Researchers find potential treatments for hemoglobinopathies

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An article published in *Experimental Biology and Medicine* (Volume 242, Issue 3, February, 2017) identifies microRNAs (miRNAs) as key factors in some hemoglobinopathies, genetic disorders characterized by alterations in the level or structure of the globin proteins that are responsible for oxygen transport in the blood. The study, led by Dr. Thais Fornari, from the Department of Internal Medicine at the University of Campinas in Brazil demonstrated that differential expression of miRNAs may be responsible for the variations in globin gene expression observed in patients with two hemoglobinopathies: hereditary persistence of fetal hemoglobin deletion type 2 (HPFH-2) and Sicilian-??–thalassemia.

HPFH-2 and Sicilian-??–thalassemia are conditions described as large deletions of the human ?-like globin cluster, with no ?-globin expression and compensatory increases in ?-globin expression. MicroRNAs (miRNAs) are small non-coding RNAs that participate in a wide range of biological processes including erythropoiesis. miRNAs silence the expression of other genes by binding to their mRNAs, and blocking protein synthesis and/or initiating mRNA degradation. Transcription factors such as BCL11A and SOX6, which regulate ?-globin gene expression, are potential targets for several microRNAs based on in silico analysis. Thus, novel miRNA-mediated pathways may explain the differences in the expressions of ?-globin in Sicilian ??–thalassemia and HPFH-2.

In the current study, Dr. Fornari and colleagues compared the miRNA profiles of erythroid cells derived from individuals heterozygous for HPFH-2 and Sicilian-??–thalassemia. Forty-nine differentially expressed miRNAs that may participate in ?-globin gene regulation and red blood cell function were identified. Twelve of these miRNAs potentially targeted the BCL11A gene, and down-regulation of BCL11A gene expression in HPFH-2 was verified by qPCR. This research suggests an important action of miRNAs in the regulation of globin expression in patients. Fornari said that these findings "may partially explain the phenotypic differences between HPFH-2 and Sicilian ??-thalassemia and the variable increases in ?-globin gene expression in these conditions. Moreover, these data support erythroid BCL11A as a therapeutic target for sickle cell disease and ?-thalassemia major patients."

Dr. Steven R. Goodman, editor-in-chief of *Experimental Biology and Medicine*, said, "Fornari and colleagues provide further evidence for the role of miRNA networks in the regulation of fetal hemoglobin expression, via altered expression of BCL11A and SOX6. These studies are important when considering these transcription factors as potential therapeutic targets".

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