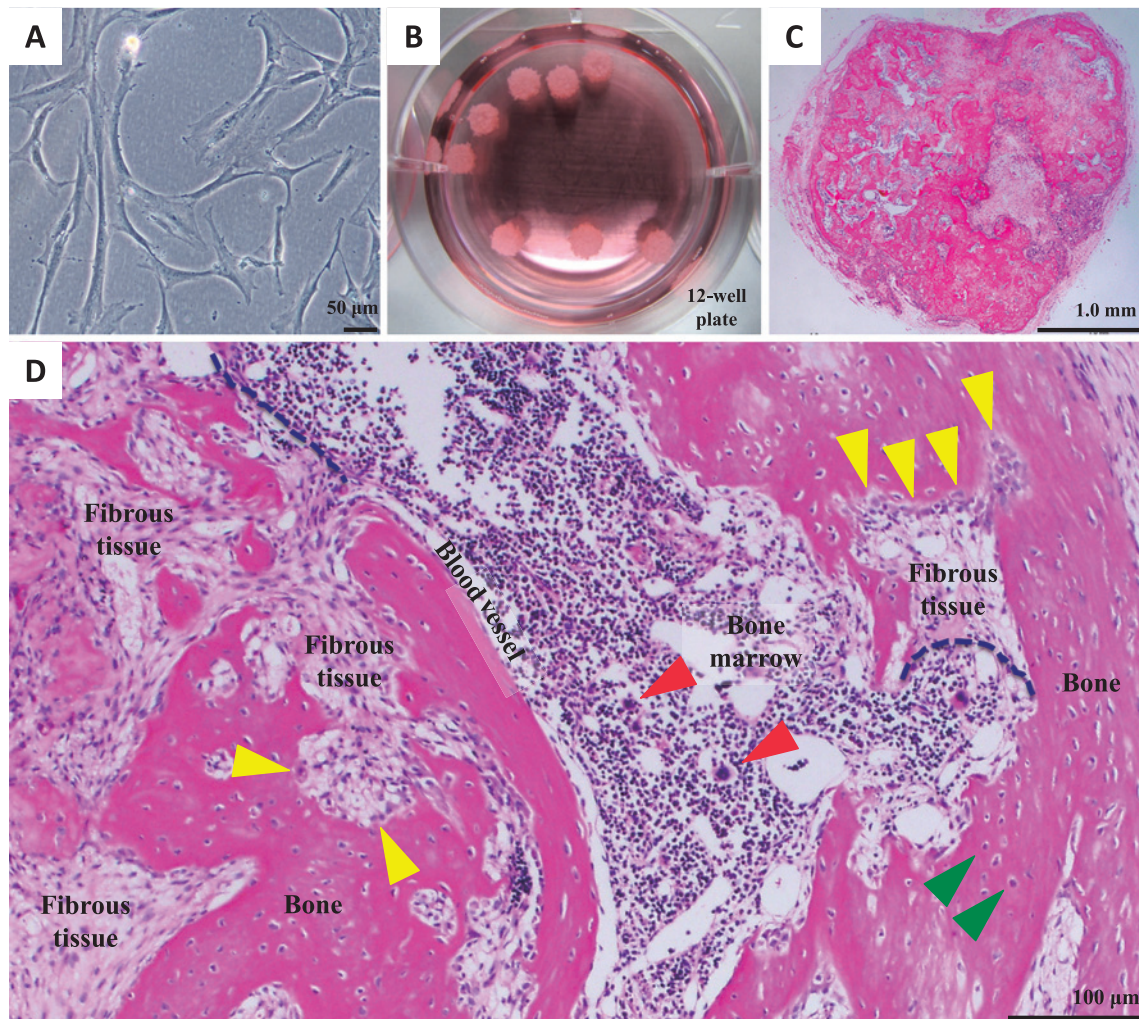


Human Mesenchymal Stromal/Stem Cell-Mediated Bone Marrow Organization



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Mesenchymal stromal/stem cells (MSCs) in bone marrow differentiate into cellular components of the hematopoietic cell niche, including osteogenic cells. A human MSC transplantation into mice (xenotransplantation model) is one of the best available *in vivo* models to recapitulate MSC-mediated bone and bone marrow

organization. In this model, MSCs isolated from bone marrow samples (purchased from AllCells, Emeryville, CA, USA) through the conventional adhesion selection method (BM-MSCs, Fig. A) were mixed with a hydroxyapatite/poly (D, L-lactic-co-glycolic acid) (HA/PLGA) scaffold (Fig. B). Thereafter, BM-MSCs embed-

ded in the HA/PLGA scaffold were implanted into the dorsal surface of 7-to-9-week-old non-obese diabetic/severe combined immunodeficiency mice. The ectopic implants were harvested and evaluated 10 weeks later. Inside the implants, BM-MSCs generated bone and bone marrow structure (Fig. C). Osteoblastic cells lined the bone surface (Fig. D, yellow arrows), and osteocytes (Fig. D, green arrows) were buried in the bone matrix. The bone marrow cavity harboured hematopoietic elements (Fig. D, red arrows). Blood vessels that were connected to fibrous tissue formed along the bone. Bone marrow elements replaced fibrous tissue with apparent borders (Fig. D, blue dotted lines).

In situ hybridization assay to detect the human-specific repetitive *Alu* DNA sequence showed that bone is derived from implanted human BM-MSCs, and bone marrow is derived from recipient hematopoietic cells¹⁾. Bone marrow contains not only cells of multiple lineages, including myeloid, erythroid, and lymphoid cells, but also hematopoietic stem/progenitor cells²⁾. The effects of pharmacological and genetic modifications of BM-MSCs on hematopoietic cell formation can be evaluated following implantation³⁾. This xenotransplantation model is a powerful tool for examining the function of human MSCs in the hematopoietic cell

niche *in vivo*.

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ヒト間葉系幹細胞により構築される骨髄組織

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