CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100469

Project Title:
Improving Cord Blood Expansion and Homing for Patients with Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
Shpall, Elizabeth

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Umbilical cord blood (CB) is used increasingly to restore marrow function in stem cell transplant patients, particularly in minorities lacking appropriately matched bone marrow donors. Two major disadvantages of CB are a low cell dose and a deficit in homing to marrow which contribute to delays in neutrophil and platelet engraftment which combat infection and bleeding, respectively, as well as high rate of complete failure to recover, which is usually fatal. We developed two novel strategies addressing the problem. The 1st is ex-vivo expansion of CB with marrow-derived mesenchymal stem cells (MSC) which function as a surrogate bone marrow niche, providing an enhanced microenvironment for expansion of CB progenitors. The 2nd strategy addresses the homing defect attributed to low levels of CB cell surface molecule fucosylation which is responsible for binding to P- and E-selectins. This binding is a key component of the mechanism by which circulating hematopoietic cells are recruited to the marrow microvasculature. We will augment CB cell surface fucosylation, thus improving homing and engraftment. With our Texas-based corporate partners who will provide unique cGMP grade products and commercialization expertise, novel technologies for CB expansion and homing will be combined to improve overall safety and survival for patients with cancer, thereby enhancing the utility of CB transplantation in Texas and beyond. If the improved expansion and homing strategies proposed in this application are successful, CB transplant (CBT) patient survival will be significantly enhanced. These improvements will broaden the utility of CBT as a curative treatment for various cancers in thousands of adult and pediatric patients who otherwise would not receive this potentially curative therapy due to the current high treatment-related mortality/morbidity. Our use of molecular imaging to evaluate the spatial and temporal trafficking CB, leading to mechanistic insights, will inform future CB and other cellular therapy studies. Once rapid and durable engraftment are achieved, this expansion/homing technology will ultimately be extrapolated to other CB populations such as immune cells. For example, virus and tumor-specific CB T cells expanded ex vivo will be efficiently recruited to the marrow, the major site of disease for many hematologic cancers, using the fucosylation technology thereby reducing both post-transplant infections and disease relapse. Success in this project will thus herald a new paradigm in CB graft engineering dedicated to optimizing the safety and efficacy of this precious resource in cancer treatment.