Abstract

Meiotic sex chromosome inactivation (MSCI) is an essential epigenetic process, which transcriptionally silences X and Y chromosomes during spermatogenesis. It is accompanied by substantial chromatin remodeling resulting in a formation of so called sex or XY body, which is a characteristic of male pachytene spermatocytes. In spite of MSCI indispensability for male fertility, its biological role and molecular nature still remain rather unclear. However, the described link between chromosomal asynapsis and transcriptional silencing demonstrated that MSCI is tightly associated with the asynapsis of largely non-homologous sex chromosomes and is a specific form of more general mechanism called meiotic silencing of unsynapsed chromatin (MSUC).

The essential role of MSCI was demonstrated using mouse models, such as carriers of X-autosome translocations, where anomalous synapsis of sex chromosomes leads to impairment of MSCI and male sterility. Intriguingly, the exclusive spermatogenic arrest is a hallmark of not only X-autosome translocations but even various autosomal rearrangements, including autosomal translocations, inversions, or other structural mutations. Because the rearranged autosomes often intimately associate with the sex body, it was suggested that such autosomal rearrangements might influence sex chromosome expression and that MSCI failure is therefore a common reason for chromosomal sterility.

In this work, we study a mouse autosomal translocation T(16;17)43H as an example of autosomal rearrangement, which in heterozygous state induces male sterility. We aim to characterize the spermatogenic arrest, which accompanies the autosomal asynapsis, to analyze the expression changes in the affected region and to analyze the impact of aberrant sex body formation on MSCI. By genetic enlargement of the region of asynapsis, we also strive to show a causative relationship between the extent of asynapsis and degree of spermatogenic failure.

MSCI is also believed to play an important role during evolution, where it accompanies the diversification of sex chromosomes. Impairment of MSCI was suggested to participate in hybrid sterility and therefore to contribute to reproductive barrier between newly formed species. To obtain an insight on MSCI divergence we compare its extent in two close mouse species *Mus musculus* and *Mus spretus* and evaluate its relationship to gene flow out of the X chromosome.