Generation and use of a humanized bone-marrow-ossicle niche for hematopoietic xenotransplantation into mice.

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Public Summary:
Xenotransplantation is frequently used to study normal and malignant hematopoiesis of human cells. However, conventional mouse xenotransplantation models lack essential human-specific bone-marrow (BM)-microenvironment-derived survival, proliferation, and self-renewal signals for engraftment of normal and malignant blood cells. As a consequence, many human leukemias and other hematologic disorders do not robustly engraft in these conventional models. Here, we describe a complete workflow for the generation of humanized ossicles with an accessible BM microenvironment that faithfully recapitulates normal BM niche morphology and function. The ossicles, therefore, allow for accelerated and superior engraftment of primary patient-derived acute myeloid leukemia (AML) and other hematologic malignancies such as myelofibrosis (MF) in mice. The humanized ossicles are formed by in situ differentiation of BM-derived mesenchymal stromal cells (MSCs). Human hematopoietic cells can subsequently be transplanted directly into the ossicle marrow space or by intravenous injection. Using this method, a humanized engraftable BM microenvironment can be formed within 6-10 weeks. Engraftment of human hematopoietic cells can be evaluated by flow cytometry 8-16 weeks after transplantation. This protocol describes a robust and reproducible in vivo methodology for the study of normal and malignant human hematopoiesis in a more physiologic setting.

Scientific Abstract:
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