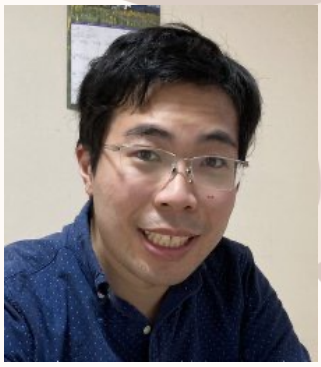
THE UNIVERSITY OF OSAKA

The Biomedical Research Seminar

Mitochondrial control of glycerolipid synthesis by a PEP shuttle



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Date | 16:00 - 17:00 on Friday, March 27

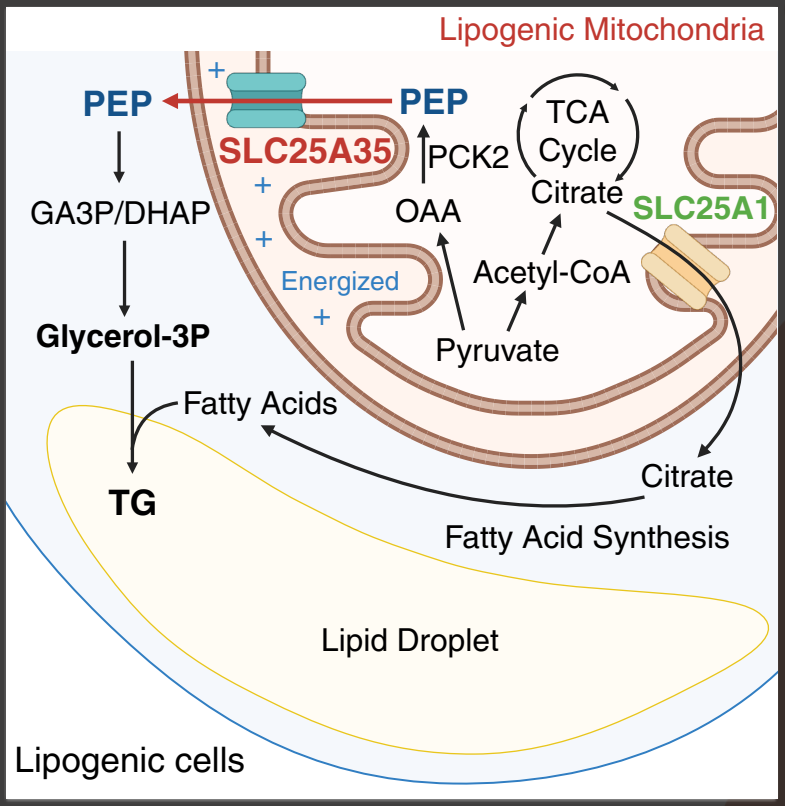
Place | 1F Auditorium, Institute for Protein Research (IPR), The University of Osaka

No registration is required. This seminar will be provided in English.

Abstract

Mitochondria provide a variety of metabolites, in addition to ATP, to meet cell-specific needs. One such metabolite is phosphoenolpyruvate (PEP), which contains a higher-energy phosphate bond than ATP and has diverse biological functions. However, how mitochondria-generated PEP is delivered to the cytosol and fulfills cell-specific requirements remains elusive.

Here, we show that SLC25A35 regulates mitochondrial PEP efflux and glyceroneogenesis in lipogenic cells that utilize the pyruvate-to-PEP bypass. Reconstitution and structural studies demonstrated PEP transport by SLC25A35 in a pH gradient-dependent manner. Loss of SLC25A35 in adipocytes impaired the conversion of mitochondrial PEP into glycerol-3-phosphate, thereby reducing glycerolipid synthesis. Significantly, hepatic inhibition of SLC25A35 in obese mice alleviated steatosis and improved systemic glucose homeostasis. Together, these results suggest that mitochondria facilitate glycerolipid synthesis by providing PEP via SLC25A35, offering lipogenic mitochondria as a target to limit glycerolipid synthesis, a pivotal step in the pathogenesis of hepatic steatosis and Type 2 diabetes.



Yamamuro T et al., *Cell, in press* "Mitochondrial control of glycerolipid synthesis by a PEP shuttle"

Speaker Information

Dr. Tadashi Yamamuro received his M.D. (Osaka University, 2013) and Ph.D. (Tamotsu Yoshimori Lab., Osaka University, 2020), followed by clinical training and research focused on cellular metabolism, aging, and autophagy. He is currently a recipient of the JSPS Overseas Research Fellowship (Japan Society for the Promotion of Science), supporting his research abroad. His work mainly centers on mitochondrial metabolism, adipocyte biology, and metabolic diseases. During his postdoc period in U.S.A., he has also received competitive research support, including funding from the American Heart Association (AHA).

Yamamuro T et al., *Nature Communications*, 2020 "Age-dependent loss of adipose Rubicon promotes metabolic disorders via excess autophagy"
Yamamuro T et al., *PLOS Genetics*, 2021 "Rubicon prevents autophagic degradation of GATA4 to promote Sertoli cell function"
Yamamuro T et al., *Autophagy*, 2022 "Loss of RUBCN/rubicon in adipocytes mediates the upregulation of autophagy to promote the fasting response"

Access to the IPR

Arranged by: Mashun Onishi (Laboratory for Membrane Systems Biology, IPR)
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