Gene variant linked to moderated symptoms of beta-thalassemia

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Beta-thalassemia is a serious, potentially life-threatening disease that affects red blood cells, cells that carry oxygen via hemoglobin throughout the body. As part of the SardiNIA Study of Aging, supported by the National Institute on Aging (NIA), a component of the National Institutes of Health, scientists have found a genetic variant in the BCL11A gene that can explain why some people with beta-thalassemia seem to be protected from most dangerous symptoms. The findings appear this week in Proceedings of the National Academy of Sciences.

While all those affected in the Sardinia study population have the same mutation in adult hemoglobin, the carrier of oxygen in the red cells, some people experience less extreme symptoms than others—mild enough that these individuals do not need to undergo regular blood transfusions, usually a necessary treatment for beta-thalassemia.

People with this blood disorder do not have enough hemoglobin binding to oxygen within their red blood cells and are therefore weakened. They are also at risk for “hemolytic crisis,” a condition in which their red blood cells are destroyed faster than their bodies can make new ones. It has been known that some individuals escape hemolytic crisis because they retain a high level of fetal hemoglobin (HbF), which is turned off at birth in most people. The persistence of fetal hemoglobin seems to substitute for the lack of adult hemoglobin sufficiently to moderate the course of the disease.

Now it has been shown that variation in the BCL11A gene, discovered through a genome-wide scan of 4,305 research participants in Sardinia and representing a founder population with a high frequency of beta-thalassemia, is strongly associated with elevated levels of HbF and is specifically more common in the individuals with less severe disease. Also in this study, researchers found the same BCL11A variant associated with persistent HbF levels among 1,242 patients from the Cooperative Study of Sickle Cell Disease, another disorder in which adult hemoglobin levels are depleted.

The study raises the possibility that manipulation of BCL11A levels might be studied as a potential therapeutic intervention to alleviate hemoglobin deficiencies that occur in people with beta-thalassemia and sickle cell anemia.

Source: NIH/National Institute on Aging