

【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Biology)



Title of Project : Post-transcriptional regulation associated with RNA modifications responsible for higher order biological processes

Tsutomu Suzuki
(The University of Tokyo, Graduate School of Engineering,
Professor)

Research Area : Biology

Keyword : RNA modification, RNA editing, mRNA, non-coding RNA

【Purpose and Background of the Research】

Higher order biological processes including development, differentiation and diseases are generated by sophisticated regulation of gene expression. Thus, it is critical to reveal the regulatory mechanism of gene expression for understanding the biological processes. It is a common knowledge that transcriptional regulation is a major factor in determining the gene expression. Recent genome wide analyses including transcriptome and proteome have revealed little correlation between the steady-state levels of mRNA and the level of the corresponding proteins. Meanwhile, non-coding RNAs, such as miRNAs or antisense RNAs, have emerged as key regulatory elements in gene expression. In addition, alternative splicing of mRNAs play a critical role to be involved in various regulation of gene expression and diversifying transcriptome. These facts indicated the presence of post-transcriptional regulation as another major factor in determining the gene expression. This project aimed to study post-transcriptional regulation associated with RNA modifications responsible for higher order biological processes. This project consists of the following subprojects: (1) Exploring RNA modifications and their functional analyses, (2) Analyzing the terminal modifications and mechanism of selective stabilization of small RNAs, (3) Studying on genes responsible for RNA modifications and investigation of molecular pathogenesis of human diseases associated with RNA modification disorder.

【Research Methods】

We employ a highly sensitive detection system for cellular RNA molecules using mass spectrometry (RNA-MS) to determine the chemical structure of novel modifications and identify the position of modifications in RNA strands. We also explore RNA-modifying enzymes, and try to reconstitute the formation of RNA modifications in vitro, leading to our better understanding how to synthesize RNA modifications at a molecular level.

【Expected Research Achievements and Scientific Significance】

We expect to reveal a hidden layer of gene expression involved in biological processes by identifying novel RNA modifications. In addition, identification of genes responsible for RNA modifications enables us to study them by biochemical and genetic approach. Genome-wide determination of inosine sites will enable us to rapidly identify alteration in status of inosines caused by cerebropathies and neurological disorders as a means to elucidate the molecular pathogenesis or to be used as diagnostic markers.

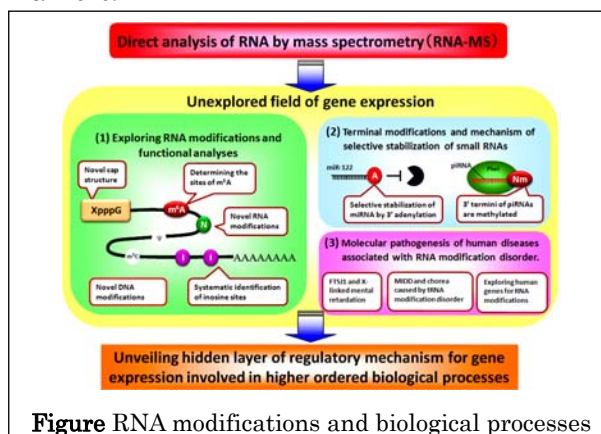


Figure RNA modifications and biological processes

【Publications Relevant to the Project】

- Ikeuchi et al. Agmatine-conjugated cytidine in tRNA anticodon essential for AUA decoding in archaea. *Nat Chem Biol.*, 6, 277-282 (2010)
- Katoh et al. Selective stabilization of mammalian microRNAs by 3'-adenylation mediated by the cytoplasmic poly(A) polymerase GLD-2. *Genes Dev.*, 23, 433-438 (2009)
- Ohara et al. The 3'-termini of mouse piwi-interacting RNAs are 2'-O-methylated *Nat Struct Mol Biol.*, 14, 349-350 (2007)

【Term of Project】 FY2010-2014

【Budget Allocation】 167, 300 Thousand Yen

【Homepage Address and Other Contact Information】

http://rna.chem.t.u-tokyo.ac.jp/index_e.html
ts@chembio.t.u-tokyo.ac.jp