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## NIH Award for Sickle Cell Study Marks Milestone Support for Junior UTHSC Investigator, CORNET Program

Memphis Tenn. (July XX, 2020) – A new research project that could impact and expand the discovery of new treatment options for sickle cell patients has just received significant federal funding. The National Heart, Lung, and Blood Institute awarded nearly \$1 million to Athena Starlard-Davenport, PhD, assistant professor of Genetics, Genomics, and Informatics in the UTHSC College of Medicine, for her project titled, "MicroRNA-based epigenetic approach to induce fetal hemoglobin". The grant, the first national award for Dr. Starlard-Davenport, is also a significant milestone for UTHSC's Office of Research: it puts the total external dollars generated from CORNET work over the \$20 million mark.

"For the past 100 years, only four drugs have been approved by the FDA for the treatment of sickle cell disease," said Dr. Starlard-Davenport. "Those patients need more treatment options depending on their symptoms and complications."

Sickle cell disease is very common; one in thirteen African Americans have the sickle cell trait and over 100,000 people in the U.S. have sickle cell disease. Individuals with sickle cell suffer from severe pain crises that increase their risk of organ failure and premature death. The sickle cell mutation causes production of abnormal sickle hemoglobin during the first year of life, when the body makes its switch from producing

fetal hemoglobin (gamma globin) to adult beta globin. Fetal hemoglobin is normal in people with sickle cell disease; it is only the adult form of sickle hemoglobin that is abnormal. Scientists have found that reversing this normal switch, i.e. turning the gamma globin gene back on, counteracts symptoms, improves health outcomes and prolongs the lifespan of sickle cell patients. To date, there is only one FDA-approved drug with proven efficacy to do that: hydroxyurea. Though another class of epigenetic modulators - DNA methyltransferase (DNMT) inhibitors - has shown promise inducing fetal hemoglobin in sickle cell patients, they produce off-target side effects. Dr. Starlard-Davenport's research is focused on a specific small molecule in this class, miRNA29b, for further study.

Dr. Starlard-Davenport has been investigating miRNA29b and fetal hemoglobin induction for four years. She got her start in 2016 with help from a new seed funding initiative launched that year by the UTHSC Office of Research: the CORNET Awards. She and her collaborator, Patricia Adams-Graves, PhD, professor of Medicine and hematologist at the Diggs-Kraus Sickle Cell Clinic at Regional One Medical Center, won a CORNET in the Clinical Awards division for their project, "Investigation of miR29 as a novel fetal hemoglobin inducer and treatment for patients with sickle cell disease."

"The CORNET award provided funding support to collect blood samples from sickle cell patients and to test whether our miRNA therapeutic could increase levels of fetal hemoglobin in vitro in cell culture and in a preclinical sickle cell models, in collaboration with Betty Pace, MD, Tedesco Distinguished Chair of Pediatric Hematology/Oncology at Augusta University," said Dr. Starlard-Davenport. "The funding was used to purchase reagents for running the necessary biochemical assays including our miRNA mimic, cell culture reagents."

The CORNET program was begun by Steven Goodman, PhD, Vice Chancellor for Research, to encourage interdisciplinary collaboration on new research that will lead to larger, national grants. In the nearly four years since their inception, the Awards have supported 52 new collaborative research teams and their groundbreaking initiatives. With this latest national award, external dollars generated from CORNET work has reached \$20,604,972, an 11.6-fold return on a \$1.78 million investment.

"This NIH award for studies to increase fetal hemoglobin expression thereby reducing sickle cell severity is important for many overlapping reasons," said Dr. Goodman. "It is the first NIH award for Dr. Starlard-Davenport. We were able to assist Athena, and her colleagues, to obtain the preliminary data that led to the award through the CORNET award program. This extramural award put the CORNET program over the \$20 million threshold in return on investment. Dr. Starlard-Davenport has been a mentee in the wonderful PRIDE program which focuses on jumpstarting the career of junior under-represented minority faculty. The Director of this PRIDE Program is Dr. Betty Pace who mentored Dr. Starlard-Davenport and is an investigator on the NIH Award. It is amazing how many stars aligned in this one NIH award to a very deserving new investigator. But most important is the impact that this study can have upon the quality of life of people around the globe who suffer from this genetic disease."

"In the initial CORNET application, my team provided preliminary results to show that miRNA29b could increase levels of fetal hemoglobin in a compatible human cell line, but we needed further preliminary data to determine what effect miRNA29b had on fetal hemoglobin induction in red blood cells from individuals with and without sickle cell disease," said Dr. Starlard-Davenport. The NIH funding she just received - \$928,317 which will be distributed over three years - will allow her team to collect blood samples from sickle cell patients and test whether this molecule increases the expression of fetal hemoglobin that blocks sickle hemoglobin and improves clinical symptoms. The longterm goal is to develop miRNA29b as a new drug for treating patients with sickle cell.

Dr. Starlard-Davenport is the principle investigator on a team of clinicians and scientists that includes, in addition to Dr. Adams-Graves and Dr. Pace, Ken Ataga, MD, director of the UTHSC Center for Sickle Cell Disease; Daniel Johnson, PhD, director of the UTHSC Molecular Bioinformatics Center; and Biaouri Li, MD, professor in the department of Pediatric Hematology/Oncology at Augusta University.

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