

BDR SEMINAR via Zoom

Takuhiro Ito

RIKEN Center for Biosystems Dynamics Research

Thursday, March 17, 2022

13:30-14:30

Zoom meeting URL will be announced on the event day by e-mail.

※This seminar is only for BDR members.

Structural biology of translation initiation: eIF2B and the integrated stress response

Summary

Eukaryotes have stress response mechanisms in the translation process. Eukaryotic translation initiation factor 2B (eIF2B) is one of the core translation initiation factors, and also plays an essential role in a mechanism called the integrated stress response (ISR), a cellular homeostasis control pathway conserved from yeast to human. eIF2B is the guanine nucleotide exchange factor specific for eIF2, which is another core translation initiation factor transferring initiator methionyl-tRNA to the ribosome in a GTP-dependent manner. Under various stressful conditions, such as viral infection and ER stress, stress-specifically activated eIF2 kinases phosphorylate a common substrate, the α subunit of eIF2, and resultant phosphorylated eIF2 [eIF2(α P)] strongly inhibits eIF2B, which triggers the ISR. Our group has led the field of the ISR regulation by determining multiple world's first three-dimensional (3D) structures, which have unveiled the fundamental mechanisms: the eIF2B catalytic mechanism of the nucleotide exchange on eIF2, the eIF2B inhibition mechanism by eIF2(α P), and the action mechanisms of a small ISR inhibitor and an ISR-regulatory viral protein. I would like to summarize these findings in the seminar.

In addition to the powerful cryo-EM single particle analysis, recent advances in cryo-electron tomography are making it possible to determine the 3D structure of molecules as they are in cells. I would like to report the progress of our analysis.



RIKEN Center for Biosystems Dynamics Research (BDR)

Host: Yasushi Okada

Laboratory for Cell Polarity Regulation, BDR
Contact: bdr-mtg@ml.riken.jp