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P-422 Maternal age affects angiogenic factors and insulin signaling pathway of human cumulus cells isolated from mature MII oocyte

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Abstract

Study question

Quality and developmental potential of oocytes decline with patient's age. Is gene expression in cumulus cells (CCs) from mature metaphase II oocytes altered as well?

Summary answer

CCs from patients (> 30 years) displayed differences in the angiogenic factors and insulin signaling pathway compared with CCs collected from patients (<30 years).

What is known already

The impact of maternal aging on the energy metabolism and post-transcriptional processes of human CCs were previously reported. However, little is known about the angiogenic factors and insulin signaling pathway according to age.

Study design, size, duration

This study includes 43 CCs isolated from mature MII oocytes collected from patients aged <30 years and 42 CCs from patients aged >30 years. Both groups of CCs were obtained from patients who underwent COS for ICSI (Period between 2010 and 2011).

Participants/materials, setting, methods

CCs from each MII oocyte were analyzed individually using whole genome U133 Plus 2.0 GeneChip Affymetrix microarrays. Significance analysis of microarray was used to analyze the array data according to age of patients with 1.5-fold cut-off and false discovery rate (FDR <5%). Validation was performed by RT-qPCR.

Main results and the role of chance

370 genes were differentially expressed (FC >1.5, FDR <0.05) between the two groups according to age. In CCs collected from patients > 30 years, the angiogenic factors including *SPP1* (4.2, p= 0.0001) and chemokine genes *CCL2* (2.9, p= 0.003), *CCL20* (2.3, p= 0.009), *CXCL2* (2.3, p= 0.04) and *CXCL5* (1.9, p= 0.03), which is known to play on important role in the human pre-ovulatory and oocyte competence, were down-regulated. Conversely, genes related to insulin signaling pathway, such as *INSR* (x2.3, p= 0.0001), *IGFBP3* (1.8, p= 0.0001), *IGFBP5* (1.7, p= 0.0001) and *IRS1* (1.7, p= 0.002) were up-regulated in CCs for patients > 30 years. Interestingly, a set of transcriptional genes involved in particular stress responses were preferentially expressed in CC-collected from patients > 30 years. Among these genes *MSRB3* (1.8, FDR = 0.0001) plays a protective role during oxidative stress.

Limitations, reason for caution

Further investigations with large number of patients are needed to confirm these results.

Wider implications of the findings

This study reveals that the expression of genes involved in angiogenic factors and insulin signaling pathway are affected in CCs with maternal age and probably explain why there is an increase in oocyte aneuploidy with age due to oxidative stress.

Study funding/competing interest(s)

Ferring supported the study but had no influence on the study design and was not involved in the analysis of the results. There were no competing interests.

Trial registration number

not applicable

Related Articles

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The Journal of Clinical Endocrinology & Metabolism 2019; 104(5):1667–1676.

Presence of aggregates of smooth endoplasmic reticulum in MII oocytes affects oocyte competence : molecular-based evidence
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Altered gene expression profile in cumulus cells isolated from mature MII oocytes from patients with polycystic ovary syndrome : P-498
Human Reproduction 2012; 27:ii302–ii337.

A pre-in vitro maturation medium containing cumulus oocyte complex ligand-receptor signaling molecules maintains meiotic arrest, supports the cumulus oocyte complex and improves oocyte developmental competence
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