

Withholding amino acid depletes blood stem cells, researchers say

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A dietary approach to depleting blood stem cells may make it possible to conduct bone marrow transplantations without the use of chemotherapy or radiation therapy, according to researchers at the Stanford University School of Medicine.

The discovery, made in collaboration with researchers at the University of Tokyo, may also become a new way to treat certain cancers without chemo or radiation, which can cause severe side effects.

The researchers showed that a diet deficient in the essential amino acid valine could effectively deplete the population of [blood stem cells](#) in mice and allow them to be successfully transplanted with blood stem cells from other mice. The researchers also showed that human blood stem cells in the laboratory were affected by a lack of access to valine, suggesting that the same therapeutic approach may work in humans.

A paper describing the findings will be published online Oct. 20 in *Science*. The lead author is Yuki Taya, a former graduate student at the University of Tokyo. The senior authors are Hiromitsu Nakauchi, MD, PhD, a professor of genetics at Stanford, and Satoshi Yamazaki, PhD, an associate professor at the Center for Stem Cell Biology and Regenerative Medicine at the University of Tokyo.

Effects of valine-deficient diet

"Bone marrow transplantation is a toxic therapy," said Nakauchi, who is also a member of Stanford's Institute for Stem Cell Biology and Regenerative Medicine. "We have to do it to treat diseases that would otherwise be fatal, but the quality of life afterward is often not good."

He added, "Relative to chemotherapy or radiation, the toxicity of a diet deficient in valine seems to be much, much lower. Mice that have been irradiated look terrible. They can't have babies and live for less than a year. But mice given a diet deficient in valine can have babies and will live a normal life span after transplantation."

The effect of a valine-deficient diet is fairly specific to blood stem cells, but there seem to be other sorts of stem cells that may also be affected, Nakauchi said, including hair stem cells and some T cells. Although other types of stem cells may also be affected, the effects are not nearly as widespread or extreme as those caused by chemotherapy or radiation therapy, he said.

Nakauchi has a particular interest in one kind of stem cell that may be affected by valine deficiency. If [leukemia stem cells](#) are also vulnerable to valine deficiency, Nakauchi said, it may open the door to a dietary therapy for these blood cancers. As with [bone marrow](#) transplantation, a dietary treatment for cancer would probably be much less toxic than chemotherapies now being used, he said.

The lightbulb

The new study came about after Yamazaki was reviewing the scientific literature and found an article in a 1946 issue of *Science*. It was co-authored by the late Stanford researcher Arthur Kornberg, who would go on to receive the 1959 Nobel Prize in Physiology or Medicine. In his 1946 research, Kornberg and his colleagues showed that certain types of anemia in rats could be treated by giving them mixtures of purified

[amino acids.](#)

Yamazaki, Nakauchi and their colleagues were intrigued and did the experiments that Kornberg did not do: testing the effects of the presence or absence of specific amino acids on blood stem cells. The researchers found that in a lab dish, a lack of valine or another amino acid, cysteine, would make the growth of mouse blood stem cells impossible.

Then, the researchers asked a company to create mouse food that was deficient in only these specific amino acids, and fed the mice this diet for four weeks. They found that the valine-deficient diet, but not the cysteine-deficient diet, depleted blood stem cells in the mice. "Unlike valine, cysteine is not an essential amino acid, which means that the body can make some of it itself," Nakauchi said. "All of our valine has to come from our diet, however."

The current dietary method complements other work recently reported by Stanford scientists for using antibodies instead of chemotherapy or radiotherapy to clear out blood stem cells in preparation for bone marrow transplantation. "The two methods might even be used together to provide an even more effective, gentler therapy," Nakauchi said.

The mechanism by which amino acid deficiency affects blood stem cells is unknown, he said, but that will be the focus of future research. Now that this amino acid has shown promise as the basis for a dietary therapy, Nakauchi thinks scientists may find other specific kinds of stem cells that are affected by the presence or absence of particular amino acids. "This work could open up a new research field of stem cell metabolism and become the basis for a whole range of dietary therapies," he said.

"It also reinforces the importance of a well-rounded diet to keep all our cells healthy," he added.

More information: "Depleting dietary valine permits nonmyeloablative mouse hematopoietic stem cell transplantation," *Science*, [science.sciencemag.org/lookup/ ... 1126/science.aag3145](https://science.sciencemag.org/lookup/.../1126/science.aag3145)

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