

Integrated Transcriptomic and Regulatory Network Analysis Identifies Candidate Molecular Signatures Associated with Recurrent Implantation Failure

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Background: Recurrent implantation failure (RIF) is a major challenge in reproductive medicine and is thought to involve complex alterations in endometrial receptivity, cellular signaling, and gene regulation. Transcriptomic profiling of endometrial tissue may help identify molecular signatures associated with implantation failure. This study aimed to identify differentially expressed genes and investigate their functional, network, and transcriptional regulatory characteristics in RIF.

Methods: The publicly available endometrial transcriptomic dataset GSE111974 was obtained from the Gene Expression Omnibus (GEO) database. The dataset includes 24 endometrial samples from women with recurrent implantation failure and 24 fertile controls. Differential expression analysis was performed using GEO2R based on the limma framework. Multiple-testing correction was applied using the Benjamini–Hochberg method, and adjusted $P < 0.05$ was considered statistically significant. Significant genes were subsequently subjected to Gene Ontology (GO)-based functional characterization and protein–protein interaction network analysis. Network organization and potential molecular modules were explored using CytoCluster. Promoter regions of selected differentially expressed genes were further analyzed for potential regulatory motifs, with motif similarity and functional annotation assessed using Tomtom and GOMO.

Results: Differential expression analysis identified 714 significantly altered probes/features between RIF and fertile control endometrial samples. These alterations included both upregulated and downregulated expression patterns. Functional and network-based analyses suggested that the identified molecular signature was distributed across multiple biological processes and interaction modules. Promoter-level analysis further indicated potentially shared regulatory elements among selected differentially expressed genes.

Conclusion: Integrated analysis of GSE111974 revealed distinct endometrial transcriptional alterations associated with recurrent implantation failure. Combining differential expression, functional annotation, network clustering, and promoter regulatory analysis may provide complementary insight into molecular mechanisms underlying impaired implantation and may help prioritize candidate biomarkers for further validation.

Keywords: Recurrent implantation failure; Endometrial receptivity; Bioinformatics