

Petr Svoboda

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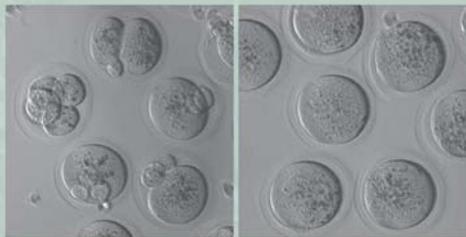
Laboratory of Epigenetic Regulations
RNA degradation, dsRNA, mobile DNA



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Research topics

Our lab explores research topics related to RNA silencing and repression of mobile elements in mammals. Current running projects include studies of activity and silencing of L1 retrotransposons, analysis of stability of maternal mRNAs in the oocyte, characterization of effects of long double-stranded RNA (dsRNA) and further analysis of RNA silencing. A representative example of our work is the study of effects of long dsRNA expression. Long dsRNA presence in mammalian cells can induce sequence-specific silencing as well as a number of sequence-independent effects resulting in general inhibition of proteosynthesis, non-specific mRNA degradation, activation of interferon-response genes, and, eventually, apoptosis. In order to understand effects of long dsRNA expression in mammalian cells, we have generated transgenic mice ubiquitously transcribing a long inverted repeat, which gives rise to a long dsRNA hairpin. We also developed a cell culture system allowing more detailed analysis of long dsRNA expression. We are currently addressing known mechanisms involving long dsRNA such as interferon pathway activation, adenosine deamination of the long dsRNA, and RNA silencing.



CagMosIR (F1 317.3 #4) WT (F1 317.3 #6)

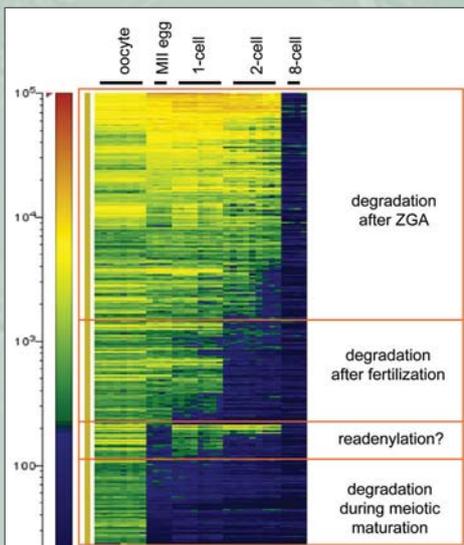
Mos null phenotype (parthenogenetic activation of *MII* oocytes) in oocytes isolated from transgenic animals carrying the *CagMosIR* transgene, which ubiquitously produces dsRNA with *Mos* sequence.

Current grant support

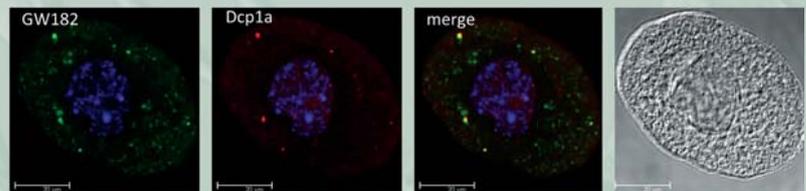
AS CR (Purkyně Fellowship); EMBO Installation Grant, GA AS CR (IAA501110701)

Selected recent papers

- Schmitter D, Filkowski J, Sewer A, Pillai RS, Oakeley EJ, Zavolan M, Svoboda P, Filipowicz W. Effects of Dicer and Argonaute down-regulation on mRNA levels in human HEK293 cells. **Nucleic Acids Res.** 2006;34:4801-4815.
- Svoboda P. Off-targeting and other non-specific effects of RNAi experiments in mammalian cells. **Curr Opin Mol Ther.** 2007;9:248-257.
- Grosshans H, Svoboda P. miRNA, siRNA, piRNA – Kleine Wiener Ribonukleinsäuren. **Bioessays.** 2007;29:940-943.
- Svoboda P. RNA silencing in mammalian oocytes and early embryos. **Curr Top Microbiol Immunol.** 2008;320:225-256.
- Sinkkonen L, Hugschmidt T, Berninger P, Gaidatzis D, Mohn F, Artus-Revel CG, Zavolan M, Svoboda P, Filipowicz W. MicroRNAs control de novo DNA methylation through regulation of transcriptional repressors in mouse embryonic stem cells. **Nat Struct Mol Biol.** 2008;15:259-267.
- Svoboda P, Stein P. (2008) RNAi experiments in mouse oocytes and early embryos. **CSH Protocols.** 2009;4(10.1101/pdb.top56).



Microarray analysis of maternal mRNA degradation



Co-localization of p-body components in meiotically incompetent oocytes. P-bodies are centres of mRNA metabolism, including degradation and storage.