MedicalXpress

Death-inducing proteins key to complications of bone marrow transplantation

December 1 2009

Treatment for a number of cancers and other medical conditions is transplantation with bone marrow from a genetically nonidentical individual (a process known as allogeneic bone marrow transplantation [allo-BMT]).

The treatment often causes an extended period of immune deficiency, resulting in susceptibility to infections and recurrence of cancers. Damage to the thymus (the part of the body where immune cells known as T cells develop) elicited by T cells from the donor bone marrow (a medical condition known as thymic GVHD [tGVHD]) contributes to the deficit in T cell immunity.

Using mouse models of allo-BMT, Marcel van den Brink and colleagues, at Memorial Sloan-Kettering Cancer Center, New York, have now identified several of the molecules required by donor-derived T cells to mediate tGVHD, some of which might prove good drug targets to improve the outcome of allo-BMT.

In the study, one series of experiments determined that donor-derived T cells required the cell death-inducing proteins FasL and TRAIL to damage the thymus and mediate tGVHD. These molecules bound to the death receptors Fas and DR5, respectively, expression of which was upregulated on thymic cells by radiation, a key step in preparing for BMT. The results identifying Fas/FasL and TRAIL/DR5 interactions as critical to tGVHD induction led the authors to suggest that targeting these pathways may provide a way to attenuate tGVHD and improve T

cell reconstitution in allo-BMT recipients.

More information: The cytolytic molecules Fas ligand and TRAIL are required for murine thymic graft-versus-host disease. View this article at: www.jci.org/articles/view/3939 … vtxU3XV6azsy7m3y7tJn

Source: Journal of Clinical Investigation