Hematopoietic stem cell transplantation in immunocompetent hosts without radiation or chemotherapy.

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Public Summary:
Hematopoietic stem cell (HSC) transplantation can cure diverse diseases of the blood system, including hematologic malignancies, anemias, and autoimmune disorders. However, patients must undergo toxic conditioning regimens that use chemotherapy and/or radiation to eliminate host HSCs and enable donor HSC engraftment. Previous studies have shown that anti-c-Kit monoclonal antibodies deplete HSCs from bone marrow niches, allowing donor HSC engraftment in immunodeficient mice. We show that host HSC clearance is dependent on Fc-mediated antibody effector functions, and enhancing effector activity through blockade of CD47, a myeloid-specific immune checkpoint, extends anti-c-Kit conditioning to fully immunocompetent mice. The combined treatment leads to elimination of >99% of host HSCs and robust multilineage blood reconstitution after HSC transplantation. This targeted conditioning regimen that uses only biologic agents has the potential to transform the practice of HSC transplantation and enable its use in a wider spectrum of patients.

Scientific Abstract:
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