

Nontechnical Abstract

Leukemia patients that develop recurrent leukemia after a bone marrow transplant from a related or unrelated donor have, until recently, had a very poor prognosis. However, it has now been shown that the administration of T lymphocytes from the bone marrow donor can reinduce a durable complete remission in such patients. Unwanted side effects of donor lymphocyte therapy include graft-versus-host disease and a decline in the blood counts and these toxicities result in significant morbidity and mortality. Strategies have been developed to introduce into the donor T cells to be used in therapy a gene from the herpes simplex virus encoding the thymidine kinase enzyme. The introduction of this gene renders the cells sensitive to the toxic effects of the common antiviral drugs ganciclovir and acyclovir and may allow the elimination of the transferred T cells in patients developing a life threatening toxicity. In the proposed study donor T cells will be modified to express the HSV TK gene and another bacterial gene that permits selection of modified cells in culture, and will be used to treat patients with leukemic relapse after allogeneic marrow transplant. Patients developing severe GVHD or myelosuppression will receive ganciclovir or acyclovir to determine if the T cells can be eliminated and the side effects reversed.