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Re-arrangements in the cytoplasmic distribution of small RNAs following the maternal-to-zygotic transition in *Drosophila* embryos

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Statement of the Problem: Regulation of small RNAs is important for modulation of extensive gene expression that takes place during early development. MicroRNAs, for example, are known to regulate gene expression post-transcriptionally and there is correlation between their co-existence in polysome and their potential role in translation regulation. However, the extent to which each type of small RNA is associated with polysomal complexes is unknown. It is also unknown whether small RNAs maintain their polysome association throughout early development.

Methodology & Theoretical Orientation: 0-1 h and 7-8 h *Drosophila* embryos were used to represent the pre- and post-maternal-to-zygotic transition (MZT) stages of development. Sucrose density gradients were used to fractionate embryonic cytoplasmic small RNAs based on their molecular weight. Fractions were pooled into four fractions based on A254 reading: translationally inactive messenger ribonucleoprotein (mRNP); 60S; monosome (80S); and polysome. Small RNAs purified from each fraction was subjected to deep sequencing along with total RNAs from unfractionated embryos. Differentially expressed small RNAs were determined based on their reads.

Findings: Deep-sequencing of RNAs purified from fractionated and un-fractionated 0-1 h and 7-8 h embryo revealed development-specific co-sedimentation of various small RNAs (i.e., endo-siRNAs, piRNAs, tRFs and miRNAs) with different polysomal fractions. We have found tRFs are main enriched in mRNPs and, transposon derived piRNAs are enriched in polysomal fractions and expressed mainly at early embryonic development while transposon derived siRNAs are mainly enriched in mRNPs and expressed mainly after MZT. We then focused on microRNAs and found out that miRNAs such as miR-1-3p, -184-39, 5-5p and 263-5p are enriched in specific fractions. However, most miRNAs did not have a specific preference for any state of the translational machinery. More interestingly, we observed dysregulation of a subset of miRNAs in fractionated embryos despite no measurable difference in their amount in unfractionated embryos, indicating a potential for developmental regulation of microRNA sub-cellular location.

Conclusions: These results suggest that there appears to be a complex interplay among the small RNAs with respect to their polysome-co-sedimentation pattern during early development in *Drosophila*.

Recent Publications

1. Goktas C, Yigit H, Cosacak M I and Akgul B (2017) Differentially expressed tRNA-derived small RNAs co-sediment primarily with non-polysomal fractions in *Drosophila*. *Genes (Basel)* 8(11):333.
2. Alberti C and Cochella L (2017) A framework for understanding the roles of miRNAs in animal development. *Development* 144:2548-2559.
3. Zhang H, Liu J, Tai Y, Zhang X, Zhang J, Liu S, Lv J, Liu Z and Kong Q (2017) Identification and characterization of L1-specific endo-siRNAs essential for early embryonic development in pig. *Oncotarget* 8:23167-23176.
4. Yuan S, Schuster A, Tang C, Yu T, Ortogero N, Bao J, Zheng H and Yan W (2016) Sperm-borne miRNAs and endo-siRNAs are important for fertilization and pre-implantation embryonic development. *Development* 143:635-647.
5. Grivna S T, Pyhtila B and Lin H (2006) MIWI associates with translational machinery and PIWI-interacting RNAs (piRNAs) in regulating spermatogenesis. *Proc Natl Acad Sci USA* 103:13415-13420.

Biography

Mehmet Ilyas Cosacak has completed BSc and MSc degrees in Molecular Biology and Genetics and currently doing his PhD to understand the molecular mechanisms of induced plasticity using zebrafish as a model organism at the German Center for Neurodegenerative Diseases (DZNE) and the Technische Universität Dresden (TUD). He is mainly interested in understanding gene regulation and molecular mechanisms in development and regeneration, as further research in these areas will help to find novel treatment options for neurodegenerative and other diseases.

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