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TEMASEK LIFESCIENCES LABORATORY

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The Auditorium (Level 1)
Hosted by: Dr Katsutomo Okamura

Importance of translation pausing in unfolded protein response

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Dr. Kenji Kohno received his Dr. degree from Univ. of Tokyo in 1980, and then moved to National Institute for Basic Biology, Okazaki, as an Assist. Prof. From 1987 to 1989, he joined Mary-Jane Gething and Joe Sambrook lab at Univ. Texas, Dallas, USA, as a research fellow. In 1989, he moved to Osaka Univ. as an Assoc. Prof. and then, in 1993, he got promoted to Professor at Nara Institute of Science and Technology (NAIST). His present interests focus on mammalian ER stress response.

The unconventional splicing of XBP1u mRNA on the endoplasmic reticulum (ER) is the sole conserved mechanism among eukaryotes to transmit the information of the disturbance of ER proteostasis to the cytosol/nucleus upon ER stress. In mammals, precursor form of XBP1 (XBP1u) mRNA is spliced by ER transmembrane stress sensor, IRE1α. The spliced form of XBP1 (XBP1s) mRNA leads to synthesize the functional transcription factor XBP1s, which upregulates the expression of Unfolded Protein Response (UPR) target genes to mitigate ER stress (1). Recently we reported that translation pausing of XBP1u mRNA ensures the efficiency of membrane targeting and cytoplasmic splicing of XBP1u mRNA (2). However, its precise molecular mechanism remains poorly understood. Here, we present evidence that SRP pathway is involved in targeting of XBP1u mRNA to the ER membrane and furthermore translation pausing is required for the recognition of XBP1u by SRP. A novel role of SRP pathway for efficient targeting of XBP1u to the ER is discussed.

Recent Publications:

1. Kimata, Y., and **Kohno, K**. Endoplasmic reticulum stress-sensing mechanisms in yeast and mammalian cells. Curr. Opin. Cell Biol. 23, 135-142 (2011)
2. Yanagitani, K., Kimata, Y., Kadokura, H. and **Kohno, K**. Translational pausing ensures membrane-targeting and cytoplasmic splicing of XBP1u mRNA. Science 331, 586-589 (2011)
3. Mathuranyanon, R., Tsukamoto, T., Takeuchi, A., Ishiwata-Kimata, Y., Tuchiya, Y., **Kohno, K.,** and Kimata, Y. Tight regulation of the unfolded protein sensor Ire1 by its intramolecularly antagonizing subdomain. J. Cell Sci. 128, 1762-1772 (2015)