

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

Integrated Disciplines (Complex Systems)



Title of Project : RNA Modifications Associated with Biological Processes

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Research Area : Complex systems

Keyword : RNA modification, RNA epigenetics, tRNA, mRNA, rRNA, ribosome

【Purpose and Background of the Research】

Higher order biological processes represented by development, differentiation, and complex metal activity are generated by sophisticated regulation of gene expression. Ill-regulated gene expression frequently results in pathological consequences. Thus, elucidating the regulatory mechanism of gene expression is required for deeper understanding of biological activities and processes, and contributes to medical and pharmaceutical applications. RNAs are decorated with various modifications introduced post-transcriptionally. Regulatory gene expression mediated by RNA modifications is also called as 'RNA epigenetics', because they are regulated spatiotemporally by expression level of RNA-modifying enzymes as well as cellular concentration of metabolites used as substrates for RNA modifications. Moreover, dysregulation of RNA modifications frequently cause human diseases, establishing a new concept of disease 'RNA modopathy'. In this project, we aim to elucidate biological processes mediated by RNA modifications and to understand molecular pathogenesis of RNA modopathies. This project comprises the following sub-projects; (1) Exploration of RNA epigenetic information and functional characterization, (2) Molecular pathogenesis of human diseases caused by aberrant RNA modifications, and (3) Crossroad between RNA epigenetics and DNA epigenetics.

【Research Methods】

Individual cellular RNAs can be isolated by our original method called 'reciprocal circulating chromatography (RCC)'. A species and site of each modification in the isolated RNA can be analyzed by a highly sensitive detection system for RNA molecules using mass spectrometry (RNA-MS). mRNA modifications will be analyzed by our new method based on RNA chemical biology. We also explore RNA-modifying enzymes, enabling us to study RNA modification biochemically as well as genetically.

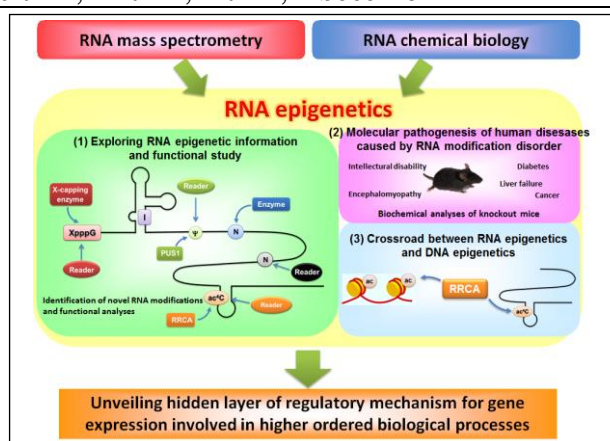


Figure 1 RNA epigenetics and biological processes

【Expected Research Achievements and Scientific Significance】

Discovery of novel RNA modifications and determination of RNA epigenetic information will reveal new regulatory mechanisms of gene expression. Identification of RNA-modifying enzymes and reader proteins that recognize RNA modifications will enable us to approach functional and physiological aspects of RNA modifications biochemically as well as genetically. Understanding of molecular pathogenesis of RNA modopathies will contribute to medical and pharmaceutical applications.

【Publications Relevant to the Project】

- Sakurai et al. A biochemical landscape of A-to-I RNA editing in the human brain transcriptome. *Genome Res*, 24, 522-534 (2014)
- Miyauchi et al. A cyclic form of N^6 -threonylcarbamoyladenine as a widely distributed tRNA hypermodification. *Nature Chem Biol.*, 9, 105-111 (2013)
- Terasaka et al. Biogenesis of 2-*agmatinyl*cytidine catalyzed by the dual protein and RNA kinase TiaS. *Nature Struct Mol Biol.*, 18, 1268-1274 (2011)

【Term of Project】 FY2014-2018

【Budget Allocation】 150, 200 Thousand Yen

【Homepage Address and Other Contact Information】

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