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

Title of Project : Regulatory Mechanisms of Meiosis in Fission Yeast

Masayuki Yamamoto
(The University of Tokyo, Graduate School of Science, Professor)

Research Area : Biology

Keyword : Cell cycle

【Purpose and Background of the Research】

Meiosis is a process to form gametes, which is essential for most eukaryotes to recombine genetic information and transmit it to the next generation. Compared to the mitotic cell cycle, however, much remains to be known about how the meiotic cell cycle is regulated.

In fission yeast we found an unusual behavior of messenger RNAs required for meiosis, which we called "selective elimination of meiosis-specific mRNA". Certain mRNAs required exclusively for meiosis carry a region termed DSR, to which a novel protein Mmi1p binds and directs the mRNAs to degradation in mitotic cells. Mmi1p is sequestered by the master meiotic regulator Mei2p to the nuclear dot in meiotic prophase, so that meiosis-specific mRNAs may execute their due function. We will investigate the molecular mechanism for selective elimination thoroughly in this project.

We have been also analyzing TOR kinase pathways in fission yeast, which has two TOR complexes (TORC1 and TORC2) like other organisms. TORC1 is essential for vegetative growth, whereas TORC2 is necessary to initiate sexual development. If the activity of TORC1 is downregulated, fission yeast cells initiate untimely conjugation and meiosis. We will analyze the TOR pathways and hope to clarify how they are linked to nutrient recognition.

【Research Methods】

1. Selective elimination, the new mechanism to destruct meiosis-specific mRNAs selectively, involves a DSR sequence on the target mRNA, an RNA-binding protein Mmi1p, and nuclear exosomes. We have shown preliminarily that polyadenylation is also required for this destruction. In this research project we try to identify additional factors relevant to the selective elimination, using molecular genetic approaches and yeast two-hybrid analyses. Then we will investigate mutual interaction of the factors, so that we may draw a scheme how selective degradation of DSR-containing mRNAs is carried out.
2. We will identify and characterize components of the two TOR pathways, in the hope to answer the following questions: (1) How do fission yeast cells recognize nutrients and transmit the signal to the TOR pathways?; (2) What are the targets of the TOR pathways that directly control sexual development?; and (3) How is it possible that two similar kinases regulate sexual development in opposite directions?

【Expected Research Achievements and Scientific Significance】

This project aims to elucidate molecular mechanisms central to the regulation of meiosis in fission yeast. Analysis of meiosis at the molecular level is far more advanced in budding and fission yeast compared to animals or plants, partly because we can induce meiosis artificially in these microbes but it is still difficult to do so in higher eukaryotes. Sophisticated analyses applicable to yeasts may also be a reason that yeasts have been widely studied in this field. Taking this advantage, we wish to scrutinize the fundamental molecular mechanisms to induce and drive meiosis. Knowledge accumulated in this study will provide an invaluable basis to examine whether a homologous mechanism is functioning in higher organisms. It may also be pertinent to point out that such knowledge will be crucial in the future when we wish to control germ cells for medical care or agricultural profits.

【Publications Relevant to the Project】

Y. Harigaya, (eight authors) and M. Yamamoto: Selective elimination of messenger RNA prevents an incidence of untimely meiosis. **Nature** 442, 45-50 (2006).

T. Matsuo, Y. Otsubo, J. Urano, F. Tamanoi and M. Yamamoto: Loss of the TOR kinase Tor2 mimics nitrogen starvation and activates the sexual development pathway in fission yeast. **Mol. Cell. Biol.** 27, 3154-3164 (2007).

【Term of Project】 FY2009-2013

【Budget Allocation】 159,800 Thousand Yen

【Homepage Address and Other Contact Information】

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