LABORATORY OF

EPIGENETIC REGULATIONS

Oocyte-to-embryo transition, RNA degradation, RNAi, miRNA, retrotransposon

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We study the mechanisms governing gene expression during mammalian oocyte-to-embryo transition (OET). OET is an orchestrated process where a highly specialized cell – the oocyte – is transformed into cells that are able to give rise to a new organism. This transformation is accompanied by extensive reprogramming of gene expression, which includes extensive post-transcriptional control of maternal mRNAs. Maternal mRNAs that are no longer needed are eliminated, while mRNAs whose products are needed for zygotic genome activation (ZGA) are maintained and translated. Our recent research focused on induction of selective mRNA degradation during resumption of meiosis, fertilization, and zygotic genome activation. Our current work aims at understanding the evolving role of small RNAs during OET.

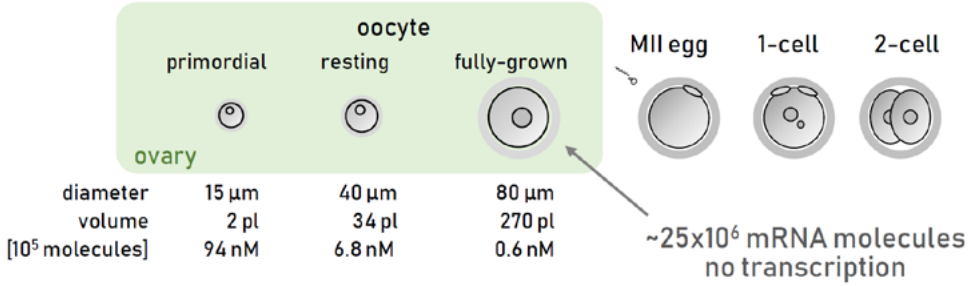

Figure 1. Oocyte-to-embryo transition in mice. Ovarian oocyte development is followed by ovulation, completion of meiosis, fertilization, and zygotic genome activation, which takes place at the 2-cell stage in mouse zygotes. An important aspect of OET is management of the massive maternal transcriptome in the large cytoplasmic volume.

Small RNAs guiding repressive ribonucleoprotein complexes represent a unique layer of control of gene expression and retrotransposon activity. Our research focuses on the role of three classes of small RNAs (microRNAs, short interfering RNAs (siRNAs) and PIWI-associated RNAs (piRNAs)) in the mammalian female germline. Mammalian oocytes offer an excellent opportunity to study the evolving co-existence of all three classes of small RNAs. While only siRNAs acting in the RNA interference (RNAi) pathway are essential for OET in mice, it is unclear whether this is exceptional or common in mammals.

We particularly focus on the molecular foundation of highly active RNAi in mouse oocytes: a unique maternal isoform of Dicer, which is responsible for highly efficient siRNA production, and an evolving set of long non-coding RNAs carrying antisense pseudogene sequences, which give rise to siRNAs, which in turn suppress complementary mRNA. Research questions we wish to answer include: Which molecular mechanisms are controlled by RNAi in mouse oocytes? How small RNA pathways operate in oocytes of other mammals, such as rat, hamster, cow, and pig? What are the consequences of ectopically enhanced RNAi in somatic cells?

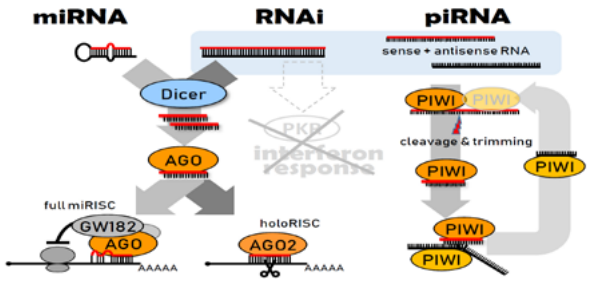

Figure 2. Schematic depiction of the three small RNA pathways that are present in mammalian oocytes. While all three pathways are present, their physiological relevance in the female germline may vary.

Selected publications:

1. Taborska E, Pasulka J, Malik R, Horvat F, Jenickova I, Jelić Matošević Z, Svoboda P* (2019) Restricted and non-essential redundancy of RNAi and piRNA pathways in mouse oocytes. *PLoS Genet*, **15**:e1008261. doi:10.1371/journal.pgen.1008261.
2. Demeter T, Vaskovicova M, Malik R, Horvat F, Pasulka J, Svobodova E, Flemr M, Svoboda P* (2019) Main constraints for RNAi induced by expressed long dsRNA in mouse cells. *Life Sci Alliance*, **2**. pii: e201800289. doi:10.26508/lsa.201800289.
3. Horvat F, Fulka H, Jankele R, Malik R, Jun M, Solcova K, Sedlacek R, Vlahovicek K, Schultz RM, Svoboda P* (2018) Role of Cnot6l in maternal mRNA turnover. *Life Sci Alliance*, **1**:e201800084. doi: 10.26508/lsa.201800084.
4. Franke V, Ganesh S, Karlic R, Malik R, Pasulka J, Horvat F, Kuzman M, Fulka H, Cernohorska M, Urbanova J, Svobodova E, Ma J, Suzuki Y, Aoki F, Schultz RM, Vlahovicek K*, Svoboda P* (2017) Long terminal repeats power evolution of genes and gene expression programs in mammalian oocytes and zygotes. *Genome Res*, **27**:1384-1394. doi: 10.1101/gr.216150.116.
5. Karlic R, Ganesh S, Franke V, Svobodova E, Urbanova J, Suzuki Y, Aoki F, Vlahovicek K*, Svoboda P* (2017) Long non-coding RNA exchange during the oocyte-to-embryo transition in mice. *DNA Res*, **24**:129-141. doi: 10.1093/dnares/dsw058.

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