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Luteinizing Hormone-Releasing Hormone Enhances T Cell Recovery following Allogeneic Bone Marrow Transplantation[1]

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Posttransplant immunodeficiency, specifically a lack of T cell reconstitution, is a major complication of allogeneic bone marrow transplantation. This immunosuppression results in an increase in morbidity and mortality from infections and very likely contributes to relapse. In this study, we demonstrate that sex steroid ablation using leuprolide acetate, a luteinizing hormone-releasing hormone agonist (LHRHa), increases the number of lymphoid and myeloid progenitor cells in the bone marrow and developing thymocytes in the thymus. Although few differences are observed in the peripheral myeloid compartments, the enhanced thymic reconstitution following LHRHa treatment and allogeneic bone marrow transplantation leads to enhanced peripheral T cell recovery, predominantly in the naive T cell compartment. This results in an increase in T cell function in vivo and in vitro. Graft-versus-host-disease is not exacerbated by LHRHa treatment and graft-versus-tumor activity is maintained. Because LHRHa allows for reversible (and temporary) sex steroid ablation, has a strong safety profile, and has been clinically approved for diseases such as prostate and breast cancer, this drug treatment represents a novel therapeutic approach to reversal of thymic atrophy and enhancement of immunity following immunosuppression.

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[4] Abbreviations used in this paper: BMT, bone marrow transplantation; HSC, hematopoietic stem cell; ERα, estrogen receptor α; LHRH, luteinizing hormone-releasing hormone; BN, bone marrow; GVDH, graft-versus-host disease; GVT, graft-versus-tumor; TCD, T cell depleted; LSK, lineage$^-$Sca-1$^+$c-kit$^+$; CLP, common lymphoid progenitor; TN, triple negative; ETP, early T cell progenitor; KGF, keratinocyte growth factor; NP, 4-hydroxy-3-nitrophenyl; CGG, chicken γ-globulin; DP, double positive; SP, single positive.