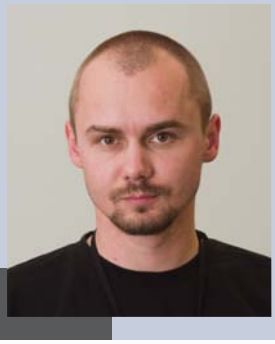

Petr Svoboda

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Laboratory of Epigenetic Regulations

RNA degradation, dsRNA, mobile DNA

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 a 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.

Current grant support

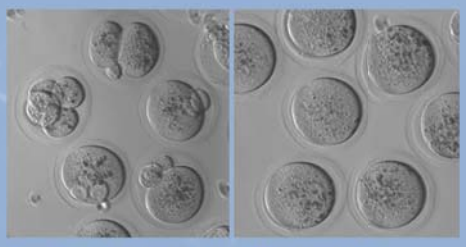
AS CR (Purkynje Fellowship); EMBO Installation Grant, GA AS CR (IAA501110701)

Selected recent papers

1. 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;34:4801-15.
2. Svoboda P. Off-targeting and other non-specific effects of RNAi experiments in mammalian-cells. **Curr Opin Mol Ther.** 2007;9:248-57.
3. Grosshans H, Svoboda P. miRNA, siRNA, piRNA – Kleine Wiener Ribonukleinsauren. **Bioessays.** 2007; 29:940-3.
4. Svoboda P. RNA silencing in mammalian oocytes and early embryos. **Curr Top Microbiol Immunol**; in press.
5. Sinkkonen L, Hugenschmidt T, Berninger P, Gaidatzis D, Mohn F, Artus-Revel C, Zavolan M, Svoboda P, Filipowicz W. MicroRNAs control de novo DNA methylation in mouse embryonic stem cells. **Nat Struct Mol Biol**; in press.

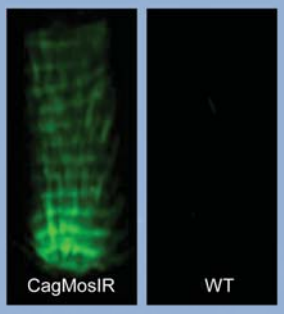
Long dsRNA expression in transgenic mice.
Structure of the CagMosIR transgene used for ubiquitous expression of a long RNA hairpin with the Mos sequence.

Petr Svoboda, PhD / Head of Laboratory
Matyáš Flemr, MSc / PhD Student
Jana Nejepínská, MSc / PhD Student
Lenka Sarnová, MSc / Diploma Student



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.



EGFP expression in somatic cells of CagMosIR transgenic mice (fluorescence of the tail tip).