

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

Broad Section G



Title of Project : Dynamic regulation of RNA modification and biological process

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Research Project Number : 18H05272 Researcher Number : 20292782

Keyword : RNA modification, mRNA, tRNA, ribosome, metabolite

【Purpose and Background of the Research】

RNA molecule has been regarded as a regulatory element in gene expression at the levels of transcription and translation, and is associated with various biological processes. RNA molecules are decorated with a wide variety of chemical modifications that are introduced after transcription. This process is also referred to as “epitranscriptome” that generates an emerging field in life science. We found some instances of RNA modifications dynamically regulated by sensing cellular metabolites which are substrates of the RNA modifications. In this project, we aim to establish a novel concept of regulatory gene expression mediated by dynamic regulation of RNA modification by sensing cellular metabolic status.

【Research Methods】

Individual RNAs are isolated by our original method called ‘reciprocal circulating chromatography (RCC)’. A species and site of each modification in the isolated RNA are analyzed by a highly sensitive detection system for RNA molecules using mass spectrometry (RNA-MS). In this project, we focus on RNA modification dynamically regulated by various cellular conditions including environmental stresses and nutrient starvation by measuring frequency of RNA modification using RNA-MS. We also explore RNA-modifying enzymes, enabling us to study RNA modification biochemically as well as genetically.

【Expected Research Achievements and Scientific Significance】

It is widely known that gene expression is transcriptionally regulated by various cellular processes including development and differentiation in spatiotemporal manner. We have been focusing on dynamic alteration of RNA modification as a novel regulatory element in gene expression. This project aims to establish a novel concept of regulatory mechanism of gene expression by dynamic alteration of RNA modification by sensing cellular metabolic status. Especially, we study RNA modifications regulated

by nutritional availability and respiratory conditions. We also study physiological importance of reversible RNA modifications. Understanding of molecular pathogenesis of RNA modopathies will contribute to medical and pharmaceutical applications.

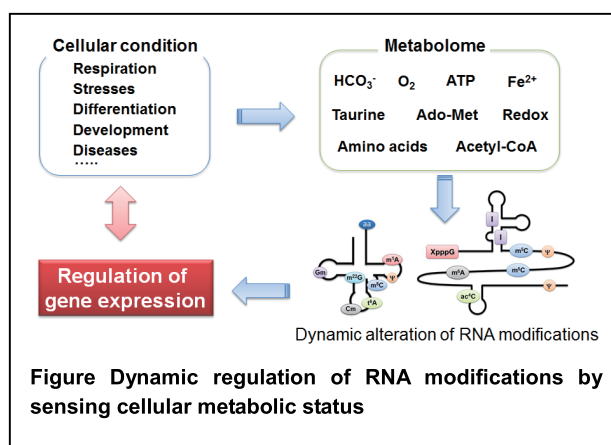


Figure Dynamic regulation of RNA modifications by sensing cellular metabolic status

【Publications Relevant to the Project】

- Taniguchi et al., Acetate-dependent tRNA acetylation required for decoding fidelity in protein synthesis. *Nature Chem Biol.*, in press (2018)
- Lin et al., CO₂-sensitive tRNA modification associated with human mitochondrial disease. *Nature Commun.*, 14, 9(1):1875 (2018)
- Nagao et al., Hydroxylation of a conserved tRNA modification establishes non-universal genetic code in echinoderm mitochondria. *Nature Struct Mol Biol.*, 24, 778-782 (2017)
- Frye et al., RNA modifications: what have we learned and where are we headed? *Nature Rev Genet.*, 17, 365-372 (2016)

【Term of Project】 FY2018-2022

【Budget Allocation】 149,800 Thousand Yen

【Homepage Address and Other Contact Information】

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