Age-related defects in B lymphopoiesis underlie the myeloid dominance of adult leukemia.

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Public Summary:
Reduced lymphopoiesis during aging contributes to declines in immunity, but little consideration has been given to its effect on the development of hematologic disease. This report demonstrates that age-related defects in lymphopoiesis underlie the myeloid dominance of adult leukemia. Using a murine model of chronic myeloid leukemia, an adult-onset malignancy that arises from transformation of hematopoietic stem cells by the BCR-ABL(P210) oncogene, we demonstrate that young bone marrow (BM) cells that were transformed with BCR-ABL(P210) initiated both a myeloproliferative disorder (MPD) and B-lymphoid leukemia, whereas BCR-ABL(P210)-transformed old BM cells recapitulated the human disease by inducing an MPD with rare lymphoid involvement. In addition, the lesser severity of MPDs initiated from old BCR-ABL(P210)-transduced BM cells revealed unappreciated defects in aged myeloid progenitors. These data demonstrate that aging affects patterns of leukemogenesis and indicate that the effects of senescence on hematopoiesis are more extensive than previously appreciated.

Scientific Abstract:
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