Scientists identify biomarker to predict immune response risk after stem cell transplants

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Researchers from Indiana University, the University of Michigan, the Fred Hutchinson Cancer Research Center and the Dana-Farber Cancer Institute have identified and validated a biomarker accessible in blood tests that could be used to predict which stem cell transplant patients are at highest risk for a potentially fatal immune response called graft-versus-host disease.

Although transplant specialists have been able to reduce its impact, graft-versus-host disease remains a leading cause of death among patients who receive a stem cell transplant from another person, known as an allogeneic transplant. Such transplants are used to treat blood and bone marrow cancers such as leukemia and multiple myeloma, often as a last resort. Graft-versus-host disease occurs when immune cells from the transplant see the patient's body as foreign and attack it.

Approximately 20,000 allogeneic stem cell transplants were performed worldwide in 2012. Thirty to 40 percent of stem cell transplant recipients whose donor is related will experience graft-versus-host disease. The percentage could rise to 60 to 80 percent if the patient and donor are not related.

The researchers found that patients with a high level of a protein named ST2 were more than twice as likely to have graft-versus-host disease that resisted standard treatment with steroids; and nearly four times as likely

to die within six months of the transplant. Their findings were reported in the Aug. 8 edition of the *New England Journal of Medicine*.

"What we found particularly significant was that this marker was a better predictor than the clinical severity of the disease when it was diagnosed," said Sophie Paczesny, M.D., Ph.D., associate professor of medicine at the IU School of Medicine and senior author of the study.

Thus, patients with low ST2 levels were more likely to respond to treatment regardless of how serious their graft-versus-host disease was graded, while patients with high ST2 levels were less likely to respond to treatment, whether their disease was graded less serious or more serious.

"This blood test, which is currently available to clinicians, will make informed treatment possible as the clinicians will now be able to adjust therapy to the degree of risk rather than treating every patient the same way," Dr. Paczesny said.

In addition, while the disease most commonly appears about 30 days after the transplant, higher ST2 levels in blood samples taken as early as 14 days after transplant—far before the clinical signs of graft-versus-host disease are apparent—were associated with an increased risk of death from the toxicity of the transplant.

Therefore, the authors noted, early identification of patients who likely won't respond to standard treatments is important and would allow physicians to consider additional therapies and early intervention. On the other hand, patients with low risk will not need to have additional medicine further suppressing their immune system. But, they cautioned, additional large prospective studies are needed to better define the levels of risk predicted by the ST2 marker.

Provided by Indiana University