New discovery may lead to effective prevention and treatment of graft-versus-host disease

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A new discovery in mice may lead to new treatments that could make bone marrow transplants more likely to succeed and to be significantly less dangerous. According to new research findings published in the *Journal of Leukocyte Biology* Brazilian scientists may have found a way to prevent the immune system from attacking transplant grafts and damaging the host's own cells after a bone marrow transplant.

Specifically, they found that a receptor for a mediator of the inflammatory process, known as platelet activating factor plays a crucial role in the development of graft-versus-host disease. Platelet activating factor receptor appears to contribute to the attraction of immune cells that lead to graft-versus-host disease. When this mechanism was blocked, there was reduced tissue damage and mortality.

"Platelet activating factor receptor antagonists may decrease suffering caused by graft-versus-host disease in patients undergoing bone marrow transplant," said Vanessa Pinho, Ph.D., a researcher involved in the work from the Departamento de Morfologia, Instituto de Ciencias Biologicas, Universidade Federal de Minas Gerais in Brazil. "As graft-versus-host disease also may decrease quality of life, patients treated with platelet activating factor receptor antagonists may live longer and with better quality of life."

To make this discovery, scientists induced graft-versus-host disease by

transferring cells between mice which were genetically incompatible. In mice subjected to graft-versus-host disease, there was significant injury to target organs, especially the liver and the intestine. In mice that received cells from genetically modified mice bred to not have platelet activating factor receptors, or in mice treated with platelet activating factor receptor antagonist, there was reduced tissue injury and reduced lethality.

"Immune rejection is one of the biggest risks of any transplant procedure, and this study sheds a new light on a receptor and pathway amenable to therapeutic intervention to reduce the serious complication of graft-versus-host disease," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology. "The next step is to take these observations from the lab and see if the potential suggested by studies in mice hold true in humans with disease."

More information: Marina G. M. Castor, Bárbara M. Rezende, Carolina B. Resende, Priscila T. T. Bernardes, Daniel isalpino, Angélica T. Vieira, Danielle G. Souza, Tarcília A. Silva, Mauro M. Teixeira, and Vanessa Pinho. Platelet-activating factor receptor plays a role in the pathogenesis of graft-versus-host disease by regulating leukocyte recruitment, tissue injury, and lethality. *J Leukoc Biol.* April 2012 91: 629-639; doi:10.1189/jlb.1111561

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