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Multipotent Mesenchymal Stromal Cells Derived from the Bone Marrow Transported Over 12 Hours Change Their Main Characteristics

Short Communication

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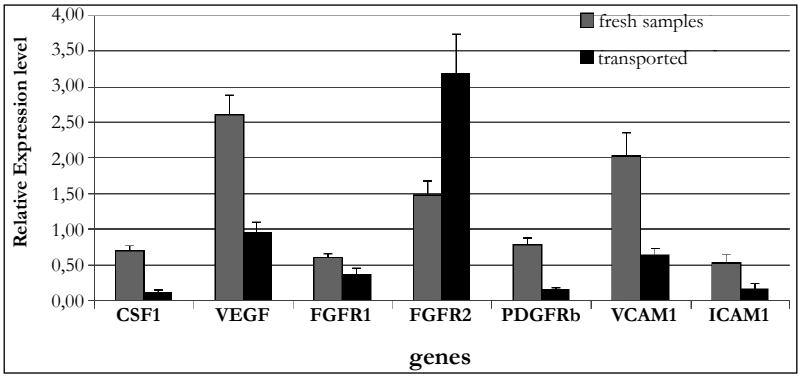
Many investigations have addressed the possibility of using multipotent mesenchymal stromal cells (MSCs) for treatment of various diseases due to their ability for tissue regeneration and unique immunomodulating capacities [1-3]. These stromal cells can be cultivated *in vitro* and represent adult, fibroblast-like cells that can differentiate into tissues of mesodermal origin [4]. Previous studies have attempted to develop the criteria for human MSC eligibility for therapeutic applications [5]. MSCs secrete various cytokines, growth factors and extracellular matrix molecules [4].

A randomized clinicaltrial (ClinicalTrials.gov NCT01941394) of MSCs application for graft versus host disease (GVHD) prophylaxis after allogeneic bone marrow transplantation has been ongoing at the National Research Center for Hematology since 2008 [6]. The trial was approved by a local ethical committee, and informed consent from donors and patients has been obtained according to the Helsinki Declaration. All donor derived MSCs (113 samples) characteristics such as cumulative cell production and relative expression level (REL) of several genes were routinely analyzed. MSCs were cultivated from bone marrow and analyzed as described [7]. Twelve of the bone marrow samples were obtained from unrelated donors. These samples had been transferred to the National Research Center for Hematology at recommended conditions at 4°C [8], a process that required more than 12 hours, usually 14-30 hours. The cumulative cell production of MSCs derived from these samples (N=12) was significantly decreased in comparison with MSCs derived from not transported (fresh, N=101) bone marrow, (5.1 ± 0.6) x 10^6 and (8.0 ± 0.9) x 10^6 per flask for 3 passages, respectively ($p < 0.01$). Dramatic changes in the REL of 7 genes were revealed in MSCs developed from transported bone marrow (Figure). The REL of CSF1, FGFR1 and PDGFRB decreased more than 3-fold ($p < 0.0001$), while those of VEGF, ICAM1 and VCAM1 decreased more than 2-fold ($p < 0.05$). The REL of FGFR2 increased 2-fold ($p < 0.01$). The observed decline in MSC production may be due to the decreased REL of growth factor and receptor genes. Increased expression of FGFR2 did not affect the production of MSCs and possibly was compensatory. Moreover, the concentration of colony-forming units fibroblast (CFU-F) in the bone marrow samples that had been transported dramatically decreased to 1.83±0.76 per 10^6 bone marrow cells ($p < 0.0001$) compared with samples from fresh bone marrow (27.0±2.8). The CFU-F concentration was found to be associated with the MSC growth parameters. The data suggests the decreased growth capacity of MSCs derived from transported bone marrow. At the same time no changes in REL of immunomodulating genes were revealed, that implies

Figure. REL of genes significantly altered in MSCs derived from transported bone marrow samples in comparison with MSCs derived from fresh bone marrow samples.



that such MSCs may be applicable for GVHD prophylaxis. Possible changes in the MSC growth characteristics should be considered for MSCs derived from bone marrow after more than 12 hours of transportation.

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