Meta-analyses to Identify Master Regulatory Elements with Potential to Induce a Pre-implantation State in Human Endometrial Cells in vitro

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Aim: To identify candidate microRNAs (miRNAs) or genes with potential to induce endometrial receptivity with different methods of meta-analyses Materials and Methods: Chapter 1: Partial correlation network between miRNAs was inferred from the miRNA microarray dataset (accession: E-GEOD-34435) of 7 biopsy samples. Chapter 2: Association scores between significantly changed miRNAs and genes from multiple previous literatures, computed as the product of TargetScan prediction cwc score and normalized inverses of aggregated ranks of miRNAs and genes, were used to build a network model. Network analyses specifically PageRank centrality were performed to identify important regulatory elements. Chapter 3: Gene expression landscape of unciliated endometrial epithelial cells was portrayed by a self-organizing map (SOM) neural network using a single-cell RNA sequencing dataset (accession: GSE111976) and important genes/metagenes were identified by autoencoder representation. Results: Partial correlation analysis identified hsa-miR-30d as one of the important miRNAs and its potential role was also confirmed by the analysis of the rank-target association score network. Transcriptional landscape further demonstrates that downregulation of direct targets of hsa-miR-30d can infer upregulation of receptivity-related genes such as DKK.

Discussion: We have shown that 3 different methods of meta-analyses can identify similar important regulatory elements including miRNAs. Furthermore, our transcriptomic landscape portrayal can also be used for different research questions such as validation of drug candidates for endometriosis.