REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Conservation of mouse Rec114 and Mei4 in programmed breaking of the genome

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Seminar Room

Programmed induction of meiotic DNA double-strand breaks (DSBs) is a universally conserved process to initiate recombination in all sexually reproducing organisms. Our knowledge of DSB formation during meiosis in higher eukaryotes is obscure although genetic screens in *S. cerevisiae* have identified at least ten proteins that are indispensable for meiotic DSBs. Out of these ten proteins, Spo11 is an evolutionarily conserved protein that catalyzes DSB formation in topoisomerase-like reaction. However, the role and conservation of other DSB proteins have remained unclear. Using phylogenomics approach we discovered that two of *S. cerevisiae* proteins, Mei4 and Rec114 are also evolutionarily conserved in most eukaryotes. Like their yeast counterparts, interaction between mouse MEI4 and REC114 proteins is well conserved. Our immunolocalization studies reveal that mouse MEI4 and REC114 appear as discrete foci on meiotic chromosome axes at the time of DSB formation and do not require SPO11 for their localization. MEI4 highly colocalizes with REC114 but does not localize with DNA repair proteins (DMC1 and RPA) that form either distinct or temporally differential foci than MEI4 in the genome. We demonstrate the functional conservation of mouse *Mei4* as *Mei4*$^{-/-}$ mice are deficient for meiotic DSB formation. We propose that MEI4 acts as a structural component of the DSB machinery that ensures meiotic DSBs to be formed in the context of chromosome axes.