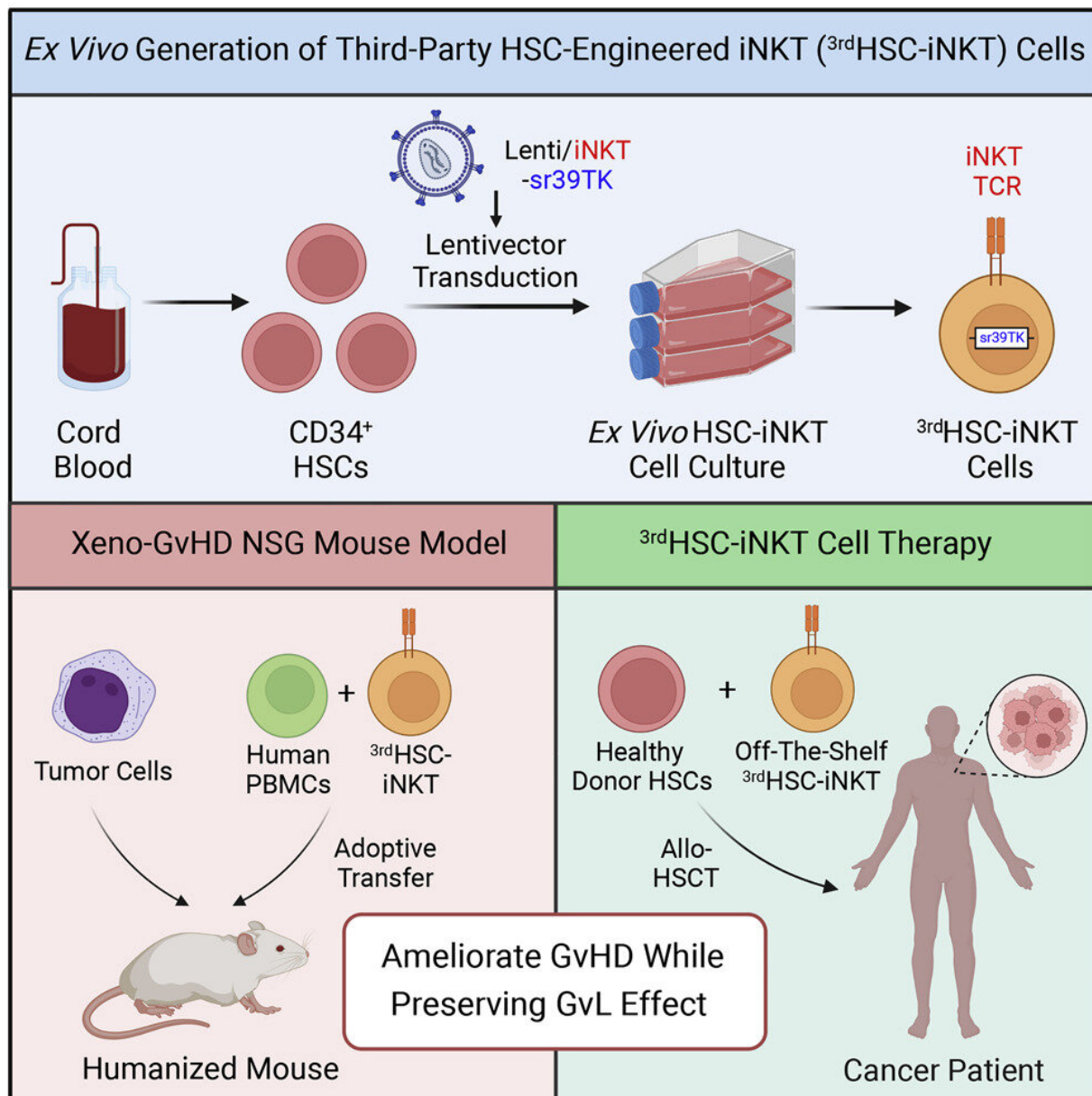


Cell therapy could improve bone marrow transplant safety

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Graphical abstract. Credit: *iScience* (2022). DOI: 10.1016/j.isci.2022.104859

UCLA researchers report a step forward in the development of an "off-the-shelf" cell therapy that could reduce the severity of graft-versus-host disease in people receiving donor bone marrow transplants for the treatment of blood cancers such as leukemia and lymphoma.

The method utilizes rare and powerful immune cells called invariant natural killer T, or iNKT, cells, which can reduce and delay the transplanted cells' attacks on healthy tissue without compromising these cells' cancer-fighting abilities. The iNKT cells are produced from [blood-forming stem cells](#) obtained from donated umbilical cord blood and could potentially be produced in large quantities, stored for extended periods and safely used to treat patients without the need for immune system compatibility.

A [bone marrow transplant](#), also known as a [stem cell transplant](#), is a procedure in which healthy blood-forming stem cells are transplanted into a person's body to help treat disease. There are two types of [bone marrow transplants](#): autologous, which use a person's own cells, and allogeneic, which use cells from a healthy donor (usually a family member).

Allogeneic bone marrow transplants are a common treatment for people with blood cancers like leukemia and lymphoma. After an allogeneic transplant, donor cells kill [cancer cells](#) while helping to restore the production of healthy blood and immune cells. Any transplant that involves cells or tissue from a donor carries the risk of [graft-versus-host disease](#), a condition in which the donated immune cells attack healthy tissue.

Graft-versus-host disease occurs in 30% to 50% of people who receive bone marrow transplants and comes in two forms: acute, which typically occurs in the first 100 days after transplant and can affect the skin, the [gastrointestinal tract](#) or the liver, and chronic, which often sets in after the first 100 days and can affect one organ or multiple.

The researchers used a method they developed to produce large numbers of genetically engineered iNKT cells from blood-forming stem cells that had been isolated from donated cord blood. To test the efficacy of these cells at preventing graft-versus-host disease, the researchers divided immune-deficient mice with leukemia or lymphoma tumors into two groups. One was injected with human immune cells and the other was injected with a combination of [human immune cells](#) and the genetically engineered iNKT cells.

While the transplanted cells helped both groups of mice clear their tumors, the group that received only immune cells developed severe graft-versus-host disease (both the acute and chronic forms) that caused weight loss, organ damage and ultimately death. The mice that received iNKT cells along with the [immune cells](#) lived nearly twice as long as those in the other group and developed slower progressing and less-severe cases of chronic graft-versus-host disease. If the same effect occurs in humans, the researchers say the slower onset of graft-versus-host disease could extend patients' lives and give them more time for currently available therapies to treat their disease.

The findings identify a potential strategy to make bone marrow transplants safer without disrupting their ability to fight cancer. While the protective effects iNKT cells have against graft-versus-host disease has been observed in patients in the clinic, this discovery has not yielded an available therapy because iNKT cells are so rare. The new study outlines a new method for producing large numbers of iNKT cells from donated cord blood. The researchers estimate one cord blood donation

could produce more than 10,000 doses of iNKT cells for clinical use.

The research was published in *iScience*.

More information: Yan-Ruide Li et al, Off-the-shelf third-party HSC-engineered iNKT cells for ameliorating GvHD while preserving GvL effect in the treatment of blood cancers, *iScience* (2022). [DOI: 10.1016/j.isci.2022.104859](https://doi.org/10.1016/j.isci.2022.104859)

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