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

Integrated Disciplines (Complex Systems)

Title of Project : Comprehensive understanding of molecular mechanism underlying the piRNA pathway

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Research Project Number : 17H06111 Researcher Number : 20322745
Research Area : Complex Systems
Keyword : PIWI, piRNA, transposon, RNA silencing, Drosophila

【Purpose and Background of the Research】

The germ cells have specific chromatin organization that enables them to express germline-specific genes. However, this permits the amplification and insertion of transposable elements, including transposons, into other sites in the genome, leading to injury in the genome, defects in gametogenesis and finally infertility. To avoid this, piRNA-mediated RNA silencing represses transposons. piRNAs are mainly derived from piRNA clusters and loaded onto PIWI proteins. Both piRNAs and PIWI proteins are necessary for repressing transposons in the germline. However, the underlying molecular mechanism remains elusive. In this study, we will dissect the molecular mechanism by mainly focusing on piRNA biogenesis and piRNA-driven transcriptional silencing of transposons.

【Research Methods】

We will use biochemical approaches to understand the mechanism underlying the piRNA pathways. We will also use techniques such as genome wide-sequencing, bioinformatics and immuno-EM. Our first goal is to understand the

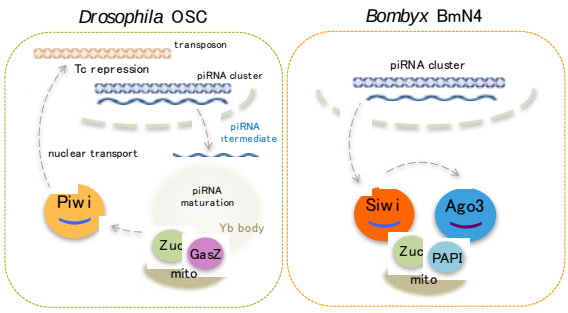

Figure 1. Model of the piRNA pathway in OSC and BmN4

molecular mechanism of piRNA biogenesis. We will focus on the primary piRNA processing pathway and the amplification loop. Our second goal is to identify the molecular functions of piRNA factors. The targeted goal of this proposal is to use biochemical-based techniques to understand the mechanisms controlling germline cell synthesis and function with a view to biotechnological and therapeutic applications.

【Expected Research Achievements and Scientific Significance】

We aim to use a unique biochemical-based aspect to understand the role of RNA silencing in germ cell fate determination, maintenance, and differentiation. Our group has established cultured OSCs, an ideal tool to perform biochemical analyses. We also have the ability to carry out RNAi-based gene screening in the OSC line, monoclonal antibody production, immunoprecipitation, and small RNA library construction. Our expertise allowed us to biochemically analyze the functions of piRNA factors in the piRNA pathways, and gain new insights into the molecular function of Piwi.

【Publications Relevant to the Project】

Matsumoto N, Nishimasu H, Sakakibara K, Nishida KM, Hirano T, Ishitani R, Siomi H, *Siomi MC, and *Nureki O. Crystal structure of silkworm PIWI-clade Argonaute Siwi bound to piRNA. ***Cell*** 167: 484-497. 2016 (*double corresponding authors)

Sumiyoshi T, Sato K, Yamamoto H, Iwasaki YW, Siomi H, and Siomi MC. Loss of l(3)mbt leads to acquisition of the ping-pong cycle in *Drosophila* ovarian somatic cells. ***Genes & Development*** 30: 1617-1622. 2016

【Term of Project】 FY2017-2021

【Budget Allocation】 155,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://www-siomilab.biochem.s.u-tokyo.ac.jp/index.html