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Researchers discover an early warning sign of transplant rejection

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A new study published today in the journal *Blood* has identified a protein that could diagnose chronic graft-versus-host disease (cGvHD), a serious, long-term complication that affects some patients after a blood and bone marrow transplant. The work was led by researchers in the Michael Cuccione Childhood Cancer Research Program at BC Children's Hospital and the University of British Columbia.

Early diagnosis is key to preventing the life-long impact of cGvHD, but currently no such test exists. In search of a diagnostic test, researchers found elevated levels of a protein, CXCL10, in the blood of transplant recipients around the time they developed cGvHD. Testing a transplant patient for this protein could provide the early diagnosis physicians urgently need.

"Diagnostic tests are desperately needed to make blood and marrow transplants safer," says Dr. Kirk Schultz, the study's principal investigator, scientist at BC Children's Hospital and professor in the Department of Pediatrics at the University of British Columbia. "At this time, there are no good tests to diagnose cGvHD and the disease can only be identified too late when it is already established. If we can diagnose it earlier and better, then treatments can be used to stop it before it becomes a chronic, disabling disease."

CGvHD develops after a blood and bone marrow transplant, which is the only effective treatment for some children suffering from childhood leukemia. The disease occurs when immune cells in the donated blood

and marrow cells recognize the child's cells as foreign and launch an immune attack against them.

"A child with leukemia can be cured with a blood and marrow transplant but then has to suffer a life-long disease, cGvHD, which causes a major decrease in their life expectancy and quality of life," says Dr. Schultz.

In the study, researchers compared blood samples from two groups of adult patients, 170 who developed cGvHD and 180 who did not. They analyzed the samples to identify proteins in the blood that could be an early sign of the disease, finding elevated levels of the inflammatory protein CXCL10. This protein appears to impact a patient's normal immune cells, preventing the body from fighting cGvHD.

CGvHD can damage the skin, liver, lungs and digestive tract. Patients with cGvHD are at greater risk for range of issues including cardiovascular disease, diabetes, obesity, and endocrine (hormone) abnormalities.

CGvHD affects approximately 30 to 50 per cent of blood and bone marrow transplant recipients. Over 1,500 children and adults receive a blood and marrow transplant each year in Canada.

This study is one of the largest analyses to date, with 350 participants at 16 Canadian, American, German and Saudi Arabian institutes. Further study is necessary before a diagnostic test for cGvHD can be put into clinical use.

More information: A. Kariminia et al, Heterogeneity of chronic graft-versus-host disease biomarkers: the only consistent association is with CXCL10 and CXCR3+ NK cells, *Blood* (2016). DOI: 10.1182/blood-2015-09-668251

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