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• **REVIEW** •

Advantages and limitations of the parthenogenetic embryonic stem cells in cell therapy

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Parthenogenetic embryonic stem cells (pESCs), as "seed cells" for regenerative medicine, are an effective way to build patient-specific pluripotent stem cells, due to the fact that characteristics of self-renewal and pluripotent are similar to embryonic stem cells (ESCs). Parthenogenetic activation can be performed at meiosis I or meiosis II describing the embryos with distinct patterns of homozygosity and heterozygosity. Heterozygous pESCs are expected to be used for autologous transplantation, while homozygous pESCs enable to be used for allogeneic gene therapy in theory but is hampered by immunological barriers defined by the recognition of natural killer (NK) cells. In this review, we describe the mechanism of deriving heterozygous and homozygous pESCs, and summarize the advantages and limitations of pESCs in the area of cell therapy.

Key words: parthenogenetic embryonic stem cells (pESCs); heterozygous; homozygous; advantages and limitations; cell therapy

Parthenogenesis is the asexual reproduction process by which an oocyte develops into an embryo without fertilization[1], which is commonly found in lower animals such as insects and amphibians but not in mammalian that can only be achieved by artificial activation. The oocytes can be developed into parthenogenetic blastocysts by the chemical, physical or combined activation method. Its mechanism is to increase the intracellular Ca^{2+} level and reduce the activity of maturation promoting factor (MPF) and cytostatic factor (CSF) to simulate the normal fertilization process, triggering the resumption of meiosis *in vitro* and

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parthenogenetic development. Parthenogenetic embryonic stem cells (pESCs), deriving from the inner cell mass (ICM) of parthenogenetic blastocysts, possess the characters of infinite proliferation and self-renewal, and retain ability to differentiate into one or more specialized type of cell or tissue. In addition, there is no requirement to destroy the living embryo and avoid the ethical controversy. Along with these special properties, pESCs are used as the "seed cells" for regenerative medicine, allowing the generation of sufficient amount of functional cells that could supply remedy for many incurable diseases in the future.

Currently, pESCs have obtained significant achievements for the regenerative medicine. Derivation of human pESC lines by chemical activation was first reported by Revazova et al. in 2007[2]. Recent Study showed that human pESCs could induce the formation of islet cells and play the hypoglycemic effect[3]; neural stem cells derived from pESCs were transplanted into the animal model of Parkinson's disease resulting in the enhancement of dopamine levels and no any adverse reaction[4]. Parthenogenetic activation can be conducted at meiosis I or meiosis II generating the various patterns of homozygosity and heterozygosity in embryos: heterozygous pESCs hold great promise for autologous transplantation due to the feature that genetic material is identical to oocytes donor, while homozygous pESCs is theoretically supposed to be used for allogeneic gene therapy but is hampered by immunological barriers defined by the recognition of natural killer (NK) cells. In this review, we summarized the mechanism of deriving different types of pESCs, and elaborated the potential advantages and limitations of pESCs in the area of cell therapy. In order to anticipate the future possibility of pESCs for histocompatible cells and tissue for clinical therapy.

The unique advantages of pESCs in gene therapy

The pluripotent property and establishment rate of pESCs

pESCs still show many unique advantages when comparing with other types of pluripotent stem cells (PSC). pESCs are similar to normal fertilized ESCs in the aspect of growth and cultivation with the characteristics of self-renewal and pluripotency. In 1995, it reported a rare phenomenon that a 14-year-old boy carried parthenogenetic cells. Genetic analysis detected chimerism in his skin fibroblasts and peripheral blood leukocytes consisting of normal biparental (46,XY) and parthenogenetic (46,XX) cells, which proved that parthenogenetic cells can promote the development of organs and perform its normal physiological function[5]. Similarly, mouse pESCs participate in the formation of most tissue except for skeletal muscle and testis when injected into another mouse blastocyst and produced the chimeric mice eventually[6]. The experiment illustrated that the mouse pESCs have multidirectional differentiation potential.

Another advantage is that pESCs have a wide range of sources and are easy-to-get.