



Molecular characterization of corona radiata cells from patients with diminished ovarian reserve using microarray and microfluidic-based gene expression profiling

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Résumé en anglais

BACKGROUND: Diminished ovarian reserve (DOR) is one of the causes of infertility in young women. In this prospective study, gene expression profiling (GEP) of corona radiata cells (CRC) was performed to identify genes deregulated in DOR patients. **METHODS:** Microarray-based GEP of CRC isolated from eight women undergoing IVF was performed to identify genes differentially expressed between patients with normal ovarian reserve and DOR patients. Microfluidic-based quantitative RT-PCR assays were used to validate selected transcripts on 40 independent patients. A principal component analysis was used to identify more homogeneous subgroups of DOR patients. In silico analyses focusing on cis-regulation were performed to refine the interactions between patient's biological characteristics and their GEP. **RESULTS:** Forty-eight transcripts were differentially expressed, including CXXC finger protein 5 (CXXC5), forkhead box C1 (FOXC1) (down-regulated in DOR) as well as connective tissue growth factor (CTGF), follistatin-like 3 (FSTL3), prostaglandin-endoperoxide synthase 2 (PTGS2) and suppressor of cytokine signaling 2 (SOCS2) (up-regulated in DOR). According to these transcripts, two DOR patients' subgroups (DOR Gr1 and Gr2) were identified. In DOR Gr2 patients, C-terminal domain 2 (CITED2), CTGF, growth arrest-specific 1 (GAS1), insulin receptor substrate 2 (IRS2), PTGS2, SOCS2 and Versican (VCAN) were expressed at significantly higher levels and CXXC5, FOXC1, guanylate-binding protein 2 (GBP2) and zinc finger MIZ-domain containing 1 (ZMIZ1) at significantly lower levels. Higher baseline estradiol (E(2)) levels were observed in DOR Gr2 patients ($P < 0.006$). The in silico analyses suggested that all 11 genes differentially expressed between DOR Gr1 and DOR Gr2 subgroups could be transcriptional targets of estrogen. **CONCLUSIONS:** Despite small sample size limitations, 12 genes deregulated in the CRC of DOR patients were identified, which could be involved in DOR pathogenesis. A DOR patient's subgroup with high baseline E(2) levels and deregulated estrogen-responsive genes was also identified.

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