Purified blood stem cells improve success of bone marrow transplants in mice, study shows

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Researchers at the Stanford University School of Medicine have challenged decades of accepted wisdom about bone marrow transplantation with a new study showing that mice receiving purified blood stem cells are less prone to complications than mice receiving stem cells plus purified T cells.

The study, led by Judith Shizuru, MD, PhD, associate professor of medicine, will be published online Aug. 2 in the Proceedings of the National Academy of Sciences.

Bone marrow transplantation has long been a powerful therapy in combating cancer and other disorders, but it also involves serious risks that make physicians wary. Patients getting bone marrow transplants must first be given powerful drugs or radiation treatments that wipe out their own bone marrow and immune cells, leaving them vulnerable to life-threatening infections.

The patient's supply of blood and immune stem cells is then replenished by bone marrow from a donor, but this bone marrow also contains mature immune cells called T cells that can see the patient's tissues as immunologically foreign. T cells that react against patient tissues cause a disorder called graft versus host disease, or GVHD, which can severely damage the patient's body.

Conventional wisdom among transplantation specialists has been that the bone marrow transplant should contain some T cells from the donor. Although the presence of mature donor T cells is known to cause GVHD, it is generally believed that these T cells can help protect the patient from infectious disease and fight cancer until the transplanted stem cells can mature into a new immune system. It is also thought that the presence of mature T cells decreases the chance that the patient will reject the graft.

"People think that T cells are a necessary evil because they help with engraftment and immune reconstitution," Shizuru said. For these reasons, patients are not given pure blood-forming stem cells as part of current therapy.

The new research by Shizuru, lead author, and research associate Antonia Mueller, MD, and their colleagues calls into question those assumptions. When they compared mice given pure stem cells with mice given a mixture of stem cells and mature T cells, they found that the mice given pure stem cells were better at forming new blood cells and faster in regenerating lymphoid tissues. T cells from the donor seemed to work against the grafted stem cells and inhibit their maturation into mature immune cells. Furthermore, Shizuru said follow-up studies showed that the donor's T cells did not help eradicate pathogens.

The current research expands on work done by Shizuru last year, in which she and her colleagues compared the effectiveness of purified stem cells with unmanipulated bone marrow cells containing low levels of T cells.

In the new study, Shizuru and her colleagues took a more precise look at the action of the mature T cells by comparing how well both groups of mice were able to regenerate bone marrow, blood and lymphoid tissues in the early post-transplant period (within one week) up through one year after transplantation.

Although the work was done in mice, Shizuru believes the results will be medically pertinent. "In our studies we tried to replicate the human system, and I believe what we have found is applicable to humans," she said.

Provided by Stanford University Medical Center