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Multiple myeloma drug could revolutionize treatment for sickle cell disease

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An established drug for recurrent multiple myeloma might effectively be repurposed to improve the survival and day-to-day lives of patients with devastating sickle cell disease, according to revealing new research by a Feinstein Institute for Medical Research scientist.

The study, by Lionel Blanc, PhD, an assistant investigator at the Feinstein Institute, will be published Dec. 17 in the journal *Blood*. Dr. Blanc's research, performed in collaboration with the New York Blood Center, Yale School of Medicine and University of Montpellier in France, was the first to identify how the drug pomalidomide increases production of fetal hemoglobin, known to interfere with the so-called "sickling" of red blood cells implicated in sickle cell disease (SCD).

Illuminating pomalidomide's mechanism of action offers proof of concept that the US Food and Drug Administration (FDA)-approved medication could potentially be used to treat SCD, representing better outcomes compared to current drug treatment for the 100,000 Americans with SCD, an inherited disorder causing poor oxygen delivery, organ damage and even death.

"We knew the drug would make fetal hemoglobin, but we didn't know to what extent or how. That was the goal of the study," explained Dr. Blanc, also an assistant professor of molecular medicine and pediatrics at Hofstra North Shore-LIJ School of Medicine and an Allied World St. Baldrick's Scholar.

"We can also say something else - that hydroxyurea, the only FDA-approved drug for sickle cell anemia, was less effective than pomalidomide and appeared to act through a different mechanism of action," he added. "The current therapy is good, but not everyone responds equally to hydroxyurea, and what we hope with pomalidomide is to improve this."

Pomalidomide, a derivative of thalidomide used in advanced cases of the cancer multiple myeloma, works by killing malignant plasma cells. But Dr. Blanc and his colleagues demonstrated in the new research, performed on stem cells taken from five SCD patients and 120 normal controls, how pomalidomide also generated fetal hemoglobin, the fetal version of the protein in red blood cells that carries oxygen to body tissues.

In patients with congenital conditions producing anemia such as SCD and beta-thalassemia, fetal hemoglobin is normal, but adult hemoglobin - produced after birth - is abnormal. Therefore, reversing their production of adult hemoglobin back to fetal hemoglobin can reverse the course of their disease.

In addition to the 100,000 US residents with SCD, the condition also affects millions globally. "I would remind people that anemia impacts 1.6 billion people worldwide, making it a global economic burden," Dr. Blanc notes.

Dr. Blanc and his colleagues in the Division of Hematology/Oncology at Cohen Children's Medical Center of New York plan to launch a clinical trial in the near future in collaboration with other institutions to test pomalidomide, which is taken orally, in young adults with SCD.

Currently, the only potential cures for SCD are gene therapy, still in the experimental stage, or stem cell transplant, but these resource-intense

treatments aren't available to the vast majority of patients, particularly in the developing world.

"Our hope is to alleviate the symptoms of sickle cell disease by using a pill that could be made available to almost all patients, worldwide," Dr. Blanc said.

Provided by North Shore-Long Island Jewish Health System