Announcement of the 10th Waseda IARBD seminar
"Orchestrating inter-organ communication and treating metabolic syndrome by targeting mRNA decay of hepatokines"

Masahiro Morita, Principal Investigator
University of Texas Health Science Center at San Antonio

The 10th seminar of the Waseda IARBD seminar series is a lecture by Masahiro Morita, Principal Investigator at The University of Texas Health Science Center, US. The lecture title is "Orchestrating inter-organ communication and treating metabolic syndrome by targeting mRNA decay of hepatokines". We look forward to your participation.

Date :	May 25, 2022
Time :	10:00-11:00 (Japan Standard Time)
Venue :	Webinar, Zoom (You will know the link after your registration.)
Lecturer :	Dr. Masahiro Morita Tenure-Track Assistant Professor, University of Texas Health Science Center at San Antonio
Title :	"Orchestrating inter-organ communication and treating metabolic syndrome by targeting mRNA decay of hepatokines"
Registration Fee :	Free
Language :	English
Registration :	Please register in the following link: *https://forms.gle/nD3GVY23YY77k1fU9*
Closing Date :	May 23, 2022
Contact :	IARBD-Office: IARBD-office@list.waseda.jp

Biography

Dr. Masahiro Morita received a Ph.D. in Science from the University of Tokyo in 2008 March under the supervision of Professor Tadashi Yamamoto, focusing on the role of mRNA decay machinery

in cancer and metabolic disorders. His postdoctoral work at Dr. Nahum Sonenberg lab at McGill University discovered that the nutrient-sensing mTORC1 pathway induces metabolic reprogramming and cell proliferation by stimulating translation of target mRNAs encoding mitochondrial proteins. In 2017, he started a Tenure-Track Assistant Professor position at the University of Texas Health Science Center at San Antonio. I published several papers in Cell Metab, Mol Cell, Nat Immunol, and PNAS from his new institution as a corresponding author.

Abstract

Hepatokines, secretory proteins from the liver, mediate inter-organ communication to maintain a metabolic balance between food intake and energy expenditure. However, molecular mechanisms by which hepatokine levels are rapidly adjusted following stimuli are largely unknown. Here, we unravel CNOT6L deadenylase switches off hepatokine expression after responding to the stimuli (e.g., exercise and food) to orchestrate energy intake and expenditure. Mechanistically, CNOT6L inhibition stabilizes hepatic *Gdf15* and *Fgf21* mRNAs, increasing corresponding serum protein levels. The resulting up-regulation of GDF15 stimulates the hindbrain to suppress appetite, while increased FGF21 affects the liver and adipose tissues to induce energy expenditure and lipid consumption. Despite the potential of hepatokines to treat metabolic disorders, their administration therapies have been challenging. Using small-molecule screening, we identified a CNOT6L inhibitor enhancing GDF15 and FGF21 hepatokine levels, which dramatically improves diet-induced metabolic syndrome. Our discovery, therefore, lays the foundation for an unprecedented strategy to treat metabolic syndrome.

References

[1] Katsumura S., et al., ***Morita, M.**, “Orchestrating inter-organ communication and treating metabolic syndrome by targeting deadenylase-dependent mRNA decay of hepatokines” (2022) *Cell Metabolism*. *Corresponding author.

[2] ***Morita, M.**, et al., “A hepatic post-transcriptional network comprising of CCR4-NOT deadenylase and FGF21 maintains systemic metabolic homeostasis” (2019) *PNAS*. *First and Corresponding author.

[3] *Hulea, L., *Gravel, S.P., ***Morita, M.**, et al., “Translational and HIF-1α-Dependent Metabolic Reprogramming Underpin Metabolic Plasticity and Responses to Kinase Inhibitors and Biguanides” (2018). *Cell Metabolism*. *First authors.

[4] ***Morita, M.**, et al., “mTOR Controls Mitochondrial Dynamics and Cell Survival via MTFP1” (2017) *Molecular Cell.* *First and Corresponding author.

[5] **Morita, M.**, et al., “mTORC1 controls mitochondrial activity and biogenesis through 4E-BP-dependent translational regulation” (2013) *Cell Metabolism*.