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

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Abstract

A major transcriptional gene activator, retinoic acid (RA), exerts its function by binding to retinoic acid receptors (RAR), which recognize retinoic acid response elements (RARE) within the regulatory regions of target genes. During embryo-fetal development, RA signaling orchestrates axial elongation, organogenesis, cell differentiation, and cell migration, starting with late gastrulation stages.

In mouse embryos, RA is synthesized starting with E7.5 by RALDH2 expressed in the paraxial mesoderm and diffuses over long distances to activate gene expression and initiate morphogenetic events in the adjacent tissues. The impact of RA on mouse embryo transcriptome homeostasis has already been described; however, little is known about the RA-dependent post-transcriptional mechanisms of gene expression regulation in the context of vertebrate embryo development.

MicroRNAs are small non-coding RNAs that operate as endogenous post-transcriptional gene expression regulators. Here, we used Exiqon qRT-PCR arrays to identify the set of 11 upregulated microRNAs in *raldh2-/-* mouse embryos at E8.5. By combining mirWalk3.0 target prediction algorithms (for 3'UTR, 5'UTR, and CDS regions), complex network analysis, and DAVID gene ontology analysis, we identified and described the signaling pathways putatively modulated by RA-microRNAs interactions during early organogenesis stages of mouse embryo development.

Our work provides a conceptual framework for future, more complex investigations of microRNAs' role as mediators of RA signaling during mouse embryogenesis.

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

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