LABORATORY OF

GERM CELL DEVELOPMENT

Fertility, sterility, spermatogenesis, meiosis, recombination initiation

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Genetic recombination is the quintessence of gametogenesis; it ensures not just the reshuffling of parental alleles and thus higher variability among the offspring, but first of all the proper segregation of chromosomes during the meiotic cell divisions and thereby fertility. The sites of meiotic double strand DNA breaks, and thus the sites of recombination, are determined in many mammals by the PRDM9 (PR/SET-domain carrying 9) protein, an epigenetic factor that carries histone-3-methyltransferase and DNA-binding activities. This protein is essential for fertility in the classical laboratory mouse, but not in the dog. In addition, a fertile human subject carrying both copies of *PRDM9* inactivated was found.
In our study published in 2019, we described the identification of male mice that produced sperm and/or offspring regardless of lacking functional PRDM9. Despite hotspots in the default sites including promoters, some spermatocytes (but no oocytes) lacking PRDM9 completed synapsis and repaired these sites to crossovers. These cells displayed a crossover rate similar to the wild type that was higher than in the wild-type spermatocytes from the previously studied mice. Fertility parameters of *Prdm9*-deficient F1 male hybrids of two mouse subspecies depended on the locus of chromosome X that also controls hybrid sterility and crossover rate. We speculated that one of the mechanisms that could rescue the effect of PRDM9 absence might be an increased efficiency of the hotspot repair.
Our mice that tolerate the loss of PRDM9 can serve as an improved model of human meiosis.

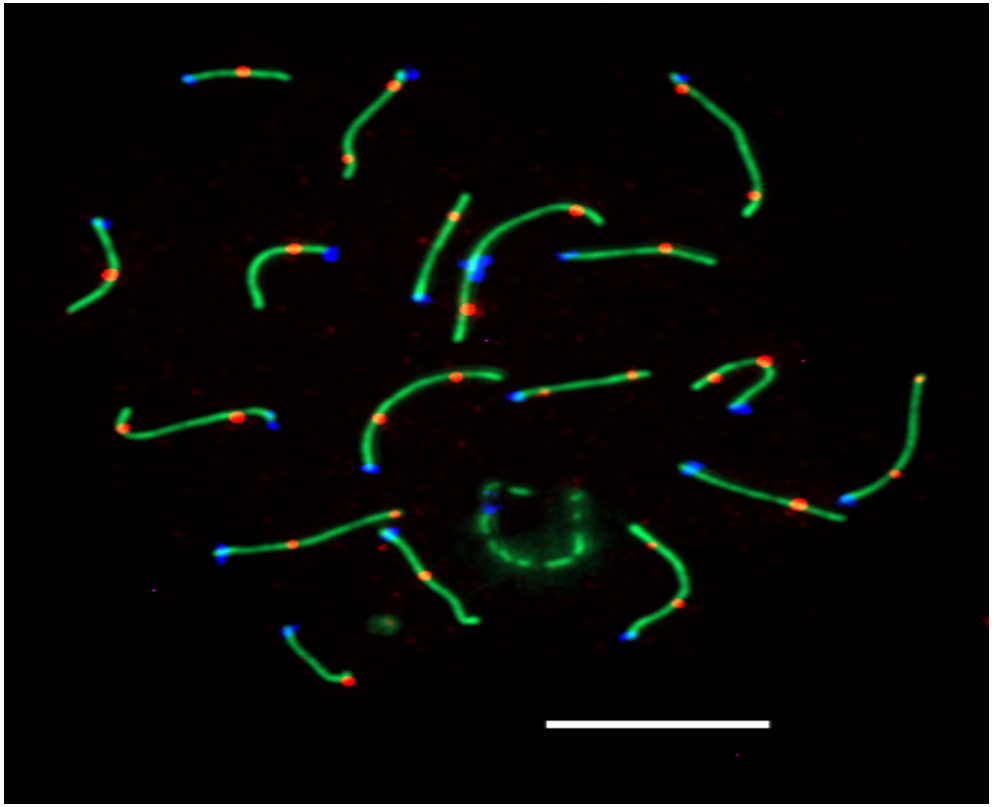
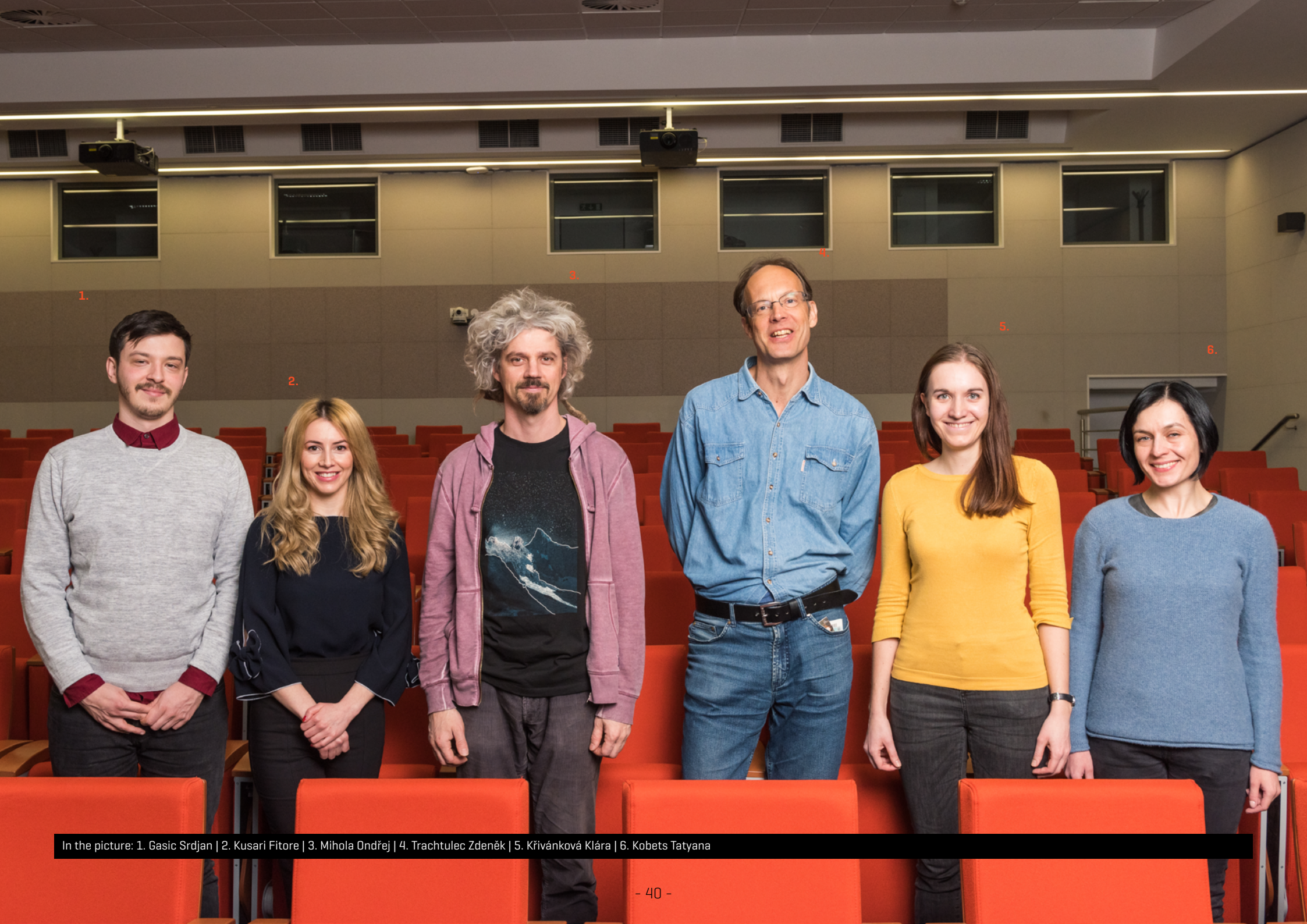


Figure 1. Immature spermatogenic cell (pachytene spermatocyte) from a *Prdm9*-deficient mouse (background strain PWD/Ph); this cell is immunolabelled for chromosomal axis protein SYCP1 (green), crossover site factor (red), and centromeres (blue); the bar represents 10 micrometers. One of the images that was used to count recombination (crossover) rates per cell.

Selected publication:

1. Mihola O, Pratto F, Brick K, Linhartova E, Kobets T, Flachs P, Baker CL, Sedlacek R, Paigen K, Petkov PM, Camerini-Otero RD, Trachtulec Z* (2019) Histone methyltransferase PRDM9 is not essential for meiosis in male mice. *Genome Res*, **29**:1078–1086.



In the picture: 1. Gasic Srdjan | 2. Kusari Fitore | 3. Mihola Ondřej | 4. Trachtulec Zdeněk | 5. Křivánková Klára | 6. Kobets Tatyana