

Bankhead-Coley Cancer Research Program

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*Immunology
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Bridge (1-year project)*

Project Title: SHIP and Immunoregulatory Cell Function

Project Summary: Doctors transplant bone marrow (BM) from a normal, healthy donor into a cancer patient for two reasons. It provides a tumor-free graft to replenish the blood cells damaged by chemotherapy and radiation. In addition, the BM graft also contains immune cells from the donor that attack tumor cells in the patient's body. Unfortunately, despite the best efforts to genetically match patients with donors, there is still sufficient difference between them that a war results between their immune systems. The patient's immune cells try to kill the incoming BM graft, while the immune cells from the donor attack vital organs. This immune war is the leading cause of treatment-related death in allogeneic BM transplantation. In addition, some patients succumb to infectious complications caused by the immunosuppressive drugs they receive to prevent this immune war. Thus, although allogeneic BM transplants can cure, they can also kill.

We have identified a gene, SHIP, that when turned off reduces immune wars between patients and donors and thus allows improved survival after the BM transplant. There are two types of cells that can prevent or limit these immune wars after BM transplant. When the SHIP gene is turned off, the activity of these "peacekeeper" cells is increased. The goal of this grant is to determine whether one or both of the "peacekeepers" are required to prevent these immune wars. Therefore, we have developed mice in which the SHIP gene is turned off in one or the other peacekeeper cells. We will perform allogeneic BM transplants with both of these mice to determine whether increases in one peacekeeper or the other are able to protect mice from life-threatening immune wars. We will also test whether the SHIP gene needs to be turned off in both peacekeepers. These studies will aid our understanding of how we might use such peacekeepers to prevent BM transplant-related deaths in cancer.