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Induced differentiation of bone marrow mesenchymal stem cells towards retinal ganglion precursor cells

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Retinal ganglion cells can hardly regenerate after apoptosis or necrosis in adult mammalian. Transplantation of retinal ganglion precursor cells provides a potential therapy for these deceases in clinic. To explore the possibility of inducing bone marrow mesenchymal stem cells (BMSC) to differentiate into retinal ganglion precursor cells, coculture of mice BMSC with mice neural retinal precursor cells (RPC) of various developmental stages was engaged. Long-term culture of RPC could be achieved with serum-free neuronal medium consisting of DMEM/F12 plus B27, EGF and bFGF. After attachment, RPC from different embryonic age displayed different differentiation potential. E13.5 RPC stretched out long and thick axon and formed network structure, while E15.5 and E17.5 RPC only showed short and thin axon. BMSC could be amplified using DMEM/F12 medium containing 10% fetal bovine serum. The cells displayed spindle shape before coculture and no expression of Pax6 and Brn3b could be detected by RT-PCR and immunofluorescence. After 3d coculture with E13.5 RPC in neuronal medium, BMSC shifted into neural appearance by displaying neurite. At the same time, expression of Pax6, Brn3b and nestin could be detected by RT-PCR and immunofluorescence. Realtime RT-PCR showed that Pax6 and Brn3b increased by 439 and 70 fold, respectively. Extended coculture with E13.5 RPC for 7d or 14d could not effectively inducing the expression of Pax6 and Brn3b in BMSC. Furthermore, BMSC returned into spindle shape after coculture with E13.5 RPC for 14d. Coculture with E17.5 RPC could also induce BMSC to adopt neural appearance, but Pax6 and Brn3b could not be detected at any time of coculture. These results suggest that coculture with E13.5 RPC for 3d could induce BMSC to differentiate into retinal ganglion precursor - like cells. But the inducing effect doesn't persist, which suggests BMSC may possess a self-feedback regulation to resist differentiation in some degree.

***Key words*:** retinal ganglion cells, bone marrow mesenchymal stem cells, differentiation

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