Laboratory of Epigenetic Regulations

RNA degradation, dsRNA, RNAi, miRNA, chromatin

Petr Svoboda

petr.svoboda@img.cas.cz

The zygotic genome activation is the first step in the execution of the genome-encoded program that forms a new organism from a single fertilized cell and it is an essential event in the life of every sexually reproducing organism. The zygotic genome activation is closely associated with formation of pluripotency, i.e. the ability of cells to differentiate into any body cell type. Pluripotency is most studied in two artificial cell types, which maintain pluripotency during *in vitro* culture: embryonic stem cells (ESCs), which are derived from the inner cell mass of the blastocyst, and induced pluripotent stem cells (iPSCs), which form upon reprogramming gene expression in somatic cells with specific pluripotency factors that include transcription factors from the core transcription factor network controlling ESC renewal and pluripotency. A similar network forms in a stepwise manner during the mouse zygotic genome activation, which initiates at the early two-cell stage.

We study reprogramming of oocytes into pluripotent blastomeres of an early embryo (oocyte-to-embryo transition). This model is the natural parallel to the artificial reprogramming of somatic cells into iPSCs. The oocyte-to-embryo transition, however, is distinct. It is a unidirectional transient process executed by cytoplasmic factors, as demonstrated by animal cloning by nuclear transfer. Our primary research interest is in post-transcriptional mechanisms underlying oocyte-to-embryo transition. These mechanisms include control of maternal mRNA stability, small regulatory RNAs in miRNA and RNAi pathways, and production of maternal transcription factors, which will control gene expression in the embryo. Our goal is to understand how control of gene expression creates developmental competence *in vivo*.

Research of pluripotency is eminent for medicine and biotechnology where pluripotency plays a role in an ever-growing number of applications. Understanding control of the oocyte-to-embryo transition will provide original insights into stem cell biology and will likely contribute to efficient and safe production of pluripotent stem cells, efficient cloning technologies, informative prenatal diagnostics, and understanding of pathology of sterility and developmental defects.

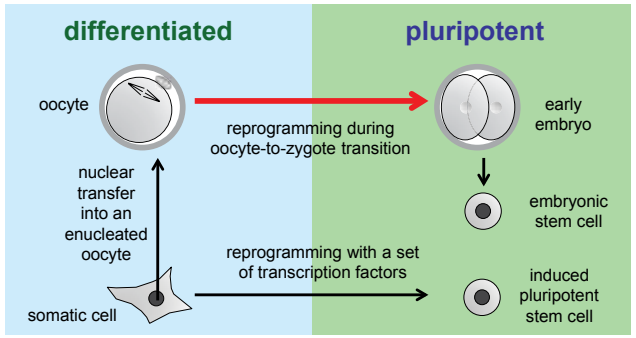

Fig. 1. Oocyte-to-zygote transition is a unique model for studying pluripotency. The mammalian oocyte is a highly specialized cell, whose cytoplasm is capable of reprogramming a genome to initiate development of a new organism. The blastomeres of the 2-cell embryo are totipotent as they can give a rise to embryonic and extraembryonic tissues. The pluripotent embryonic stem cells, which have potential to give a rise to any body cell type, are derived from the blastocyst, the final preimplantation embryo stage carrying the first defined cell lineages.

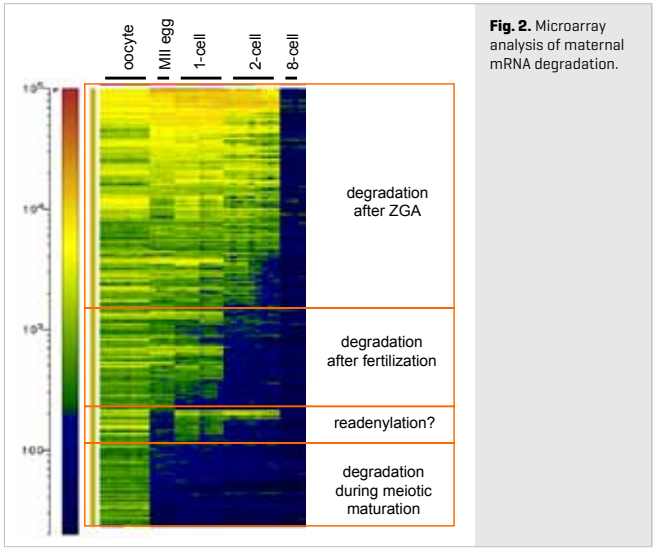

Fig. 2. Microarray analysis of maternal mRNA degradation.

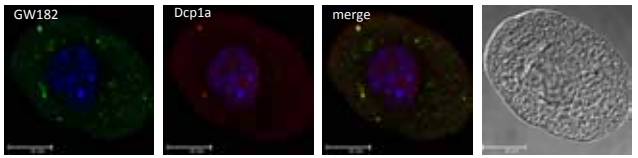

Fig. 3. Colocalization of p-body components in meiotically incompetent oocytes. P-bodies are centres of mRNA metabolism, including degradation and storage.

- EMBO, 1483 – EMBO Installation Grant, 2007-2011, P. Svoboda
- Ministry of Education, Youth and Sports of the Czech Republic, ME09039 – Role of posttranslational mechanisms in reprogramming mouse oocytes to pluripotent cells, 2009-2012, P. Svoboda
- GA CR, GA204/09/0085 – RNA silencing and long dsRNA in mammalian cells, 2009-2013, P. Svoboda
- GA CR, GAP305/10/2215 – Control of chromatin and pluripotency by microRNAs, 2010-2013, P. Svoboda
- GA Charles University, 18110 – Development and characterization of microRNA pathway inhibitor, 2010-2012, K. Podolská

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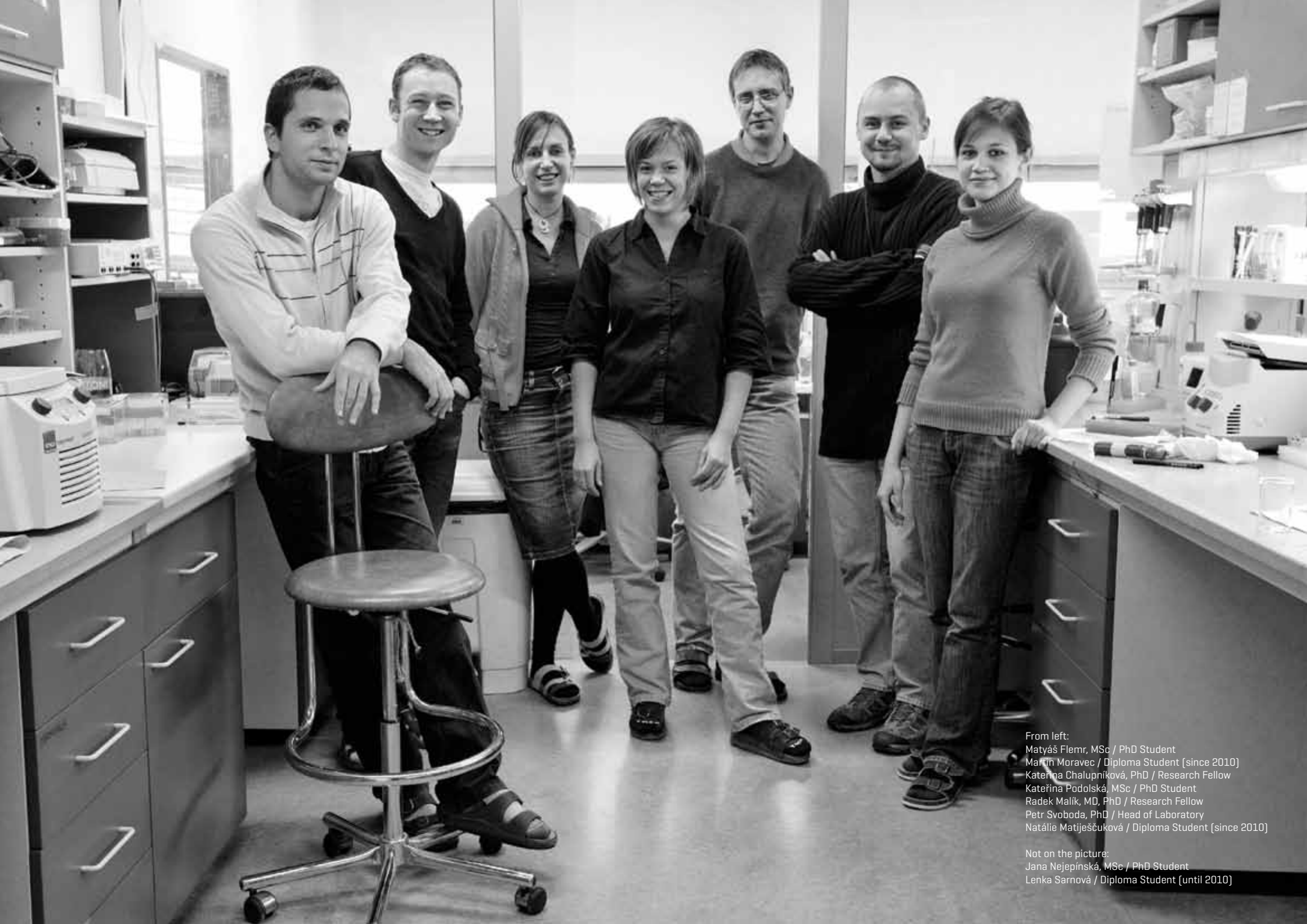

From left:
Matyáš Flemr, MSc / PhD Student
Martin Moravec / Diploma Student (since 2010)
Kateřina Chalupníková, PhD / Research Fellow
Kateřina Podolská, MSc / PhD Student
Radek Malík, MD, PhD / Research Fellow
Petr Svoboda, PhD / Head of Laboratory
Natálie Matiješčuková / Diploma Student (since 2010)

Not on the picture:
Jana Nejepínská, MSc / PhD Student
Lenka Sarnová / Diploma Student (until 2010)