**Stem Cell Exosomes and Nrf2 Signaling: A Novel Paradigm for Therapeutic Intervention in premature ovarian insufficiency**

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Premature ovarian insufficiency (POI) is a gynecological endocrine disease marked by impaired ovarian function occurring before the age of 40. POI is characterized by a change in menstrual function, low levels of estrogen and elevated gonadotropin levels. These factors give rise to a range of clinical manifestations including infertility, amenorrhea and perimenopausal symptoms. Oxidative stress is a critical factor in the induction of lipid peroxidation, affecting both the structure and function. It leads to alterations in proteins and DNA, ultimately promoting apoptosis, which plays an important role in the pathogenesis of premature ovarian failure. Nuclear factor erythroid 2–related factor 2 (Nrf2), a transcription factor, is able to mitigate damage caused by oxidative stress through various signaling pathways. The positive effects resulting from the activation of the Nrf2 signaling pathway in different disorders have been documented in various types of literature. Over past decade, positive results have been observed in restoration of ovarian function in POI models using different types of stem cells-exosomes. Exosomes are nano-sized membrane extracellular vesicles which can be released from various types of cells. Exosomes originating from inflammatory or injury cells can have detrimental effects on recipient cells, while exosomes derived from stem cells not only facilitate the repair and regeneration of damaged tissues but also inhibit inflammation and provide protective effects against various diseases, suggesting they may serve as an alternative strategyof stem cells transplantation. Exosomes have a fundamental role in communication between cells, through the transfer of proteins, bioactive lipids and nucleic acids. Studies have confirmed that exosomes derived from stem cells could act as Nrf2 effective agonists. However, limited studies have explored the Nrf2 role in therapeutic effects of stem cell-derived exosomes in POI. This review provides a comprehensive overview of the existing knowledge concerning the role of Nrf2 signaling pathways in the effects exerted by stem cell exosomes in POI.

**Keywords:** Premature ovarian insufficiency; Nrf2; Exosomes; Stem cells