

# Researchers highlight potential gene therapy approach to sickle cell disease

11 December 2012

Researchers at Dana-Farber/Children's Hospital Cancer Center (DF/CHCC) have taken the first preliminary steps toward developing a form of gene therapy for sickle cell disease. In an abstract presented on Dec. 10 at the 54th annual meeting of the American Society of Hematology, the research team—led by DF/CHCC's Raffaele Renella, MD, PhD, Stuart H. Orkin, MD, and David A. Williams, MD—announced that they had demonstrated in an animal model the feasibility of activating a form of hemoglobin unaffected by the sickle cell mutation.

The study was included as part of the meeting's Best of ASH session on Dec. 11. At this session, the meeting's scientific co-chairs present what they consider to be the best abstracts of the 4,000-plus presented at the conference.

"This work builds on the transformative basic research discovery of the role of BCL11A in maintaining [fetal hemoglobin](#) silencing by the Orkin laboratory with a near-term goal of curing sickle cell disease using [gene therapy](#)," said Williams, chief of the Division of Hematology/Oncology at DF/CHCC and senior author on the abstract. "We have had important recent successes in applying this type of gene therapy in treating several other [genetic diseases](#) at Boston Children's Hospital."

The team's work builds on previous research, published by Orkin's laboratory, suggesting that strategies targeting a [molecular switch](#) called BCL11A have the potential to correct sickle cell disease.

First described over 100 years ago, sickle cell disease (or sickle cell anemia) is an inherited [blood disease](#) caused by a single mutation in one of the components of hemoglobin, the oxygen-carrying protein in [red blood cells](#). The mutation reduces the protein's ability to carry oxygen and forces the cells to curve into a distinctive crescent or sickle shape.

Our bodies can actually manufacture two forms of hemoglobin: the adult form susceptible to the sickle cell mutation, and a fetal form that is largely produced during development and for a short time after birth. BCL11A is a transcription factor that facilitates that shift in hemoglobin production. Fetal hemoglobin expression significantly reduces the symptoms and complications of sickle cell disease because it prevents the intracellular abnormalities caused by the sickle mutation.

In their abstract, Renella, Orkin, Williams and their colleagues reported on their efforts to develop a combined lentiviral gene transfer/RNA interference approach capable of turning down BCL11A in vitro in human and mouse cells and in vivo in a mouse bone-marrow transplant model. Among their findings, the researchers documented a five- to 20-fold increase in fetal hemoglobin production in treated mice.

The team is quick to note that they have not yet attempted to correct disease in a model of sickle cell using this approach. Such efforts would be carried out in future studies.

"There are many approaches to sickle cell disease, and while we've shown we can develop viral vectors, knock down BCL11A, and induce fetal hemoglobin production, it's all been done in non-disease model systems," cautioned Renella, a fellow in the Williams laboratory at DF/CHCC. "What we don't yet know is whether we can stop production of sickled cells in a sickle cell system. Further experiments will show us if that is possible."

Provided by Children's Hospital Boston

APA citation: Researchers highlight potential gene therapy approach to sickle cell disease (2012, December 11) retrieved 8 September 2022 from <https://medicalxpress.com/news/2012-12-highlight-potential-gene-therapy-approach.html>

*This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.*