

2nd GLOBAL CONFERENCE ON REPRODUCTION, FERTILITY AND GYNECOLOGY

April 29-30, 2025 | VIENNA, AUSTRIA



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Role of Hyaluronic Acid Metabolism in Endometrial Receptivity: Insights from RNAseq and Cellular Models

Abstract:

Despite long-term research, the percentage of successfully implanted embryos during in vitro fertilization (IVF) process stays low (ca. 30%) creating a significant number of patients with so called non-receptive endometrium pathological condition. The extracellular matrix (ECM) of the endometrium, the initial interface between the embryo and the endometrial lining, may play a crucial role in embryo implantation. This matrix contains various adhesive molecules that facilitate temporary adhesion, allowing subsequent biological processes to support implantation. Hyaluronic acid (HA), a key ECM component, has been identified as critical in this interaction. This study investigates the role of HA metabolism in endometrial receptivity by analyzing RNA sequencing (RNAseq) datasets from the GEO database. We utilized two endometrial epithelial cell lines as models of receptive and non-receptive endometria: RL95-2 cells, which are moderately differentiated and resemble luminal epithelium in a receptive state, and AN3CA cells, which are poorly differentiated and resemble glandular, thus non-receptive endometrium. Through PCR, proteomics, immunohistochemistry (IHC), and flow cytometry, we assessed differences in HA metabolism between these cell lines. We compared datasets from GEO database of endometrial samples from healthy women with successful pregnancies to those with repeated IVF failures, revealing significant downregulation of HA metabolism in the latter group. The results from in vitro experiments indicated alterations in HA-related gene expression and protein levels, consistent with the differential HA gene expression observed in human endometrial samples. These findings suggest that impaired HA metabolism may contribute to the non-receptive state of the endometrium, providing a potential target for enhancing implantation success in assisted reproduction techniques (ART).

Keywords: endometrium, receptivity, hyaluronic acid, extracellular matrix

Biography :

I am a PhD student focused on female infertility related to non-receptive endometrium. With a bachelor's degree in molecular biology and a master's in immunology, I investigate the mechanisms of endometrial receptivity at the cellular level. Utilizing diverse in vitro methods, my research aims to uncover the underlying factors that contribute to infertility, ultimately seeking to enhance our understanding and treatment of this critical issue.