IMCB Invited Speaker

Speaker : **Dr. Christian Zierhut**
Postdoc, The Rockefeller University, USA

Date : 29 July 2013 (Monday)

Time : 10:00AM - 11:00AM

Venue : IMCB Seminar Room 3-46, Level 3, Proteos, Biopolis

Host : Prof. Wang Yue

Seminar :

Cell cycle transitions in the absence of nucleosomes

Eukaryotic nuclear DNA is packaged into large structures known as chromatin. This structure's fundamental unit is the nucleosome, formed by DNA wrapped around the histone proteins H2A, H2B, H3 and H4. By limiting accessibility to DNA,nucleosomes may act inhibitory to many processes, but by recruiting proteins they may also act stimulatory, and post-translational histone modifications provide added regulatory complexity. However, because of the essential nature of histones and their extremely long half-lives, these effects are hard to analyse in genetic model organisms. Furthermore, histones directly regulatetranscription, and therefore pleiotropic effects cannot be excluded following histone manipulations. To bypass these problems, I have developed a method to deplete H3 and H4 from Xenopus laevis egg extracts that faithfully recapitulate chromosome physiology in the absence of transcription. Using these extractsthat are incapable of forming nucleosomes, I have analysed the contributions of nucleosomes to mitosis, nuclear envelope formation, DNA damage checkpoint signalling and DNA damage processing/repair. Although DNA damage responses are only mildly affected by the absence of nucleosomes, both mitotic spindle formation and nuclear envelope formation require nucleosomes. There are two main pathways that induce spindle formation, one centred around RanGTP and one centred around the kinase Aurora B, and both are defective in the absence of nucleosomes. Using add-back of phosphomimetic histones, H3T3 phosphorylation was found to be necessary and sufficient for Aurora B activation. At exit from mitosis, membranes can associate with nucleosome-free chromatin, but formation of nuclear pore complexes (NPCs) is defective in the absence of nucleosomes. This can be attributed to a defect in the generation of a chromatin-bound intermediate in NPC formation on nucleosome-free DNA. Indeed, the first nucleoporin to bind chromatin and which is required for the association of most others,ELYS, is absent from nucleosome-free DNA in extract, and can bind nucleosomes but not naked DNA in vitro. These results thus suggest that recognition of nucleosomes by ELYS triggers the formation of nuclear pores upon exit from mitosis. Together, our results comprise the first study of how chromatin as a whole directly affects chromosome physiology, and allow us to generate a framework for nucleosome functions throughout the cell cycle.

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