



Laboratory of Mouse Molecular Genetics

Mouse genomics, hybrid sterility, *Prdm9*, meiotic silencing, chromosome substitution strains

Jiří Forejt

jiri.forejt@img.cas.cz

www.img.cas.cz/research-groups/jiri-forejt

We identified the first vertebrate hybrid sterility gene *Prdm9* [Meisetz], encoding a meiotic histone H3 lysine-4 tri-methyltransferase. Positional cloning was confirmed by a rescue experiment using the intact *Prdm9* transgene in bacterial artificial chromosomes with the "fertility" *Hst1^f* allele. Identification of the *Prdm9* hybrid sterility gene reveals a role for epigenetics in speciation, and opens a window to a systems approach to the hybrid sterility gene network. To characterize the incompatibilities underlying hybrid sterility, we phenotyped reproductive and meiotic markers in males with altered copy numbers of *Prdm9*. A partial rescue of fertility was observed upon removal of the B6 allele of *Prdm9* from the azoospermic [PWD x B6]F1 hybrids, whereas removing one of the two *Prdm9* copies in PWD or B6 background had no effect on male reproduction.

Chromosome substitution, or consomic strains C57BL/6J-Chr # PWD/Ph/ForeJ, recently constructed in our laboratory, are used for dissecting the genomic architecture of sterility of *Mus m. musculus* x *Mus m. domesticus* hybrids. They are also employed in phenome analysis in collaboration with The Jackson Laboratory, Bar Harbor, Maine, USA [Dr. K.L. Svenson]. We study meiotic X-chromosome inactivation by genome-wide expression profiling and by monitoring transcription profiles and histone modifications in meiotic and postmeiotic testicular cells of carriers of male-sterile autosomal rearrangements and in male-sterile inter-species hybrids.

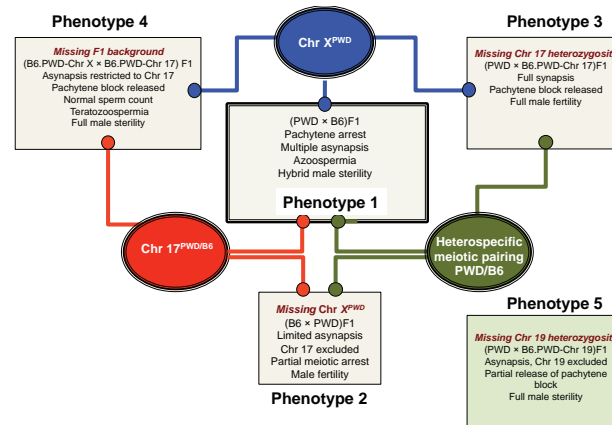


Fig. 1. Genetic architecture of hybrid sterility of [PWD x B6]F1 hybrids. Five basic hybrid sterility phenotypes are controlled by three major genomic determinants. Interaction of all five components is required to attain full pachytene block.



- AS CR, Premium Academiae - Premium Academiae, 2007-2013, J. Forejt
- GA CR, GAP305/10/1931 - Identification of interactors of the meiotic histone methyltransferase Hybrid sterility 1 [PR-domain 9], 2010-2013, Z. Trachtulec
- GA CR, GPP305/11/P630 - Epigenetic regulators of gene expression in mouse spermatogenesis, 2011-2013, O. Mihola
- COST Action [BM0901], project LD11079 European systems genetics network for the study of complex genetic human diseases using mouse genetic reference populations [SYSGENET], 2010-2013, J. Forejt



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4. Dzur-Gejdošová M, Simeček P, Gregorova S, Bhattacharyya T, Forejt J. Genetic architecture of hybrid sterility in the house mouse. **Evolution** 2012 66: 3321-3335.
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From the left:

Irena Chvátalová, MSc / Research Assistant · Petr Šimeček, PhD / Postdoctoral Fellow · Tanmoy Bhattacharyya, MSc / PhD Student · Prof. Jiří Forejt, MD, DSc / Head of Laboratory · Petr Flachs, MSc / PhD Student · Zdeněk Trachtulec, PhD / Research Fellow
Hana Vágnerová / Secretary · Václav Gergelits / Diploma Student (since 2012) · Ondřej Mihola, PhD / Postdoctoral Fellow · Mária Dzur-Gejdošová, MSc / PhD Student · Petr Jansa, PhD / Research Fellow

Not in the picture:

Vladana Fotopulosová, MSc / Research Assistant (maternity leave) · Soňa Gregorová, MSc / Research Assistant · Jana Perlová / Technician · Eliška Škaloudová / Diploma Student (since 2012)