

# Anti-sickling therapies should be focus for sickle cell science

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Pain is an undeniable focal point for patients with sickle cell disease but it's not the best focus for drug development, says one of the dying breed of physicians specializing in the condition.

Rather scientists need to get back to the crux of the disease affecting 1 in 500 [black Americans](#) and find better ways to prevent the hallmark sickling that impedes [red blood cells' oxygen delivery](#), damaging [blood vessel walls](#) and organs along the way, said Dr. Abdullah Kutlar, Director of the Sickle Cell Center at the Medical College of Georgia at Georgia Regents University.

"We have one drug that reduces sickling and we need more," said Kutlar, the 2013 Roland B. Scott, M.D., Lecturer for the 7th Annual Sickle Cell Disease Research and Educational Symposium and National Sickle Cell Disease Scientific Meeting April 14-17 in Miami.

"Pain is very important to someone who is suffering, but by using pain as an end point, we are missing opportunities and wasting drugs that could be very helpful," he said. "Moving forward, I suggest we develop new combination therapies that have anti-sickling capabilities at their center," said Kutlar, noting such cocktail approaches have worked well for cancer and HIV.

Kutlar completed an extensive historical review of patient and study outcomes in preparation for the lecture honoring the late Howard University physician who made it his mission to improve the lives of

children with sickle cell disease. Scott's contributions include prompting the National Sickle Cell Control Act of 1972, which established the first federally-funded comprehensive sickle cell centers, including the one at MCG led by Dr. Titus H.J. Huisman.

No doubt Scott, Huisman and others have made a tremendous difference to patients, whose [average life expectancy](#) has gone from the teens to the 50s in the past 30 years, Kutlar said. Much of that progress grew out of focusing on the basics, including developing hydroxyurea, still the only [Food and Drug Administration](#)-approved drug that targets sickling.

Approved 15 years ago, [hydroxyurea](#) works by increasing expression of fetal hemoglobin, which can't sickle. However, it's still not widely used – about 35 percent of Kutlar's adult patients take it, for example – probably for a combination of reasons that include a side effect of weight gain and unsubstantiated concerns that it increases cancer risk. He and his colleagues need to do a better job communicating the benefits of this drug in addition to finding new ones, Kutlar said. Reduced sickling means less damage to blood vessels and organs, he said, noting that the major cause of death in adults and children is acute chest syndrome, a severe pneumonia resulting from cumulative lung damage. A handful of new anti-sickling drugs are in various stages of development, including a thalidomide- derivative pioneered by MCG researchers that also enhances fetal hemoglobin expression.

Other good endpoints for drug development include downstream effects of sickling, such as the unnatural adhesion of red blood cells to blood vessel walls, Kutlar said. Unfortunately work was recently halted on a drug that reduced adhesion but not pain, Kutlar said.

Pain needs to be the primary endpoint only for pain medications, he noted. The good news is that many new pain medications are available for these patients, whose pain crises can be severe enough to require

hospitalization and whose chronic pain can impair daily living. However, that circles back to the complex causes of pain. The pain initially likely results from tissues crying out for more oxygen and later from nerve and organ damage resulting from ongoing impaired oxygen supplies. Pain control can get even more complex and difficult because regular use of opiates, a common analgesic for sickle cell patients, actually increases [pain](#) sensitivity, Kutlar said.

In addition to finding better therapies, physicians who treat sickle cell patients need to help cultivate the next generation of caregivers, Kutlar said. He's in the minority in that he opted to take care of patients with sickle cell disease rather than pursue the more common – and generally more professionally lucrative – hematology path: treating cancer. "We don't have enough hematologists, period," said Kutlar. The problem does have a good cause: the reality that more patients are living longer. However, the number of physicians to treat adult patients is dismal. Helping cultivate the next generation is a focus of a study led by Kutlar and Dr. Robert W. Gibson, a GRU occupational therapist and medical anthropologist. They are reaching out to primary care physicians – who also are in short supply in this country – as a permanent medical home for patients as they reach adulthood. Kutlar and Gibson are co-principal investigators on \$7 million, five-year grant from the National Center on Minority Health and Health Disparities of the National Institutes of Health supporting this initiative as well as the search for new drugs and more.

MCG physicians follow about 1,500 adults and children with sickle cell disease.

Provided by Medical College of Georgia

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