Blood test serves as 'crystal ball' for heart transplant patients

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A new UCLA-led study shows that a blood test commonly used to determine whether heart transplant recipients are rejecting their new organ can also predict potential rejection-related problems in the future.

Reporting in the online edition of the peer-reviewed journal *Transplantation*, researchers demonstrate how the AlloMap test, which uses a blood sample to measure changes in the expression of roughly a dozen genes, can be used over a period of time to assess the risk of dysfunction or rejection of a transplanted heart—months before such an event may occur.

"For the first time, we can use genomic testing over multiple patient visits to go beyond intuition to understand not just how patients are doing now but how they are likely to be a few months from now," said Dr. Mario Deng, medical director of UCLA's Integrated Advanced Heart Failure–Mechanical Support–Heart Transplant Program and the study's principal investigator. "It's another step toward personalized medicine."

The discovery that transplant recipients' white blood cells contain this prognostic information on rejection, independent of how their transplanted heart may be functioning currently, could potentially improve care and outcomes, the researchers said. The findings represent a significant step in the movement toward using genomic-based testing to predict future clinical events and bolster the importance of similar tests being developed for recipients of other organs.

In the U.S., approximately 2,000 patients receive lifesaving heart transplants each year, and monitoring their immune systems for signs of rejection is a critical part of follow-up care. Until recently, however, the only way to diagnose rejection was through a heart-muscle biopsy, a painful and potentially risky procedure in which a heart catheter is inserted through a vein in the neck.

That changed with the development of the AlloMap gene-expression profiling test, which received clearance from the Food and Drug Administration in 2008. The test is now routinely used by a majority of U.S. heart transplant centers to monitor low-risk patients during follow-up care, resulting in a substantial reduction in the number of biopsies.

AlloMap, which is based on research Deng led in conjunction with more than a dozen of the largest U.S. heart transplant centers and the Brisbane, Calif.–based biotech company XDx, measures the expression levels of 11 genes from a patient's blood sample, each of which is known to be associated with rejection risk.

"The AlloMap was the first FDA-cleared test allowing transplant centers to rule out rejection at the time of the visit," Deng said. "But until now, it has never been used to predict future events."

The current study is based on data originally collected by leading transplant centers and published in the New England Journal of Medicine in 2010. For that study, 600 heart transplant recipients were randomly assigned to be monitored for potential episodes of rejection either through routine biopsy or through the AlloMap test. The study found that AlloMap was equally as effective as biopsy at detecting rejection or dysfunction, and it resulted in increased patient satisfaction because it was less invasive.

The new study demonstrates for the first time the ability of the AlloMap

test, when used over time, to predict future events.

Deng and colleagues noted that using gene-expression profiling to predict the future likelihood of patients experiencing rejection-related problems with their transplanted heart could change the way such patients are treated.

For example, those deemed to be at low risk for adverse events could be given lower doses of immunosuppressive drugs, which could reduce the significant side effects. On the other hand, patients found to be at high risk could be evaluated at shorter time intervals to determine the causes of the test-result variability, specifically to rule out rejection.

As of now, there are no similar tests to monitor the potential for rejection in other types of transplanted organs, but Deng said that active collaborative and multidisciplinary research programs at UCLA and elsewhere are working to bring genomic testing to these fields.

Provided by University of California, Los Angeles