Project number　39

The functional role of human OSER1 in preserving mitochondrial homeostasis and the health of the mitochondrial pool

［1］Research group

Principal Investigator (PI)：
Lene Juel Rasmussen
(University of Copenhagen, Denmark)
Host researcher at IDAC：
Akira Yasui
(IDAC Tohoku University)
Co-investigator：
Shinichiro Kanno
(IDAC Tohoku University)

Expenditure report of research funds：
Consumables 130,000 YEN
Travel cost 0 YEN

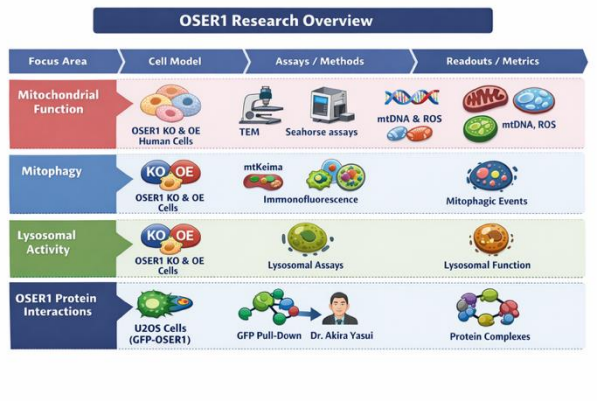
［2］Research setup

We investigated the role of OSER1 in maintaining mitochondrial homeostasis and quality. Using OSER1-deficient and overexpressing human cells, we evaluated mitochondrial function via TEM, Seahorse assays, Mitosticks, and quantitative analysis of mtDNA and mitochondrial ROS. Mitophagy, which selectively removes damaged mitochondria, was assessed using mtKeima/flow cytometry, and immunofluorescence will co-localize lysosomal, mitochondrial, and autophagy markers to quantify autophagic and mitophagic events. Lysosomal activity, critical for mitochondrial homeostasis, was also be measured.
To identify OSER1-interacting protein complexes, we collaborated with Dr. Akira Yasui. GFP-tagged OSER1 plasmids was transfected in U2OS cells, and interacting proteins was identified. These interactions was further validated in our lab through cellular and biochemical assays.

Summary Table:

Focus Area	Cell Model	Assays / Methods	Readouts / Metrics
Mitochondrial Function	OSER1 KO & OE human cells	TEM, Seahorse assays, Mitosticks, mtDNA quantification, ROS measurement	Mitochondrial structure, respiration, ROS levels, mtDNA content
Mitophagy	OSER1 KO & OE cells	mtKeima/flow cytometry, immunofluorescence (mitochondria + lysosome + autophagy markers)	Number of autophagic/mitophagic events per cell
Lysosomal Activity	OSER1 KO & OE cells	Lysosomal activity assays	Lysosome-mediated degradation efficiency
OSER1 Protein Interactions	U2OS cells (GFP-OSER1 overexpression)	GFP pull-down (collaboration with Dr. Akira Yasui), cellular & biochemical validation	Identification and functional validation of OSER1-interacting protein complexes

We had regulary joint meeting with Dr Akira 3-4 times per year.



［3］Research outcomes

（3－1）Results

Dr Yasui's group identified several interesting OSER1 interacting proteins. These results were followed up in Dr Rasmussen's group by cellular and biochemical assays dependent on the nature of the protein complex (manuscript in preparation).

（3－2）Future perspectives

In 2024, we identified OSER1 as a novel, evolutionarily conserved longevity gene (DOI: 10.1038/s41467-024-51542-z). The findings in this project advance our understanding of OSER1-mediated redox regulation in healthy aging. This project will shed light on human oxidative stress responses and their impact on lifespan, healthspan, and reproduction. Given the high interest in longevity and healthy aging research, these results are expected to attract significant attention.

［4］List of research achievements

Zhiquan Li, Shinichiro Kanno, Akira Yasui, and Lene Juel Rasmussen. 2026. The conserved YM-rich domain of OSER1 mediates its recognition of oxidative damage. Manuscript in preparation.