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— From Innovation to Impact —

Session PO3-11c - Reproductive Biology III

Add To Itinerary

S-247 - Transcriptomic Changes and Paracrine Factors Involved in Ovarian Rejuvenation Induced by Stem Cell.

March 16, 2019, 8:00 AM - 10:00 AM | Hall Maillot

Categories
+11.3 - Basic Reproductive Biology: Ovarian Biology, Reproductive Aging

Keywords
Stem cells,ovarian rejuvenation,paracrine signaling

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Abstract

Introduction: Human bone marrow-derived stem cells (BMDSC) induced tissue regeneration and fertility rescue in mouse and human damaged ovaries. In fact, promoted follicular growth to the secondary stage together with enhanced ovarian stroma proliferation and blood vessel formation in xenografted ovarian cortex (OC) from Poor Responder (PR) patients. However, the underlying mechanisms remained unknown. We aimed to investigate transcriptomic changes and factors implicated in follicular rescue induced by stem cells in OC from PR women.

Methods: OC from PR were grafted into ovariectomized SCID mice. A week later, animals received a tail vein injection of PBS (Control), $1x10^6$ human BMDSC or $3x10^5$CD133+ selected cells. On day 7 (D7) and D14 after stem cell infusion, ovarian grafts were recovered. RNA was then isolated, pooled and analyzed by three RT^2 Profiler PCR Arrays Qiagen including cell differentiation/survival, angiogenic and growth factors. Only good quality genes in all comparisons were considered. Principal component analysis (PCA) was done in R software and functional interpretation with KEGG and GeneCards databases.

Results: When transcriptomic profile was analyzed, the PCA showed that experimental conditions were clearly separated by both the time (principal component 1 (PC1): 66.8%) and the received treatment (PC2: 15.4%) from a total of 100 good quality genes. A global downregulation was induced by both BMDSC and CD133 treatments on day 7. Nevertheless, on day 14 BMDSC induced the upregulation of 64% of the considered genes and CD133 of the 37%, underlining higher regenerative properties of BMDSC. Interestingly, most common genes between treatments were PI3K pathway´s genes and stem cell secreted factors such TIMP1 and TIMP2. Twenty-nine genes were exclusively upregulated by BMDSC, as KITLG (fold change, FC:8.8), TIMP3 (FC:4.3) and THBS1 (FC:2.8).

Conclusion: Stem cell infusion induced transcriptomic changes in genes related to follicular recruitment, cell differentiation, survival and vascularization according to the histological findings previously described by our group. Our results suggested that these paracrine factors could have a key role in the positive ovarian effects induced by stem cell infusion, but further validation is needed prior to its clinical application in women with impaired ovarian reserve.
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