The TopoVIB-Like protein family is required for meiotic DNA double strand break formation

Meiotic recombination is induced by the formation of DNA double strand breaks (DSBs) catalyzed by SPO11, the ortholog of the subunit A of TopoVI DNA topoisomerase (TopoVIA). TopoVI activity requires the interaction between A and B subunits; however whether SPO11 functions alone or through association with another subunit has remained an open question for the last 18 years. Here, we identified a conserved family of plant and animal proteins that we named TopoVIB-Like. They show strong similarity with TopoVIB and have a GHKL domain potentially involved in ATP binding and a transducer domain interacting with SPO11. We further provide evidence that the meiotic recombination proteins Rec102 (S. cerevisiae), Rec6 (S. pombe) and Mei-P22 (D. melanogaster) are TopoVIB homologs, but without GHKL domain. We then demonstrated that mouse TOPOVIBL interacts and forms a complex with SPO11 and is required for meiotic DSB formation. We conclude that the meiotic program has evolved through the combined specialization and differentiation of TopoVI subunit homologs expressed specifically in meiotic cells and with a modified biochemical activity to promote the formation of DSBs.

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