Distinct Bone Marrow Sources of Pleiotrophin Control Hematopoietic Stem Cell Maintenance and Regeneration.

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Public Summary:
Bone marrow perivascular cells and vascular cells are essential for blood stem cell maintenance, but the roles of distinct cells during blood stem cell regeneration are less understood. Here we show that perivascular cells and vascular cells dichotomously regulate HSC maintenance and regeneration via secretion of pleiotrophin (PTN). Perivascular cells are the key source of PTN during steady-state blood formation, whereas vascular cells and bone cells are not required sources. Following stress or injury with radiation, PTN expression is increased in bone marrow vascular cells, and PTN - expressing blood vessels increase in the bone marrow. Moreover, bone marrow vascular cells are the key source of PTN necessary for blood stem cell regeneration whereas perivascular cells are not a required source of PTN in this process. These findings reveal complementary regulation of blood stem cell maintenance and regeneration by bone marrow perivascular cells and vascular cells.

Scientific Abstract:
Bone marrow (BM) perivascular stromal cells and vascular endothelial cells (ECs) are essential for hematopoietic stem cell (HSC) maintenance, but the roles of distinct niche compartments during HSC regeneration are less understood. Here we show that Leptin receptor-expressing (LepR+) BM stromal cells and ECs dichotomously regulate HSC maintenance and regeneration via secretion of pleiotrophin (PTN). BM stromal cells are the key source of PTN during steady-state hematopoiesis because its deletion from stromal cells, but not hematopoietic cells, osteoblasts, or ECs, depletes the HSC pool. Following myelosuppressive irradiation, PTN expression is increased in bone marrow endothelial cells (BMECs), and PTN(+) ECs are more frequent in the niche. Moreover, deleting Ptn from ECs impairs HSC regeneration whereas Ptn deletion from BM stromal cells does not. These findings reveal dichotomous and complementary regulation of HSC maintenance and regeneration by BM stromal cells and ECs.