BDR SEMINAR (Kobe & online hybrid)

Andrey Parkhitko

Aging Institute, University of Pittsburgh

Tuesday, September 8, 2026

15:00-16:00

1F Auditorium, DB Building C, Kobe / Broadcast online via

※This seminar is open only for BDR Members

Targeting Age Related Metabolic Dysfunction to Extend Health Span

Summary

Methionine metabolism is a central regulator of protein synthesis, mitochondrial function, antioxidant defense, and other critical cellular processes. Tight regulation of methionine flux through the methionine metabolism pathway is essential for healthy cellular function. Restricting methionine in the diet (in the absence of cysteine) provides multiple benefits. Methionine restriction (MetR) improves cognitive function in wild-type and AD models, ameliorates atherosclerosis, improves cardiovascular health, demonstrates anti-cancer effects, and increases lifespan across different species. Accordingly, human population studies demonstrate positive associations between methionine intake and type 2 diabetes, acute coronary events, and mild cognitive impairment. However, dietary prescriptions that require daily adherence to low-methionine diets are generally poorly tolerated in human patients, a challenge that is compounded by the extreme dietary changes required to achieve MetR. Given these inherent challenges, one theoretical alternative would be to design a pharmacologic mimetic of the downstream molecular effector(s) of SAAR. However, the lack of validated downstream effectors precludes the development of effective MetR mimetics. Among the challenges that delay identifying of downstream effectors and developing pharmacological strategies to achieve MetR are the lack of high- or semi-high-throughput reporters; the highly divergent requirements for sulfur amino acids between in vitro and in vivo conditions, which preclude the use of cell lines; and the ability of altered methionine levels to affect the function of a wide variety of downstream methyltransferases (more than 300 in the human genome) via reduced production of S-adenosylmethionine (SAM). Our work in Drosophila provides the tools and insights needed to overcome all these challenges. We have developed and validated highly selective luciferase-based reporters that respond to both increased and decreased levels of methionine in the diet, allowing us to use semi-high-throughput in vivo screening to identify novel potential downstream effectors of MetR. We also collected and screened a library comprising all MTs predicted in the Drosophila genome and identified the arginine-specific methyltransferase PRMT5 as one of the downstream effectors of MetR.

RIKEN BDR

RIKEN Center for Biosystems Dynamics Research (BDR)

Host: Fumiaki Obata

Laboratory for Nutritional Biology

Contact: fumiaki.obata@riken.jp