

Circulating Mesenchymal Stem Cells in Fracture Patients

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INTRODUCTION: A part of mesenchymal stem/ stromal cell (MSCs) population participating in fracture healing can be recruited from distant sites in response to chemotactic factors [1]. Both clinical and experimental studies have suggested that committed osteoblast progenitors circulate in the peripheral blood and home in to sites of fracture repair [2-3]. We report here the presence of pluripotent mesenchymal cells in the systemic circulation of fracture patients.

METHODS: Peripheral blood (PB) samples (20 ml) and bone marrow (BM) aspirates were taken before surgery from 42 patients:

- elderly females (n=19) undergoing cemented semi-arthroplasty for hip fracture (mean age 84 yrs, range 76-95)
- age-matched elderly females (n=10) undergoing cemented total hip arthroplasty (THA) for osteoarthritis (mean age 80 yrs, 75-85)
- younger adults (n=13) undergoing ORIF or nailing for a lower extremity fracture (mean age 37 yrs, 19-60).

Postoperatively, PB samples were collected at 2-4 days and at 6 weeks. Mononuclear cells (MNCs) were isolated by density centrifugation and plastic adherent cells were re-plated for several passages for calculations of population doublings (PD). Osteoblastic and adipogenic differentiation assays were performed using established protocols. Expression pattern of cell surface markers was investigated by immunostaining and FACS analysis (Finnish Red Cross Blood Service).

RESULTS: We found plastic adherent MSCs in peripheral blood samples of 4/19 hip fracture patients and 5/13 lower extremity fracture patients. Circulating MSCs were found 2-4 days post fracture. No MSCs were found in the systemic circulation before or after elective THA surgery. PB derived adherent cells fulfilled the profile of pluripotent MSCs [4] in morphology, colony formation, proliferation through several passages and differentiation into osteoblasts and adipocytes (Fig. 1). There

were no statistical differences for any parameter between BM and PB derived MSCs.

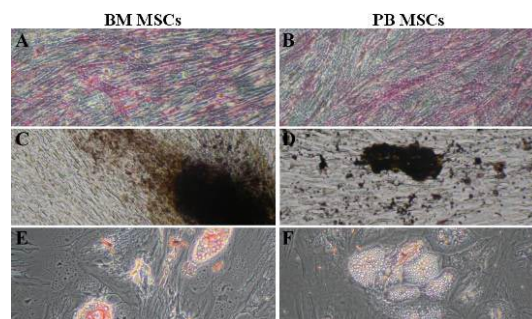


Fig 1. Differentiation of bone marrow (BM) and peripheral blood (PB) derived MSCs. Osteoblastic differentiation demonstrated by ALP staining (A-B) and von Kossa positive mineralized nodules (C-D). Adipocytic differentiation demonstrated by accumulation of lipid droplets (E-F).

Table 1. Detection of MSCs in bone marrow (BM) and systemic circulation (PB)

	BM	PB
Hip fracture surgery	19 (100%)	4 (21%)
Hip OA surgery	10 (100%)	0 (0%)
Lower extremity fracture surgery	13 (100%)	5 (38%)

DISCUSSION & CONCLUSIONS:

Circulating MSCs were not found before or after elective THA, but fracture seems to mobilize MSCs into circulation even in very old patients. The temporary presence of circulating MSCs in response to a fresh fracture is further evidence that these cells may participate in fracture repair.

REFERENCES: ¹Einhorn et al. JBJS Am 2008;90:438-42. ²Eghbali-Fatourehchi et al. NEJM 2005;352:1959-66. ³Shirley et al. J Orthop Res 2005;23(5):1013-21. ⁴Dominici et al. Cytotherapy 2006;8:315-7.

ACKNOWLEDGEMENTS: The study was supported by Academy of Finland and Turku University Hospital (EVO).