ANTIOXIDANT GENE EXPRESSION OF PEROXIREDOXIN DECREASES IN GRANULOSE CELLS FROM OOCYTES OF YOUNG WOMEN WITH LOW OVARIAN RESERVE

***Rocío Nuñez-Calonge,[1] Leonor Ortega,[1] Susana Cortes,[1] Lisa Rancan,[2] Elena Vara,[2] Pedro Caballero Peregrin,[1] Jesús Fernandez-Tresguerres[3]**

1. Clínica Tambre, Madrid, Spain
2. Departamento de Bioquímica y Biología Molecular III, Universidad Complutense, Madrid, Spain
3. Departamento de Fisiología, Universidad Complutense, Madrid, Spain
**Correspondence to rocio@clinicatambre.com*

Disclosure: The authors have declared no conflicts of interest.
Citation: EMJ Repro Health. 2017;3[1]:XX-XX. Abstract Review No. ARXX.

Keywords: Oxidative stress, low ovarian reserve, peroxiredoxin (PRDX), granulose cells (GC).

INTRODUCTION

Recent studies carried out by our team have shown that an increase in oxidative stress may have a negative impact on ovarian response.[1] Peroxiredoxins (PRDX), a family of peroxidases, are associated with various biological processes such as the detoxification of oxidants and cell apoptosis.[2] The latest studies have suggested that *PRDX2*, *PRDX3*, and *PRDX4* have the ability to protect against oxidative stress and apoptosis.[3] *PRDX1* may play an important role in the regulation of cell signalling pathways induced by reactive oxygen species, whereas *PRDX5* would act as a scavenger.[4] Nevertheless, little attention has been given to the role of *PRDX* in female infertility.

OBJECTIVE

The aim of this work was to investigate gene expression of *PRDX* (1–6) in granulose cells (GC) and cumulus cells (CC) from peri-ovulatory follicles of young women who experienced a low response in controlled ovarian stimulation cycles (COH), when compared with fertile donors from the same age cohort.

MATERIALS AND METHODS

This prospective study compared the mRNA expression of *PRDX* (1–6) and caspase 3 in 56 oocyte-cumulus and 62 oocyte-granulose complexes retrieved from six healthy, fertile oocyte donors and five patients (≤5 oocytes retrieved) after gonadotropic stimulation from July–December 2016. All study participants were <35 years of age and stimulated with the same protocol (follicle-stimulating hormone receptor and triggering with gonadotropin-releasing hormone analogues). mRNA was extracted using the TaqMan® Gene Expression Cells-to-CT Kit (AM1729, Applied Biosystems, California, USA) and mRNA expression of *PRDX* genes and endogenous controls were measured by quantitative reverse transcription polymerase chain reaction (qRT-PCR) using TaqMan probes. No parametric tests were used to identify any significant differences between patients and healthy donors. Statistical significance was set at $p<0.05$.

RESULTS

Following this study, we found that *PRDX1*, *PRDX2*, *PRDX3*, *PRDX4*, *PRDX5*, and *PRDX6* are expressed in GC and CC. The results obtained from comparative RT-PCR analysis revealed that the mean relative levels of mRNA coding for *PRDX2*, *PRDX3*, *PRDX4*, and *PRDX6* were significantly decreased in GC from women with low response in COH compared with healthy oocyte donors (*PRDX2* p=0.03; *PRDX3* p=0.022; *PRDX4* p=0.014; *PRDX6* p=0.014). mRNA expression of both *PRX1* and *PRX5* was much stronger in GC from the patient group compared with the expression observed in GC from the donor group (*PRDX1* p=0.05; *PRDX5* p=0.02). Also, an increase of caspase-3 expression in GC ($p<0.001$) was observed in the patient group, compared to the donor group. No significant differences were found in the levels of mRNA coding for *PRDX* (1–6) and caspase-3 in CC from young women with low response compared with oocyte donors.

CONCLUSIONS

From our study, we can conclude that *PRDX* are differentially expressed in GC and CC. Our results suggest a lower antioxidant capacity and increased apoptosis level in GC of women with low response to COH compared with fertile donors, as well as a role for PRDX in human GC function and in the pathogenesis of low ovarian reserve in women undergoing infertility treatment with COH-*in vitro* fertilisation (IVF). These results suggest that antioxidant capabilities are diminished during low ovarian response, leading to an increase in oxidative damage in the ovary in a similar way to age-related oxidative damage. These findings could lead to the development of new therapeutic strategies for the treatment of low ovarian reserve.

REFERENCES

1. Núñez-Calonge R et al. Oxidative stress in follicular fluid of young women with low response compared with fertile oocyte donors. Reprod BioMed Online. 2016;32(4):446-56.
2. Rhee S et al. Peroxiredoxins: a historical overview and speculative preview of novel mechanisms and emerging concepts in cell signaling. Free Radic Biol Med. 2005:38(12): 1543-52.
3. Fujii J, Ikeda Y. Advances in our understanding of peroxiredoxin, a multifunctional, mammalian redox protein. Redox Rep. 2002;7(3):123-30.
4. Ishii T, Yanagawa T. Stress-induced peroxiredoxins. Subcell Biochem. 2007;44:375-84.