Opinion

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Endoplasmic reticulum stress and ovarian failure

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The endoplasmic reticulum (ER) as a unique highly well-structured organelle within eukaryotic cells plays important roles in several specific cellular functions including protein synthesis, folding and transport, lipid trafficking and metabolism and Ca^{2+} storage.[1-3] Accumulation of unfolded or misfolded proteins in the ER lumen due to several physiological or pathological conditions including hypoxia, ischemia/reperfusion injuries, neurodegeneration, viral infections, glucose deprivation and abnormal Ca^{2+} regulation as well as inflammation and oxidative stress can lead to induction of ER stress.[4-7] Additionally, a series of cytoprotective intracellular signaling pathways known as unfolded protein response (UPR) will be activated by cells to combat with ER stress and reorganize ER homeostasis which can also cause cellular dysfunctions and trigger cell death.[8]

The ER homeostasis plays vital roles in ovarian folliculogenesis, cumulus cells survival, cumulus-oocyte complex interactions and oocyte quality as well as pre-implantation embryo development and implantation and ER stress-induced disruptions in ER homeostasis can lead to several pathologies that negatively impact on female fertility.[9]

It is well documented that oocyte growth and granulosa cells proliferation in the ovarian tissue bring about hypoxic conditions resulting in ER dysfunctions and eventually ER stress and UPR.[10] Accordingly, it has been shown that ovarian granulosa cell apoptosis during early follicular atresia is associated with ER stress.[11] Further, previous reports have indicated that ER stress and UPR are critical causative factors of pro-fibrotic remodeling in tissue fibrosis.[12-14] and ER stress in granulosa cells of patients with polycystic ovary syndrome contributes to the induction of pro-fibrotic growth factors during ovarian fibrosis.[14]

Taken together, it seems that ER stress can cause ovarian failure and subsequent fertility impairments.[15] probably through induction of tissue fibrosis, oxidative stress and inflammation (Figure 1). Thus, safe ER stress inhibitors should be considered in the therapeutic strategies for ovarian disorders treatment to promote female reproductive health.

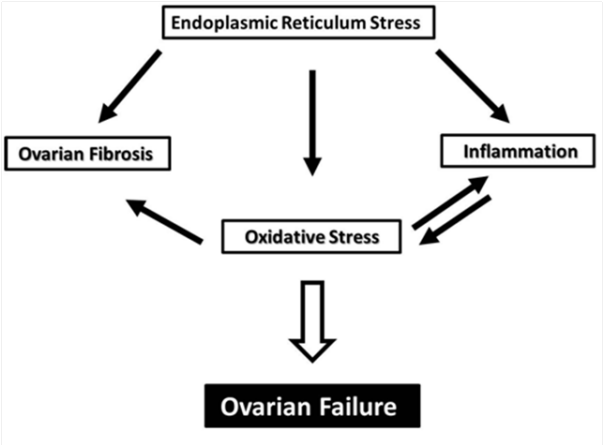

Figure 1 Possible mechanisms of endoplasmic reticulum stress-induced ovarian failure.

Acknowledgments

None.

Conflicts of interest

None.

References

1. Schroder M, Kaufman RJ ER stress and the unfolded protein response. *Mutat Res*. 2005; 569(1–2):29–63.
2. Duan XQ, Li YH, Zhang XY, Zhao ZT, Wang Y, et al. Mechanisms of intracellular calcium homeostasis in MC3T3–E1 cells and bone tissues of Sprague–Dawley rats exposed to fluoride. *Biol Trace Elem Res*. 2016 ; 170(2) 331–339.
3. Xu Y, Wang C, Su J, Xie Q, Ma L, et al. Tolerance to endoplasmic reticulum stress mediates cisplatin resistance in human ovarian cancer cells by maintaining endoplasmic reticulum and mitochondrial homeostasis. *Oncol Rep*. 2015; 34(6):3051–3060.
4. Marjon PL, Bobrovnikova–Marjon EV, Abcouwer SF Expression of the pro–angiogenic factors vascular endothelial growth factor and interleukin–8/CXCL8 by human breast carcinomas is responsive to nutrient deprivation and endoplasmic reticulum stress. *Mol Cancer*. 2004; 3: 4.
5. Xu C, Bailly–Maitre B, Reed JC Endoplasmic reticulum stress: cell life and death decisions. *J Clin Invest*. 2005; 115(10): 2656–2664.
6. Zhou Y, Sun P, Wang T, Chen K, Zhu W, et al. Inhibition of calcium influx reduces dysfunction and apoptosis in lipotoxic pancreatic β–Cells via regulation of endoplasmic reticulum stress. *PLoS One*. 2015; 10(7): e0132411.
7. Gao Y, Jia P, Shu W, Jia D The protective effect of lycopene on hypoxia/reoxygenation–induced endoplasmic reticulum stress in H9C2 cardiomyocytes. *Eur J Pharmaco*. 2016;l 774:71–79.
8. Ron D, Walter P Signal integration in the endoplasmic reticulum unfolded protein response. *Nat Rev Mol Cell Biol*. 2007; 8(7): 519–529.
9. Guzel E, Arlier S, Guzeloglu–Kayisli O, Tabak MS, Ekiz T, et al. Endoplasmic reticulum stress and homeostasis in reproductive physiology and pathology. *Int J Mol Sc*. 2017;i 18(4).

10. Harada M, Nose E, Takahashi N, Hirota Y, Hirata T, et al. Evidence of the activation of unfolded protein response in granulosa and cumulus cells during follicular growth and maturation. *Gynecol Endocrinol.* 2015; 31(10): 783–787.

11. Lin P, Yang Y, Li X, Chen F, Cui C, et al. Endoplasmic reticulum stress is involved in granulosa cell apoptosis during follicular atresia in goat ovaries. *Mol Reprod Dev*. 2012; 79(6): 423–432.

12. Lenna S, Trojanowska M The role of endoplasmic reticulum stress and the unfolded protein response in fibrosis. *Curr Opin Rheumato*. 2012;l 24(6): 663–668.

13. Tanjore H, Lawson WE, Blackwell TS Endoplasmic reticulum stress as a pro–fibrotic stimulus. *Biochim Biophys Acta*. 2013; 1832(7): 940–947.

14. Takahashi N, Harada M, Hirota Y, Nose E, Azhary JM, et al. Activation of endoplasmic reticulum stress in granulosa cells from patients with polycystic ovary syndrome contributes to ovarian fibrosis. *Sci Rep*. 2017; 7(1):10824.

15. Galgani M, Insabato L, Calì G, Della Gatta AN, Mirra P, et al. Regulatory T cells, inflammation, and endoplasmic reticulum stress in women with defective endometrial receptivity. *Fertil Steril*. 2015;103(6): 1579e1–1586.e1.

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