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Melatonin enhances autologous adipose-derived stem cells to improve mouse ovarian function in relation to the SIRT6/NF-κB pathway

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Abstract

Background: Premature ovarian insufficiency (POI) is the main cause of female infertility. Adipose-derived stem cells (ADSCs) are ideal candidates for the treatment of POI. However, some deficient biological characteristics of ADSCs limit their utility. This study investigated whether melatonin (MLT)-pretreated autologous ADSCs were superior to ADSCs alone in the treatment of the POI mouse model.

Methods: Autologous ADSCs were isolated and cultured in MLT-containing medium. Surface markers of ADSCs were detected by flow cytometry. To determine the effect of MLT on ADSCs, CCK-8 assay was used to detect ADSCs proliferation and enzyme-linked immunosorbent assay (ELISA) was used to detect the secretion of cytokines. The POI model was established by intraperitoneal injection of cyclophosphamide and busulfan. Then, MLT-pretreated autologous ADSCs were transplanted into mice by intraovarian injection. After 7 days of treatment, ovarian morphology, follicle counts, and sex hormones levels were evaluated by hematoxylin and eosin (H&E) staining and ELISA, and the recovery of fertility was also observed. The expressions of SIRT6 and NF-κB were detected by immunohistochemical (IHC) staining and quantitative real-time polymerase chain reaction (qRT-PCR).

Results: Flow cytometry showed that autologous ADSCs expressed CD90 (99.7%) and CD29 (97.5%). MLT can not only promote the proliferation of ADSCs but also boost their secretory function, especially when ADSCs were pretreated with 5 μM MLT for 3 days, improving the interference effect. After transplantation of autologous ADSCs pretreated with 5 μM MLT, the serum hormone levels and reproductive function were significantly recovered, and the mean counts of primordial follicle increased. At the same time, the expression of SIRT6 was remarkably increased and the expression of NF-κB was significantly decreased in this group.

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