

Safety switch preserves beneficial effects of cell therapy

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Researchers in the Center for Cell and Gene Therapy at Baylor College of Medicine, Houston Methodist and Texas Children's Hospital have found that a single dose of an otherwise harmless drug can safely control the severe and often lethal side effects associated with haploidentical stem cell transplantation. Due to the immune-compromising nature of haploidentical stem cell transplantation, where the stem cells are only half matched, patients are at an increased risk of viral infection and of a lethal complication called graft versus host disease, when the graft cells, which have immune potential, attack the tissues of the person whose original immune system has been eliminated as part of treatment. Investigators have now shown how a molecular "switch" (inducible caspase 9 or iC9) that is activated by a single dose of a bio-inert chemical is able to clear all symptoms of graft versus host disease without jeopardizing the ability of the infused graft to fight infection.

The team presented results from a Phase 1 clinical trial today in a presentation at the American Society of Gene and Cell Therapy annual meeting in New Orleans. The results were simultaneously published in the American Society of Hematology journal, *Blood*.

The clinical study is the Center's most recent quest to pioneer the safety and efficacy of T cell therapy, which harnesses the [immune system](#) and specially modified T cells to attack and destroy cancers of the immune system such as leukemia and lymphoma, as well as restore immunity in serious immunodeficiency disorders.

"We've shown that the therapy (T cells with antiviral specificity and a "kill-switch" in the form of iC9) works, fighting viruses that threaten immune compromised patients," said Dr. Xiaoou Zhou, post-doctoral associate in the Center, and a lead and corresponding author on the report. "We have also shown that the 'switch' can turn off the T-cells that reproduce out of control, attacking the patient as [graft](#) versus host disease. This study was the first to look at any potential effect on the ability of the T cells to fight infection. We found there was no compromise."

"This switch allows us to eliminate the donor cells that cause [graft versus host disease](#) but leave behind the component that fights viral infection," said Dr. Malcolm Brenner, professor in the Center and a corresponding author on the report.

The study included 12 patients (range between 2 to 50 years-old) who underwent haploidentical stem cell transplants and were administered donor-derived iC9-T cells between 30-90 days after transplant.

Removing all T-cells increases the risk of [graft rejection](#), relapse and viral infection. Attempts have been made to save or add desirable T-cells, and the suicide "switch" can eliminate these therapeutic T-cells if they become problematic.

Four patients who received the T-cell therapy developed graft versus host disease, and treatment with the chemical resolved symptoms within 6 to 48 hours. Even after the problematic T cells were killed, the remaining T cells were able do their job without causing further graft versus host disease.

In a surprise finding, Zhou and colleagues showed for the first time that the iC9-T cells can eliminate the uncontrolled [cells](#) in not only the peripheral blood but also in the central nervous system.

In the current study, one patient also developed a potentially life-threatening graft versus host disease-associated cytokine release syndrome, which was rapidly resolved with the administration of one dose of the chemical drug.

"This is an important advance for patients who develop a life threatening complication called graft versus host disease," said Zhou. "This could lead to rapid resolution for those patients without compromising their T cell therapy."

The chemical drug and the inducible caspase 9 suicide gene "switch" it activates are currently being developed by Bellicum Pharmaceuticals.

Provided by Baylor College of Medicine

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