

Natural enzyme provides potential new approach for treating graft-vs-host disease

January 17 2012

A natural enzyme derived from human blood plasma showed potential in significantly reducing the effects of graft-vs.-host disease, a common and deadly side effect of lifesaving bone marrow transplants.

Researchers from the University of Michigan Comprehensive Cancer Center looked at the drug alpha-1-antitrypsin, which is approved by the U.S. [Food and Drug Administration](#) for use in people who have a genetic mutation that makes them deficient in a certain enzyme. This drug has been used in many of these patients over extended periods of time and is known to cause minimal side effects.

More important, there are no known reports of increased susceptibility to infections. This is key for people with graft-vs.-host disease, where existing treatment options tend to suppress the immune system, putting patients at risk of infection. Graft-vs.-host disease is a major complication of bone marrow transplants using marrow from a donor, called an allogeneic transplant. This often-deadly side effect is what makes the procedure so risky.

"If we can get graft-vs.-host disease under control, we can more effectively use allogeneic [bone marrow transplant](#) to treat people with leukemia and lymphoma as well as other blood disorders. It would be a curative therapy for people who otherwise have no hope," says senior study author Pavan Reddy, M.D., associate professor of hematology/oncology at the U-M Medical School.

In this study, which appears in the [Proceedings of the National Academy of Sciences](#), researchers used alpha-1-antitrypsin in mice that received allogeneic bone marrow transplants. The drug significantly reduced mortality from graft-vs.-host disease, compared to control mice who did not receive the drug.

In addition, alpha-1-antitrypsin reduced the number of [inflammatory cells](#) called T Effector cells that are known to be present in graft-vs.-host disease. It also increased the number of T-regulatory cells, which immunologists believe play a positive role in immune responses.

"It's likely the balance between the T-regulatory cells and the T Effector cells that leads to graft-vs.-host disease. Alpha-1-antitrypsin appears to have tipped that balance favorably," says lead study author Isao Tawara, M.D., Ph.D., a research investigator at the U-M Medical School.

The U-M researchers collaborated on this work with researchers from the University of Colorado and from Ben Gurion University of the Negev in Israel. The researchers are beginning to discuss a possible clinical trial using alpha-1-antitrypsin in post-transplant patients with graft-vs.-host disease for whom conventional therapies are no longer working.

More information: *Proceedings of the National Academy of Sciences*, Vol. 109, No. 2, pp. 564-569

Provided by University of Michigan

Citation: Natural enzyme provides potential new approach for treating graft-vs-host disease (2012, January 17) retrieved 21 July 2024 from <https://medicalxpress.com/news/2012-01-natural-enzyme-potential-approach-graft-vs-host.html>

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