Dr K Tanaka - Signalling mechanism that coordinate meiotic differentiation -RAS and cell cycle regulators-

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Meiosis is fundamental to living organisms that employ a sexual reproduction system for their propagation. We study the signalling mechanisms required to coordinate meiotic differentiation. The two main areas of this are.

Analysis of RAS mediated signal transduction cascades

The Ras proteins are widely conserved and they regulate signalling pathways that control cellular growth and differentiation. Most importantly, mutations in RAS genes are frequently associated with human cancers. Despite extensive research to uncover the molecular nature of Ras proteins, the means by which Ras-mediated signal transduction cascades are integrated in cells still requires further rigorous studies. Active RAS proteins interact with a number of target molecules to transduce a variety of different signals. Also, de-sensitisation or negative feedback mechanisms operate in concert with the signalling processes to make the signals to be temporal and specific.

We employ a genetically tractable model organism, the fission yeast. In this organism, the mating factor signalling pathway, which triggers meiotic differentiation, involves the RAS and the downstream MAP kinase cascade. Intriguingly, constitutive activation of RAS gives different phenotypes to the constitutively activated MAP kinase cascade. Thus, fine-tuning of the signalling is expected to be crucial for the concerted signal transduction. This will generate various mutants in the RAS and MAP kinase cascades to analyse spatial and temporal regulation of the signaling events.

Functional study of the mechanisms regulating the onset of meiosis

Meiosis generates four gametes by co-ordinating extensive chromosome pairing and recombination with two successive rounds of chromosome segregation in the absence of intervening DNA synthesis. Disordered meiotic divisions lead to inaccurate chromosome segregation resulting in production of malfunctioning gametes. They may contribute to abortive embryos or to embryos containing abnormal chromosome numbers. One such example in humans is Down's Syndrome, which arises when an extra copy of chromosome 21 is introduced into the genome of the gamete.

This work aims to dissect individual steps leading up to the onset of meiotic division using fission yeast as a model organism. Fission yeast is a genetically tractable organism and has made a significant contribution to the understanding of cell cycle regulation. We will examine how known mitotic cell cycle regulators contribute to meiotic differentiation and how regulators for meiotic recombination ensure the accurate progression of meiosis.

References

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