Small RNA Regulation in Drosophila

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Title of project or programme

Small RNA Regulation in Drosophila

Principal Investigators of project/programme grant

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- United Kingdom

Source of funding information

Medical Research Council

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01-04-2007

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36

The project/programme is most relevant to

- Spinal muscular atrophy (SMA)

Keywords

Drosophila, small RNAs, U body, P body, Spinal Muscular Atrophy

Research abstract in English

The overall aim of this project is to understand how various small RNAs may be related and how the spatial dynamics of small RNAs influence gene function using the fruit fly Drosophila melanogaster as

a model system. Study of small RNA regulation promises to provide new insights into the molecular mechanism of human diseases such as Spinal Muscular Atrophy (SMA), a devastating neurodegenerative disorder.

Small RNAs play critical roles at multiple levels of gene expression, such as chromatin architecture, transcription, and RNA processing, turnover and translation. Recent studies suggest that many human diseases are caused by dysfunction of specific small RNAs.

We have recently demonstrated that uridine-rich small nuclear RNAs (U snRNAs), the major components for pre-mRNA processing, are concentrated in discrete cytoplasmic foci, which we have called U bodies. The enrichment of snRNA, snRNA-associated proteins and the SMA determining factor – Survival Motor Neuron protein (SMN) in the U body suggest that it might be the site for snRNA-protein assembly. Intriguingly, U bodies always associate with cytoplasmic processing bodies (P bodies), which are specialized foci containing small interfering RNAs (siRNAs), microRNAs (miRNAs), and factors for mRNA degradation and translational repression. While the U body exhibits a different pattern and composition from the P body, there are mounting evidences to suggest a functional relationship between these two bodies: 1) U bodies always touch P bodies; 2) both bodies contain Sm/Lsm proteins, which are important for RNA metabolism; 3) both bodies reside at subdomains of the endoplasmic reticulum; and 4) Disruptions of P body components cause reorganization of U bodies.

Focusing on nervous and reproductive systems in Drosophila, we aim to illuminate how various small RNA pathways interact in U bodies and P bodies. What is the significance of the U body-P body interaction? What events are occurring underneath the physical contact of these two bodies? How do these two organelles keep their own identities? Do small RNAs have a common maturation site or share a common way station? Do various small RNAs have any cross-talk at all? What processes are reflected by the U body-P body interaction? What are the consequences when the interaction goes wrong? By taking advantage of the genetic tractability and the wealth of information available for Drosophila, we are now able to precisely dissect those cellular problems in a developmental manner.

Lay Summary