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

Broad Section H

Title of Project : Analysis of immune regulatory mechanisms mediated by mRNA metabolism

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Research Project Number : 18H05278 Researcher Number : 10379092
Keyword : immune reaction, cytokine, mRNA decay

【Purpose and Background of the Research】

Immune cells eliminate pathogens by evoking immune responses by recognizing pathogens via a set of receptors such as Toll-like receptors and antigen-receptors. Cytokines are mediators of immune responses, although their production is tightly controlled to prevent inflammatory diseases. We previously identified Regnase-1 as an RNase essential for the suppression of excess immune responses. Regnase-1 post-transcriptionally controls abundance of mRNAs related with immune responses by directly degrading them. Furthermore, the studies on Regnase-1 and Roquin revealed that immune responses are fine-tuned by spatiotemporally-regulated decay of mRNAs in cells. The immune-related mRNAs are controlled not only by 3' untranslated regions (UTR) recognized by Regnase-1, but also via the coding regions and the modification of mRNAs. Although the abundance of immune-related mRNAs is determined by highly complex mRNA metabolism, the mechanism of regulation is not understood yet. In this research, we aim to elucidate the dynamic network of mRNA metabolism in immune regulation.

【Research Methods】

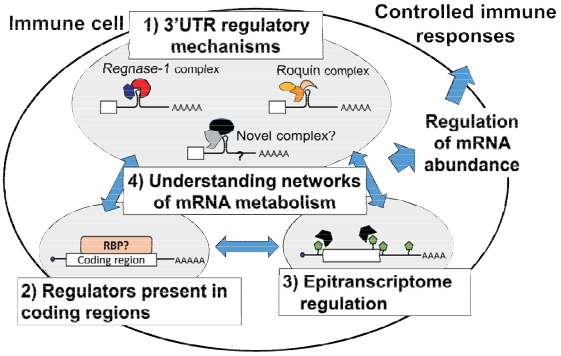

Fig. 1. Scheme of this research

In this research, we will analyze mechanisms of mRNA regulation in immune responses via following points of view.

1) Analysis of spatiotemporal regulation of immune-related mRNAs via 3' UTR.
2) Analysis of molecular mechanisms of immune-related mRNAs hidden in protein coding regions.
3) Roles of mRNA epitranscriptome in the regulation of immune reactions.

Then, the networks between immune regulatory systems studied in 1) ～3) will be integrated by in silico analysis such as machine learning.

【Expected Research Achievements and Scientific Significance】

We will try to understand dynamic mRNA metabolism networks in the control of immune responses. Further integration between mRNA regulation and transcription networks, complete understanding of gene expression networks of immune reactions will be achieved. In addition, our study will lead to the precise prediction of immune responses, which might be leading to the development of novel therapies targeting mRNA metabolisms.

【Publications Relevant to the Project】

・Yoshinaga M, Nakatsuka Y, Vandenbon A, Ori D, Uehata T, Tsujimura T, Suzuki Y, Mino T, Takeuchi O. Regnase-1 Maintains Iron Homeostasis via the Degradation of Transferrin Receptor 1 and Prolyl-Hydroxylase-Domain-Containing Protein 3 mRNAs. ***Cell Rep.*** 19:1614-1630. 2017
・Mino T, Murakawa Y, Fukao A, Vandenbon A, Wessels HH, Ori D, Uehata T, Tartey S, Akira S, Suzuki Y, Vinuesa CG, Ohler U, Standley DM, Landthaler M, Fujiwara T, Takeuchi O. Regnase-1 and Roquin Regulate a Common Element in Inflammatory mRNAs by Spatiotemporally Distinct Mechanisms. ***Cell.*** 161:1058-73. 2015

【Term of Project】 FY2018-2022

【Budget Allocation】 148,900 Thousand Yen

【Homepage Address and Other Contact Information】

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