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Downregulated microRNAs as mediators of retinoic acid-dependent transcriptome homeostatic mechanisms in mouse embryos

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Abstract

Retinoic acid (RA) is an important transcriptional gene expression regulator which functions as a ligand for retinoic acid receptors (RAR), which bind retinoic acid response elements (RARE) within the regulatory regions of target genes. During antenatal development, RA signaling starts at late gastrulation stages and is required for cell differentiation, cell migration, axial elongation and organogenesis.

In mouse embryos, the most important source of RA is RALDH2, expressed in the paraxial mesoderm starting with E7.5. RA has been shown to travel over long distances and to activate gene expression and orchestrate morphogenetic events in axial and paraxial tissues of neuroectodermal and mesodermal origin. Several *ex vivo* and *in vivo* studies have described the impact of RA on transcriptome homeostasis; however, little is known about the post-transcriptional mechanisms altered by RA in the context of vertebrate embryo development.

The aim of this study was to provide a better understanding of these mechanisms. Here we used Exiqon qRT-PCR arrays to analyze the small RNA profile in E8.5 *raldh2-/-* embryos and identified a set of 26 downregulated microRNAs. MicroRNAs are small non-coding RNAs that regulate gene expression at post-transcriptional level. In order to identify the signaling pathways putatively modulated by RA-microRNAs interactions during early organogenesis stages, we combined mirWalk3.0 target prediction algorithms (for 3'UTR, 5'UTR, and CDS regions), complex network analysis, and DAVID gene ontology analysis.

Further, more complex investigations are needed in order to understand the transcriptomic impact certain microRNAs have on RA signaling during mouse embryogenesis.

Keywords: mouse embryo, gene regulation, miRNA, retinoic acid

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