room, 1st Floor, Science South Building

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