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Ex vivo generation of germ cells from marrow derived mesenchymal stem cells in rat

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Germ cells must develop along distinct male or female paths to produce the spermatozoa or oocyte required for sexual reproduction. Mesenchymal stem cells (MSCs) have the capacity to transdifferentiate into multilineage cells, such as muscle of mesoderm, lung and liver of endoderm, and brain and skin of ectoderm origin. Here we show that the bone marrow derived stromal cells can transdifferentiate to germ cell-like cells suggesting that bone marrow can be a potential source of germ cells that could sustain sperm/oocyte production. The bone marrow derived cells were characterized using MSC specific markers (CD73, CD90 and CD105) by molecular, immunocytochemistry and FACS analysis and termed them rBM-MSC. These rBM-MSCs were subjected to insitu differentiation into germ cells (GCs) with the help of retinoic acid. Briefly, the semi confluent cells were treated with low glucose DMEM medium with FBS and supplemented with 10-6 M RA for a period of 21 days. At the end of the treatment, the existence of germ-like cells in the cultures were confirmed by assessments of changes in cell morphology, expressions of GC-specific marker genes i.e. Stella and Fregilis by RTPCR, FACS and immunocytochemistry. Further, the differentiated cells also expressed the known molecular markers of spermatogonial stem cells viz c-kit, Stra8, dazl, Daz, Tex18 and Tp2. The study revealed that the mesenchymal stem cells derived from bone marrow have the potentiality to differentiate into germ cells and opens the possibilities for use of these cells in reproductive medicine.

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