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Laboratory of Mouse Molecular Genetics

Meiotic silencing, aneuploidy, genomics, hybrid sterility genes

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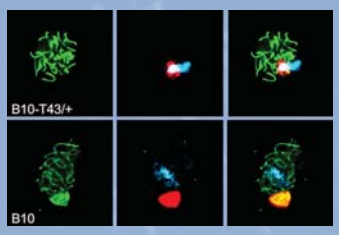
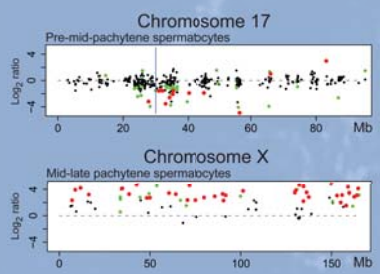


Meiotic synapsis and XY body in pachytene spermatocytes of B10-T43/+ sterile males and B10 controls. Synaptonemal complexes are green, phosphorylated histone H2AX is red and chromosome 17 is light blue.



Distribution of gene expression changes (Log2 scale) along chromosome 17 and X between sterile and fertile males. Expression differences significant at P<0.05 in green, at P<0.01 in red

Research topics

We study **Meiotic X-chromosome inactivation** by genome-wide expression profiling and by monitoring X-chromosome histone modifications in meiotic and postmeiotic testicular cells of carriers of male-sterile autosomal rearrangements and in male-sterile inter-species hybrids.

Genetic architecture of hybrid male sterility is analysed on the model of PWD/Ph x C57BL/6 sterile male hybrids. The candidate genes are evaluated by transgenic rescue for the *Hst1* locus and by positional cloning and expression profiling of sorted testicular cells for the *Hstx1* locus.

We have established a **New mouse model of human aneuploidy syndromes**. The Ts43H segmental trisomy of proximal 30 MB of mouse chromosome 17 encompasses over 300 protein-coding genes. Phenome analysis of aneusomic animals is realized by collaboration with Dr. M. Hrabe de Angelis, GSF, Munich.

Chromosome substitution strains C56BL/6.PWD, recently constructed in our laboratory, are used for phenome analysis in collaboration with The Jackson Laboratory, Bar Harbor, Maine, USA (Dr. K. L. Svenson) and for the genetics of gene expression in a systems genetics project with the Max-Planck-Institute for Molecular Genetics in Berlin (Dr. H. Lehrach).

We analyse **Haplotype structure and conserved synteny** in the *Hst1* region of mouse chromosome 17 by sequencing 33 loci from 80 chromosomes of five (sub)species of mice. Conservation of a complex pattern of alternative and antisense transcripts at the *Pdcd2* locus in the *Hst1* region suggests its biological importance.

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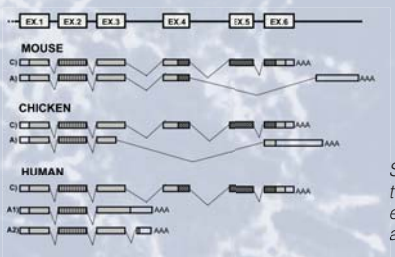
Selected recent papers

1. Mihola O, Forejt J, Trachtulec Z. Conserved alternative and antisense transcripts at the programmed cell death 2 locus. **BMC Genomics.** 2007;8:20.
2. Homolka D, Ivanek R, Capkova J, Jansa P, Forejt J. Chromosomal rearrangement interferes with X-chromosome inactivation. **Genome Res.** 2007;17:1431-7.
3. Pialek J, Vyskočilova M, Bimova B, Havelkova D, Pialkova J, Dufkova P, Bencova,V, Dureje L, Albrecht T, Hauffe HC, Macholan M, Munclinger P, Storchova R, Zajicova A, Holan V, Gregorova S, Forejt J. Development of unique house mouse resources suitable for evolutionary studies of speciation. **J Heredity.** Epub Oct 26,2007.
4. Pravenec M, Kazdova L, Landa V, Zidek V, Mlejnek P, Simakova M, Jansa P, Forejt J, Kren V, Qi N, Wang J-M, Chan D, Aitman T, Kurtz TW. Identification of mutated Srebf1 as a QTL influencing risk for hepatic steatosis in the spontaneously hypertensive rat. **Hypertension.** 2008;51:148-153.



Schematic representation of the constitutive (C) and alternative (A) transcripts encoding PDCD2 in the mouse, chicken and human.