A large team of medical researchers at Novartis Biomedical Research has developed a possible treatment for people with sickle cell disease. In their project, published in the journal Science, they conducted an exhaustive study to find a degrader of the WIZ transcription factor for fetal hemoglobin induction and tested it in animal models.

Douglas Higgs and Mira Kassouf with the University of Oxford have
published a Perspective piece in the same journal issue, outlining the work by the team on this effort.

Sickle cell disease is caused by a mutation in the gene responsible for creating adult hemoglobin. The mutation leads to misshapen red blood cells (they form in crescent shapes, rather than disks) which in turn results in problems transporting oxygen and cells sticking together, causing pain.

Two therapies have been developed in recent years to treat the disease. Both involve gene editing and have proven to be very effective. Unfortunately, they both cost so much that few people can afford them. So medical research teams including those at pharmaceutical giant Novartis have continued to look for other ways to treat the disease.

One of the main avenues of research has revolved around the development of a drug that could switch on fetal hemoglobin in adults. Researchers believe such a drug would offer a cure to people with the disease by transporting oxygen in a new way. Unfortunately, resulting treatments come with negative side effects, such as suppressing bone marrow stem cell production, leading to anemia.

In this new effort, the team at Novartis devoted their considerable resources to finding a drug that could switch on fetal hemoglobin without causing other problems. More specifically, they set themselves the task of finding a compound that would bind to the protein cereblon.

They eventually found one called dWIZ-1 and, after refinement, found that giving it to animal models raised fetal hemoglobin levels from a baseline of 17% to 45%—a level that the team believes would greatly reduce symptoms in humans.

More testing of the compound is required to ensure that it does not
produce any negative side effects, but the team is confident that they have found a compound that could be made into pill form that will greatly reduce the symptoms of sickle cell disease.


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