The role of mitochondria in human reproduction: mitochondria in endometriosis

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Endometriosis is a common disorder presented with infertility, and often affects young women in the childbearing age. The etiology and pathogenesis of this important disease are poorly understood; it is defined as an ectopic location for endometrial tissue outside of the uterine cavity. It still remains an open question as to what extent the peritoneal environment influences the establishment and/or progression of endometriosis. In our study, the significantly higher amounts of oxidative damage were detected in endometriotic lesions than in controlled normal endometrium, including mitochondrial DNA (mtDNA) rearrangement, 8-OH-deoxyguanosine (8-OH-dG), and lipoperoxide contents. Our central hypothesis proposes that the declined efficacy in the maintenace of antioxidant capacity and mitochondrial genome integrity might be associated with the pathogenesis of endometriosis. Recently, mitochondrial estrogen receptor (mtER-β) and p53 was found in the endometriotic tissues and the putative function is unclear. Our studies showed that the proportion of ER-β inside mitochondria and the mtDNA copy number were increased in the endometriotic tissues. The mtER-β and mtDNA interaction was found to be augmented in the endometriotic tisssue. Additionally, the primary endometriotic cells harbored less normal p53 mRNA segments and the dimmer type of p53 after gonadotropin releasing hormone (GnRH) agonist treatment. In vitro assay showed that diarylpropionitrile (DPN, an mtERβ agonist) could promote mitochondrial biogenesis and attenuate the mitochondrial dysfunction and reactive oxygen species generation in the endometriotic cells. Meanwhile, the mitochondrial p53 was increased after treated with E2 or DPN. We speculate that mtER-β can promotes the endometriotic cell survival by enhancing mitochondrial respiration capacity and changing its susceptibility to apoptosis, and p53 can interact with mtDNA to maintain mitochondrial DNA integrity in the endometrial cells. The regulation of mitochondrial ERβ and p53 needs tightly control and the disruption of ERβ and p53 function may contribute to the pathogenesis and tumoriogenesis of endometriosis. The results will unravel the relationship between the ER and p53 in mitochondria, which may promote the new directed therapies of endometriosis and tumor formation.