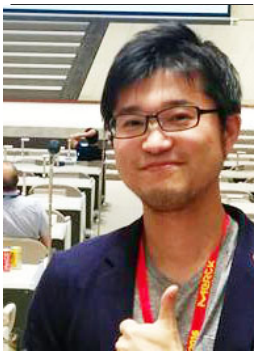


RNA Systems Biochemistry Laboratory
Chief Scientist: Shintaro Iwasaki (Ph.D.)

(0) Research field

CPR Subcommittee: Biology

Keywords:

Translation, RNA, translation inhibitor, RNA binding protein, next-generation sequencing

(1) Long-term goal of laboratory and research background

"The central dogma of molecular biology", which represents information flow from DNA to RNA to protein, has been most basic principle in life. Recent quantitative and comprehensive analysis revealed that the amount of RNA could not simply correlate with protein abundance in cells, suggesting that "translation control" significantly contributes to gene expression more generally than as we previously expected. Our laboratory tackles to unveil the unknown mechanisms of translation control, by the combination of next-generation deep sequencing and classical biochemistry. Especially we harness a technique called ribosome profiling, which enables to measure cellular translation status in a genome-wide manner. Applying this technology to a variety of living organisms, we aim to reveal diverse biological phenomena controlled by protein synthesis regulations.

(2) Current research activities (FY2019) and plan (until Mar. 2025)

Translation control in plants

The sessile nature of plants requires them to adapt the external environment alteration and to drastically change gene expression. Collaborating with Matsui laboratory from CSRS RIKEN, we revealed the dynamic of translation control in response to light, in *Arabidopsis* (Representative research achievements 2 and 4). We found numerous open reading frames from long non-coding RNAs, that has been overlooked for a long time (Representative research achievements 2).

Co-translational mRNA decay

Recent studies showed that mRNA decay are coupled with translation. Especially, the general decay rates were reported to be determined with the optimality of the codons; more with non-optimal codons, more unstable mRNAs. However, our understanding of the codon optimality-mediated mRNA decay was largely restricted in yeast. Collaborating with Takeuchi laboratory from Kyoto University, we unveiled that mammals also employ the similar mechanism for mRNA decay (Representative research achievements 3).

Discovery of Hero proteins

Collaborating with Tomari laboratory from The University of Tokyo, we reported the novel protein class, termed Heat-resistant obscure (Hero) proteins (Representative research achievements 1). In contrast to our stereotypic view of proteins, this group of proteins is not denature by heat. Surprisingly, Hero proteins have unique functions, such as for maintenance of enzymatic activity of other proteins, prevention of neurodegenerative aggregation in neurons, extension of life span in flies, etc. Hero proteins are thought to be constituents of hidden cellular environments.

Future direction

Although the pre-exiting techniques for RNA/translation, such as ribosome profiling, are powerful, they have the limitation and challenges. Thus, we aim to develop novel methods with even more high sensitivity, resolution, throughput, and specificity. The development of a RNA labeling technique proximal to RNA binding protein (Representative research achievements 4) is such an example. Exemplified by Hero proteins, hidden cellular environments are warrant to be studied.

(3) Members as of March, 2020

(Chief Scientist)
Shintaro Iwasaki

(Research scientist)
Eriko Matsuura

(Visiting researcher)
Yuichi Shichino

(Technical Staff)
Mari Mito

(Junior Research Associate)
Yusuke Kimura

(International Program Associate)
Chen Mingming, Apostolopoulos Antonios

(Research Fellow)
Shiho Makino

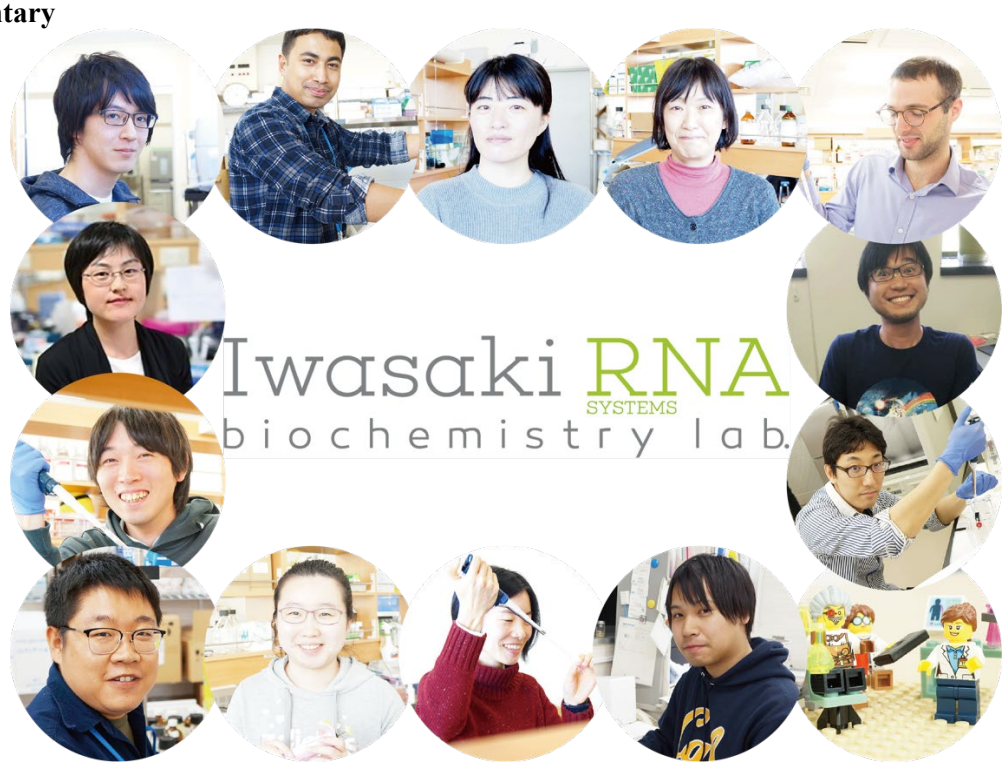
(Student Trainee)
Hironori Satito, Tomoya Fujita, Han Peixun

(Assistant)
Rie Yokoyama

(4) Representative research achievements

1. "A widespread family of heat-resistant obscure (Hero) proteins protect against protein instability and aggregation", Tsuboyama K*, Osaki T, Suzuki-Matsuura E, Kozuka-Hata H, Okada Y, Oyama M, Ikeuchi Y, **Iwasaki S**, and Tomari Y*. *PLoS Biol.* 18(3):e3000632. (2020)
2. "Translational landscape of protein-coding and non-protein-coding RNAs upon light exposure in *Arabidopsis*", Kurihara Y, Makita Y, Shimohira H, Fujita T, **Iwasaki S**, and Matsui M*. *Plant Cell Physiol.* 61(3):536-545. (2020)
3. "Codon bias confers stability to human mRNAs", Hia F, Yang SF, Shichino Y, Yoshinaga M, Murakawa Y, Vandenbon A, Fukao A, Fujiwara T, Landthaler M, Natsume N, Adachi S, **Iwasaki S**, and Takeuchi O*. *EMBO Rep.* e48220 (2019)
4. "Proximity RNA labeling by APEX-Seq reveals the organization of translation initiation complexes and repressive RNA granules", Padrón A, **Iwasaki S**, and Ingolia NT*. *Mol Cell.* 75(4):875-887. (2019)
5. "The plant translatome surveyed by ribosome profiling", Fujita T, Kurihara Y*, and **Iwasaki S***. *Plant Cell Physiol.* 60(9):1917-1926 (2019)

Supplementary



Laboratory Homepage
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