Some 12 million people in sub-Saharan Africa have sickle cell disease, and many die in childhood, from infections.

protein, CCR5, that gives the virus a toehold as it establishes an infection.

But those are complex and risky interventions. Doctors must remove stem cells from the body, add or modify their genes, and then reinfuse the cells back into the body after using chemotherapy to wipe out a patient’s original stem cells. In sub-Saharan Africa, where medical infrastructure is limited, those procedures are largely out of reach. Yet the region is home to more than 12 million people with sickle cell disease and 25 million living with HIV—two-thirds of the world’s total for both diseases.

The new collaboration will instead seek to put gene therapy or gene editing into a one-time infusion. The strategy would enlist a harmless virus or nanoparticles to ferry sophisticated molecular tools into the body. “The potential beauty of in vivo gene editing is that it might be given ultimately as a single shot, curing everyone in a scalable manner,” says Steven Deeks, a leading HIV cure researcher at the University of California, San Francisco (UCSF).

Although several labs are working on such in vivo gene therapy or editing to modify blood stem cells in animals, “A major challenge is modifying enough cells,” says Harvard University stem cell scientist Stuart Orkin. He estimates that at a minimum 20% of a patient’s blood stem cells within the bone marrow would have to be modified to cure sickle cell, which would be “a real stretch.”

Mike McCune, an immunologist who has long worked on HIV/AIDS at UCSF and recently joined the Gates Foundation, came up with the idea for the collaboration and approached NIH. McCune, who has worked with Deeks, says he realized existing strategies won’t be enough to defeat HIV in Africa. “Antiretroviral treatment alone is not going to cut it,” he says. The foundation was already talking about investing in in vivo gene editing for sickle cell. Merging the two disease efforts made sense, McCune says.

Collins met in December 2018 with Bill Gates, co-chair of the foundation, to hash out details. Each institution will fund its own grants, but they will share information about proposals each is considering so they can identify redundancies and gaps. The Gates Foundation can act more quickly and is freer to collaborate with industry if it wants. NIH, for its part, has a vast clinical trials network throughout sub-Saharan Africa, where the collaboration aims to launch trials in 7 to 10 years. “I don’t think this is traditionally something the foundation or the NIH would do on its own,” McCune says.

Hematologist Alexis Thompson of the Northwestern University Feinberg School of Medicine in Chicago, Illinois, who is working on sickle cell gene therapy trials, calls the NIH-Gates collaboration “phenomenal.” But she says a low-tech need is more urgent: expanded screening of newborns in Africa for sickle cell so those afflicted can receive antibiotics. Many die before age 5 from bacterial infections because the sickled cells impair the spleen’s immunological function. “It’s almost being able to crawl or walk before you sprint,” Thompson says. Gates and NIH say that outside the collaboration, they plan to support screening efforts.

The new effort also hopes to develop other genome-based strategies to cure these diseases, including cutting-edge approaches such as excising HIV from genomes. “This might be science fiction now, but one day may be a real possibility,” Deeks says. ■
ne of the most contagious human pathogens, the measles virus is dangerous enough by itself, with sometimes-fatal complications including pneumonia and brain inflammation. Two detailed studies of blood from unvaccinated Dutch children who contracted measles now reveal how such infections can also compromise the immune system for months or years afterward, causing the body to “forget” immunity it had developed to other pathogens in the past.

To what extent this “immune amnesia” increases illness and deaths from other infections isn’t clear. But the results are another good reason to immunize children against the virus, the studies’ authors and other infectious disease experts say. The findings are particularly sobering now that measles cases are increasing sharply—by more than 30% globally from 2017 to 2018—because of undervaccination and misguided vaccine safety concerns. “If we allow [measles] outbreaks to happen, we are knowingly creating pockets of people who are susceptible to other diseases as well,” says Velislava Petrova at the Wellcome Sanger Institute in Hinxton, U.K., who led one study.

“These two studies provide further strong evidence for the highly immunosuppressive effects of measles infection and the power of measles vaccination to counter it,” adds population biologist Bryan Grenfell of Princeton University, whose group in 2015 reported early evidence for the effect.

That finding was based on population data showing that mortality from other pathogens increases after a measles outbreak. Experiments in animals have also suggested the measles virus impairs immunity. So Petrova’s group and another, headed by Stephen Elledge of Harvard University, decided to explore this phenomenon more closely in people. Both teams chose a well-known cohort of children from an Orthodox Protestant community in the Netherlands whose parents had opted out of all vaccines for their children for religious reasons.

Michael Mina, a Harvard virologist who also worked on the population study, teamed up with Elledge to analyze blood samples from 77 of the children before and after they became infected during a 2013 measles outbreak in the Netherlands. Tomasz Kula, a postdoc in Elledge’s lab, had developed a technology called VirScan that enabled the team to test the antibodies in the infected children’s blood against antibody targets representing most known human pathogenic viruses.

Before the children contracted measles, their blood contained antibodies to many common pathogens. “These were really healthy kids,” Mina says. After the disease, the children lost, on average, about 20% of their antibody repertoire. Some fared much worse, losing more than 70% of their immunity to viral pathogens, the research-
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