Some Assembly Required: How to Build a Meiotic DNA-Breaking Machine

Human reproductive success and the development of healthy offspring depend on accurate transmission of genetic material from parent to child. During meiosis, the specialized cell division that gives rise to sperm and eggs, homologous maternal and paternal chromosomes exchange genetic information through the process of homologous recombination, which initiates with DNA double-strand breaks (DSBs) made by the Spo11 protein in collaboration with a suite of accessory factors. Although Spo11 and its partner proteins have been known for more than 25 years, the roles of these factors in DSB formation remain poorly understood. Moreover, the structures and activities of the higher order nucleoprotein assemblies that carry out DSB formation have remained enigmatic. Toward overcoming these obstacles, we recently reported purification of recombinant complexes of yeast DSB-promoting proteins, including a “core complex” of Spo11 with its direct binding partners Rec102, Rec104, and Ski8 and separate complexes of the evolutionarily conserved Rec114, Mei4, and Mer2 proteins (Claeys Bouuaert et al. Nature Struct Mol Biol 2021; Nature 2021). Recent progress in biochemical, single molecule biophysical, and structural characterization of these protein complexes from yeast and their orthologs in mice will be presented.

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Host: Melina Schuh / Jochen Rink