SOMATIC GENOME EDITING IN SICKLE CELL DISEASE: REWRITING A MORE JUST FUTURE*

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Genome-editing technologies promise novel therapies for hematologic disorders. Sickle cell disease ("SCD"), the most common inherited blood disorder, has been identified as one condition where somatic genome editing may provide a cure to alleviate the burden and suffering of the disease. SCD has been slated as one of the first targets for Phase I clinical trials. Given the legacy of discrimination and health inequities for individuals living with the disease and individuals living with sickle cell trait ("SCT"), carriers of one sickle cell gene, policymakers and scientists developing genome-editing research and clinical programs must consider the history of SCD. This Article surveys the social and legal context of SCD and current somatic genome-editing research. It maintains that development and access to curative genetic therapies should be based on the principle of fairness. Equitable application of human genome editing must serve as the core legal, ethical, and social compass that guides the implementation of somatic genome-editing research and clinical treatment. Proactive steps must be taken to ensure that SCD globally is not left behind in the development of genome-editing technologies.

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INTRODUCTION

> *Approximately 1,000 children in Africa are born with SCD every day and more than half will die before they reach five.*[1]

In 1910, Dr. James Herrick described a blood cell irregularity in his article, "Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia," in the *Archives of Internal Medicine*: this "peculiar" phenomenon later came to be known as SCD.[2] The identification of this disease within the Western medical community was an important milestone in the science of human genetics. Today, SCD is used to describe several inherited blood disorders, including sickle cell anemia, HbSC, and HbSβ-thalassaemia.[3] Throughout the history of SCD—the most common single-gene disease—treatment of this community has been intertwined with race and inequities in health care.

While the pharmacological revolution of the last twenty-five years failed to benefit the SCD community, during the last five years promising new drugs and genetic curative treatments have emerged.[4] While acknowledging the promise and potential of novel genetic therapies to end suffering of those with SCD, this Article considers the historical context of the disease and how that history affects current ethical, legal, and social implications of the research.

The National Academies of Sciences, Engineering, and Medicine 2017 Report on Human Genome Editing identifies fairness as an important principle, requiring

> that like cases be treated alike, and that risks and benefits be equitably distributed (distributive justice). Responsibilities that flow from adherence to this principle include (1) equitable distribution of the burdens and benefits of research and (2)

1. AM. SOC'Y OF HEMATOLOGY, STATE OF SICKLE CELL DISEASE: 2016 REPORT 22 (2016), http://www.scdcoalition.org/pdfs/ASH%20State%20of%20Sickle%20Cell%20Disease%202016%20Report.pdf [https://perma.cc/KQ7E-372W].

2. James B. Herrick, *Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia*, 5 ARCHIVES INTERNAL MED. 517 (1910), *reprinted in* 74 YALE J. BIOLOGY & MED. 179, 179 & cmt. a (2001).

3. Catherine Booth, Baba Inusa & Stephen K. Obaro, *Infection in Sickle Cell Disease: A Review*, 14 INT'L J. INFECTIOUS DISEASES e2, e2–e3 (2010).

4. *See, e.g.*, Chris Morris, *The Story Behind the New Sickle Cell Drug That Was 25 Years in the Making*, CNBC (Aug. 7, 2017, 9:58 AM), https://www.cnbc.com/2017/08/07/new-sickle-cell-anemia-drug-endari-by-emmanus-is-fda-approved.html [https://perma.cc/N9QY-R2JD].

> broad and equitable access to the benefits of resulting clinical applications of human genome editing.[5]

Fairness, which includes equitable access, must be at the forefront in developing both policies and clinical trials. The commitment of every stakeholder engaged in the research, development, production, and provision of the new technology will be required to address this challenging goal—essentially, that grand scientific advances in biotechnology must translate into health care for underserved patients. The pharmaceuticals industry, government regulators and policymakers, legislators, bioethicists, health-care professionals, and insurers cannot operate in isolation; each must invite the voices of patients and their advocates to join in collaborative dialogue and policymaking.

This Article describes the discrimination that SCD patients have faced in the past and proposes a fairness-based framework to guide future treatment and research to ensure equitable access to somatic gene editing in the SCD community.[6] Part I of the Article discusses current advances in gene editing and its potential to cure disease. Part II provides an overview of SCD and how somatic genome editing may someday cure individuals with the disease. Part III contemplates the legacy of discrimination endured by the SCD community, which may inform the community's concerns regarding inequitable access to new treatments. Part IV considers the importance of engaging in

5. NAT'L ACADS. OF SCIS., ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 12 (2017); *see also* NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH 10, https://videocast.nih.gov/pdf/ohrp_belmont_report.pdf [https://perma.cc/NND4-RLRY] ("[W]henever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.").

6. Somatic Genome Editing is

> the alteration of cells that cannot contribute to gamete formation and thus cannot be passed on from the individual to offspring. In contrast, germline genome editing, . . . refers to genome editing that occurs in a germ cell or embryo and results in changes that are theoretically present in all cells of the embryo and that could also potentially be passed from the modified individual to offspring. In theory, modification of gamete-producing cells at any point in development could permit this. Because human germline genome editing has potential effects on both the treated individual and subsequent generations of persons, it entails ethical considerations beyond those of somatic genome modification.

Kelly E. Ormond et al., *Human Germline Genome Editing*, 101 AM. J. HUM. GENETICS 167, 169 (2017).

conversations with the SCD community about its thoughts, beliefs, hopes, and fears relating to curative genetic therapies and how such engagement may forestall perpetual health inequities. Part V provides an overview of current legal protections relating to genetic information and its limitations concerning diagnosed genetic diseases. Part VI considers the idea of equity and gene editing, spotlighting new approaches to ensure inclusion and affordability for the SCD community.

I. GENOME EDITING AND THE POTENTIAL OF CURING DISEASE

Genome editing is a "group of [techniques] that give scientists the ability to change an organism's" genome by removal or change in genetic material, specifically deoxyribonucleic acid ("DNA") or ribonucleic acid ("RNA").[7] In humans, a vector to edit a gene can either be delivered outside the body (*ex vivo* treatment) or the vectors can be injected into the body (*in vivo* treatment).[8] These techniques "allow genetic material to be added, removed, or altered at particular locations in the genome."[9]

In 2012, Jennifer Doudna, Emmanuelle Charpentier, and their colleagues published a groundbreaking report on how Clustered Regularly Interspaced Short Palindromic Repeats ("CRISPR"), when combined with an enzyme called CRISPR protein 9 ("Cas9"), could be programmed to edit the DNA of virtually any living organism.[10] Enthusiasm about CRISPR—a naturally occurring, ancient defense mechanism deployed by bacteria to destroy invading viruses—stems from its precision and low cost relative to comparable techniques.[11] Feng Zhang and his colleagues were the first to use genome-editing techniques in eukaryotic cells including human cells.[12] In 2015, *Science* named CRISPR as the "Breakthrough of the Year," describing it as a "molecular marvel" and recognizing the exponential growth in the

7. *What Are Genome Editing and CRISPR-Cas9?*, NIH: GENETICS HOME REFERENCE, https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting [https://perma.cc/JHJ6-E7VV] (last updated Apr. 30, 2019).

8. *How Does Gene Therapy Work?*, NIH: GENETICS HOME REFERENCE, https://ghr.nlm.nih.gov/primer/therapy/procedures [https://perma.cc/63KF-66VV] (last updated Apr. 30, 2019).

9. *What Are Genome Editing and CRISPR-Cas9?*, *supra* note 7.

10. Martin Jinek et al., *A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 SCIENCE 816, 816 (2012).

11. *Id.*; *see also* Mark Shwartz, *Target, Delete, Repair*, STAN. MED., Winter 2018, at 20, 27 (explaining that "CRISPR has made gene editing cheap, easy and accessible").

12. Le Cong et al., *Multipex Genome Engineering Using CRISPR/Cas Systems*, 339 SCIENCE 819, 820 (2013).

scientific community's understanding of the tool and how it could be applied within various clinical, environmental, and ecological contexts.[13]

The medical utility of CRISPR gene editing has continued to develop at a rapid pace. In 2016, doctors in China began using CRISPR-Cas9 to edit immune cells from lung cancer patients to inactivate the protein PD-1, which therefore made immunotherapy more effective.[14] In mid-2017, researchers successfully used a variation of the CRISPR tool to correct the mutation underlying Duchenne muscular dystrophy ("DMD"), both in patient-derived induced pluripotent stem cells ("iPSCs") and in *mdx* mice (which have the same dystrophin mutation as human patients).[15] Around the same time, another research team demonstrated, for the first time, the way in which CRISPR could be used to halt HIV-1 replication and eliminate the virus from infected cells in animal models.[16] With the fast-moving development of the science, clinical trials are being developed to treat diseases using somatic genome editing.[17]

The first somatic gene-editing clinical trials in the United States occurred in 2017, when the first U.S. patient received an *in vivo* zinc finger nucleases ("ZFNs")-based editing therapy for Hunter syndrome (mucopolysaccharidosis type II).[18] Additional genome-editing trials using ZFNs are now open for other rare genetic conditions, such as mucopolysaccharidosis I,[19] hemophilia B,[20] and β-thalassemia.[21]

13. John Travis, *Making the Cut: CRISPR Genome-Editing Technology Shows Its Power*, 350 SCIENCE 1456, 1456–57 (2015).

14. David Cyranoski, *CRISPR Gene Editing Tested in a Person*, 539 NATURE 479, 479 (2016).

15. Yu Zhang et al., *CRISPR-Cpf1 Correction of Muscular Dystrophy Mutations in Human Cardiomyocytes and Mice*, 3 SCI. ADVANCES, no. e1602814, Apr. 12, 2017, at 1, 1.

16. Ramona Bella et al., *Removal of HIV DNA by CRISPR from Patient Blood Engrafts in Humanized Mice*, 12 MOLECULAR THERAPY: NUCLEIC ACIDS 275, 275 (2018).

17. Martina C. Cornel et al., *Moving Towards a Cure in Genetics: What Is Needed to Bring Somatic Gene Therapy to the Clinic?*, 27 EUR. J. HUM. GENETICS 484, 484 (2019).

18. Jocelyn Kaiser, *A Human Has Been Injected with Gene-Editing Tools to Cure His Disabling Disease. Here's What You Need to Know*, SCIENCE (Nov. 15, 2017, 6:00 PM), https://www.sciencemag.org/news/2017/11/human-has-been-injected-gene-editing-tools-cure-his-disabling-disease-here-s-what-you [https://perma.cc/6T23-TP49].

19. *Ascending Dose Study of Genome Editing by the Zinc Finger Nuclease (ZFN) Therapeutic SB-318 in Subjects with MPS I*, CLINICALTRIALS.GOV, https://clinicaltrials.gov/ct2/show/NCT02702115 [https://perma.cc/2T3W-4HH2] (last updated June 7, 2018).

20. *Ascending Dose Study of Genome Editing by Zinc Finger Nuclease Therapeutic SB-FIX in Subjects with Severe Hemophilia B*, CLINICALTRIALS.GOV,

The discovery of the CRISPR-Cas9 system for genome editing, and its application to human cells, has accelerated progress in genome editing.[22] The first U.S.-based CRISPR-Cas9 clinical trial began recruiting cancer patients for an *ex vivo* approach in 2018.[23] The eagerly awaited results from these clinical trials will act as the first indications of the safety and efficacy of CRISPR-Cas9 genome-editing approaches.[24] Trials using both ZFNs and CRISPR-Cas9 gene editing are in the pipeline for SCD.

II. SCD AND SOMATIC GENOME EDITING

As gene-editing technology advances, it becomes more likely that a technique like CRISPR can be used to develop a cure for SCD. This part provides an overview of SCD, the genome-editing-based approaches being developed to treat it, and the reaction of the SCD community to these new approaches.

A. Background of SCD

SCD is the most common monogenic disorder, caused by a single-point mutation.[25] This mutation is located in the sixth codon of

https://clinicaltrials.gov/ct2/show/NCT02695160 [https://perma.cc/7EUJ-3XER] (last updated Feb. 12, 2019).

21. *A Study to Assess the Safety, Tolerability, and Efficacy of ST-400 for Treatment of Transfusion-Dependent Beta-thalassemia (TDT)*, CLINICALTRIALS.GOV, https://clinicaltrials.gov/ct2/show/NCT03432364?term=genome+editing&rank=6 [https://perma.cc/UCS6-7VEE] (last updated Feb. 4, 2019).

22. Jennifer A. Doudna & Emmanuelle Charpentier, *The New Frontier of Genome Engineering with CRISPR-Cas9*, 346 SCIENCE 1077, 1077 (2014).

23. *NY-ESO-1-redirected CRISPR (TCRendo and PD1) Edited T Cells (NYCE T Cells)*, CLINICALTRIALS.GOV, https://clinicaltrials.gov/ct2/show/NCT03399448 [https://perma.cc/F6V6-YZLQ] (last updated Mar. 4, 2019).

24. *See* Mary Ellen Perry et al., *Genome Editing to 'Re-Write' Wrongs*, 17 NATURE REVIEWS: DRUG DISCOVERY 689, 689–90 (2018). The range of potential applications makes the results of particular interest:

> The relative ease of targeting by interchangeable guide RNAs is likely to be particularly important for rare monogenic diseases. There are thousands of such diseases, and each can result from different mutations in different individuals. Following the discovery of Cas9, researchers have identified homologues in other species with improved properties, such as reduced size and increased specificity. In addition, engineered versions of Cas9 and related proteins, including nuclease-free versions of Cas9 coupled to DNA or RNA-modifying enzymes, have been developed. Of note are base editors that can correct the most common disease-causing single-base mutations without creating a double-strand break in DNA.

Id. at 689.

25. Frédéric B. Piel, Martin H. Steinberg & David C. Rees, *Sickle Cell Disease*, 376 NEW ENG. J. MED. 1561, 1561 (2017) [hereinafter Piel et al., *Sickle Cell Disease*].

the β-hemoglobin subunit.[26] SCD is "a group of inherited diseases . . . characterized by mutations in the gene encoding the hemoglobin subunit β (*HBB*)."[27] Sickle erythrocytes, or red blood cells, can lead to recurrent vaso-occlusive episodes that are the hallmark of the disease.[28]

The burden of the disease is highest in sub-Saharan Africa; however, the disease is also common in the Mediterranean basin, the Middle East, and India.[29] The prevalence is estimated to be between 300,000 and 400,000 infants born globally each year, the majority in sub-Saharan Africa.[30] It is also estimated that 100,000 people in the United States live with the disease.[31] Individuals living with SCD with the same genotype can clinically present very differently.[32] Common complications are acute pain events, acute chest syndrome, stroke, leg ulcers, priapism, and sickle cell retinopathy.[33] The disease burden on the body can result in end organ damage.[34]

The number of individuals living with the disease is expected to increase globally.[35] In high-income countries, this increase reflects migration[36] and gains in life expectancy among affected persons in these countries that result from health interventions such as newborn screening, penicillin prophylaxis, pneumococcal immunization, and education about disease complications.[37] In many African countries, where the frequency is the highest, the overall number of births is expected to double between 2010 and 2050.[38] Worldwide, the growth in the number of babies born with the disease is expected to increase

26. Nicola Conran, Carla F. Franco-Penteado & Fernando F. Costa, *Newer Aspects of the Pathophysiology of Sickle Cell Disease Vaso-Occlusion*, 33 HEMOGLOBIN 1, 1 (2009).

27. Gregory J. Kato et al., *Sickle Cell Disease*, 4 NATURE REVIEWS: DISEASE PRIMERS, no. 18010, Mar. 15, 2018, at 1, 1.

28. Piel et al., *Sickle Cell Disease*, *supra* note 25, at 1565.

29. Kato et al., *supra* note 27, at 2.

30. Frédéric B. Piel et al., *Global Burden of Sickle Cell Anaemia in Children Under Five, 2010–2050: Modelling Based on Demographics, Excess Mortality, and Interventions*, 10 PLOS MED., no. e1001484 July 2013, at 1, 4 [hereinafter Piel et al., *Global Burden*].

31. *See Sickle Cell Disease*, CENTERS FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/ncbddd/sicklecell/data.html [https://perma.cc/L54L-9CJC].

32. Kato et al., *supra* note 27, at 11.

33. *Id.* at 1, 3, 4.

34. *Id.* at 5.

35. Piel et al., *Global Burden*, *supra* note 30, at 4.

36. Stephan Lobitz et al., *Newborn Screening for Sickle Cell Disease in Europe: Recommendations from a Pan-European Consensus Conference*, 183 BRIT. J. HAEMATOLOGY 183, 648, 650 (2018).

37. Russell E. Ware et al., *Sickle Cell Disease*, 390 LANCET 311, 311 (2017).

38. Piel et al., *Global Burden*, *supra* note 30, at 4.

by more than 30% by 2050.[39] Currently, in low-income countries, 90% of children with SCD do not survive to adulthood.[40]

The molecular basis of SCD has been studied for many years and is well understood. While a cure exists in the form of hematopoietic stem cell transplantation ("HSCT"), it can be difficult to find donor matches.[41] Furthermore, HSCT remains an expensive procedure with the prospect of serious complications, such as graft versus host disease ("GVHD").[42] The limitations of treatments and procedures like HSCT combined with the devastating nature of SCD and documented poor access to high-quality care, has sparked hope that the era of gene editing and gene therapy will change the tide for patients who have historically been disenfranchised by the biomedical system.[43] Recent improvements in understanding the molecular pathways controlling production of red blood cells and fetal-to-adult hemoglobin switching offer new therapeutic options.[44] Substantial resources are being directed into discovering a gene-editing cure using these new mechanisms.[45] To this end, SCD may facilitate a turning point for gene-editing and gene-therapy research.

B. SCD and Genome Editing

There are two dominant genome-editing approaches under current exploration for treatment of SCD.[46] The first, described as "[t]he holy grail of genome editing for the β-hemoglobinopathies[,] is the correction of the β-globin mutation . . . ."[47] Using CRISPR-Cas9 to repair the β-globin gene, preclinical studies have successfully used a viral approach to edit hematopoietic stem cells from patients with

39. *Id.*

40. AM. SOC'Y OF HEMATOLOGY, *supra* note 1, at 23.

41. Courtney D. Fitzhugh et al., *Hematopoietic Stem Cell Transplantation for Patients with Sickle Cell Disease: Progress and Future Directions*, 28 HEMATOLOGY/ONCOLOGY CLINICS N. AM. 1171, 1178 (2014).

42. Javier Bolaños-Meade & Robert A. Brodsky, *Blood and Marrow Transplantation for Sickle Cell Disease: Overcoming Barriers to Success*, 21 CURRENT OPINION ONCOLOGY 158, 158 (2009).

43. Katherine Bourzac, *Erasing Sickle-Cell Disease*, NATURE OUTLOOK: BLOOD, Sept. 28, 2017, at S28, S30.

44. Selami Demirci, Naoya Uchida & John F. Tisdale, *Gene Therapy for Sickle Cell Disease: An Update*, 20 CYTOTHERAPY 899, 899 (2018).

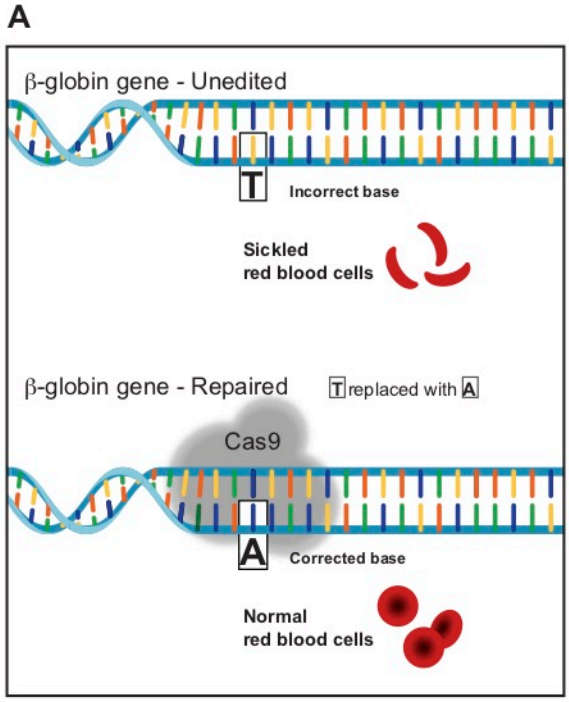
45. Edward J. Benz Jr., *The Cure Sickle Cell Initiative: Catalyzing Progress via Innovative Interfaces Between NIH, Patients, Academics, ASH, and the Private Sector*, HEMATOLOGIST, Nov.–Dec. 2018, at 1, 1.

46. Demirci et al., *supra* note 44, at 904.

47. *Id.*

SCD in the lab.[48] The researchers have also shown that they can successfully transplant the repaired cells into blood stem cells of mice.[49]

Figure 1. Genome Editing Approaches for SCD: Approach A



Approach A: Schematic of β-globin mutation correction using CRISPR-Cas9. The correction is made by changing the single nucleotide mutation thymine to adenine (T to A), which changes glutamic acid to valine at codon 6 of the β-globin (*HBB*) gene. (Image Credit: Darryl Leja, National Human Genome Research Institute).

The second approach entails disrupting *BCL11A*, a region of the DNA known to suppress the production of fetal hemoglobin, a form

48. Rasmus O. Bak, Daniel P. Dever & Matthew H. Porteus, *CRISPR/Cas9 Genome Editing in Human Hematopoietic Stem Cells*, 13 NATURE PROTOCOLS 358, 358 (2018).

49. *See, e.g.*, *id.* at 363; Mark A. DeWitt et al., *Selection-Free Genome Editing of the Sickle Mutation in Human Adult Hematopoietic Stem/Progenitor Cells*, 8 SCI. TRANSLATIONAL MED., no. 360ra134, Oct. 12, 2016, at 1, 1.

of hemoglobin associated with reduced disease severity.[50] In 1949, Janet Watson and colleagues reported that the blood of infants with SCD delayed sickling in comparison to the mothers' blood.[51] This was later determined to be caused by the high levels of fetal hemoglobin ("HbF") in the infants' blood.[52] Genome-wide association studies identified that the *BCL11A* gene variant was strongly associated with modulating HbF levels.[53] The *BCL11A* gene variant is a prime target for genome editing.[54] Research studies in mouse models have established that perturbation of the *BCL11A* enhancer with gene editing can result in HbF levels to clinically ameliorate the disease.[55]

50. Daniel E. Bauer et al., *An Erythroid Enhancer of* BCL11A *Subject to Genetic Variation Determines Fetal Hemoglobin Level*, 342 SCIENCE 253, 254 (2013).

51. Janet Watson, Albert W. Stahman & Francis P. Bilello, *The Significance of the Paucity of Sickle Cells in Newborn Negro Infants*, 215 AM. J. MED. SCI. 419 (1948), *reprinted in* 3 OBSTETRICAL & GYNECOLOGICAL SURV. 819, 819 (1949).

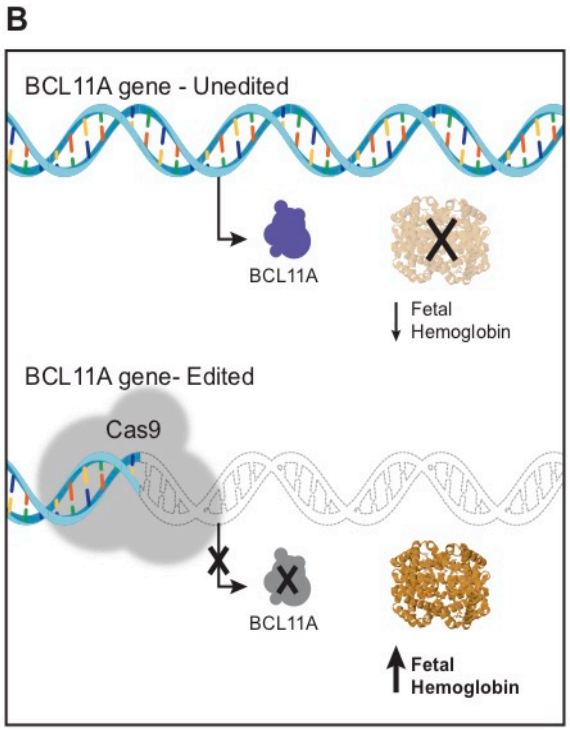
52. C. Lockard Conley et al., *Negro Families in Baltimore*, 21 BLOOD 261, 278 (1963); G. Stamatoyannopoulos et al., *A New Form of Hereditary Persistence of Fetal Hemoglobin in Blacks and Its Association with Sickle Cell Trait*, 46 BLOOD 683, 683 (1975).

53. Bauer et al., *supra* note 50, at 253.

54. Stuart H. Orkin & Daniel E. Bauer, *Emerging Genetic Therapy for Sickle Cell Disease*, 70 ANN. REV. MED. 257, 260 (2019).

55. Matthew C. Canver et al., BCL11A *Enhancer Dissection by Cas9-Mediated* in Situ *Saturating Mutagenesis*, 527 NATURE 192, 196 (2015); Vijay G. Sankaran et al., *Human Fetal Hemoglobin Expression Is Regulated by the Developmental Stage-Specific Repressor* BCL11A, 322 SCIENCE 1839, 1839 (2008); Manuela Uda et al., *Genome-Wide Association Study Shows* BCL11A *Associated with Persistent Fetal Hemoglobin and Amelioration of the Phenotype of β-thalassemia*, 105 PNAS 1620, 1620 (2008).

Figure 2: Genome Editing Approaches for SCD: Approach B



Approach B: Schematic of gene editing to control silencing the *BCL11A* gene, a region of the DNA known to suppress the production of fetal hemoglobin. The use of CRISPR-Cas9 to disrupt *BCL11A* allows for the production of high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. (Image Credit: Darryl Leja, National Human Genome Research Institute)

Besides these two novel approaches, other curative genetic therapies are moving forward. Sickle cell *ex vivo* gene therapy, inserting a normal, functional gene to replace an abnormal gene, can modify an individual's genome.[56] In March 2017, Jean-Antoine Ribeil and colleagues reported the results of the first SCD patient who received this therapy in France, stating that the patient achieved "complete clinical remission with correction of hemolysis and biologic

56. Orkin & Bauer, *supra* note 54, at 264.

hallmarks of the disease."[57] In that study, a research team endeavored to insert a functional β-globin into a patient's hematopoietic stem cells, *ex vivo*, through the use of a lentiviral vector.[58] This breakthrough, along with the decades of foundational study dedicated to understanding the molecular basis underlying this disease, may pave the path for SCD to lead the implementation of these new technologies into clinical care.[59]

C. Cure for SCD and Engagement of the Community

Disorders of the blood constitute an area of active gene-therapy and gene-editing research currently underway.[60] In January 2018, the National Institutes of Health ("NIH") launched a $190 million, six-year research initiative to remove the implementation barriers of somatic gene editing in clinical care.[61] These endeavors include improving current delivery mechanisms, genome editors, and assays for testing the safety and efficacy of genome-editing tools.[62] With this program, the NIH hopes to accelerate the field and expedite the translation of gene-editing treatments into meaningful clinical applications.[63] On September 13, 2018, the NIH launched a new initiative to help speed the development of cures for SCD.[64] Dr. Gary H. Gibbons, director of NIH's National Heart, Lung, and Blood Institute ("NHLBI"), stated, "Our scientific investments have brought us to a point where we have many tools available to correct or compensate for the defective gene that causes [SCD]. We are now ready to use these tools to speed up our quest for a cure."[65]

With advancements in gene therapy and a potential genome-editing cure for SCD on the horizon, we are likely to witness a

57. Jean-Antoine Ribeil et al., *Gene Therapy in a Patient with Sickle Cell Disease*, 376 NEW ENG. J. MED. 848, 849 (2017).

58. *Id.* at 848.

59. *Id.* at 854.

60. *See, e.g.*, Canver et al., *supra* note 55, at 196; DeWitt et al., *supra* note 49, at 9.

61. News Release, Nat'l Insts. of Health, NIH to Launch Genome Editing Research Program (Jan. 23, 2018), https://www.nih.gov/news-events/news-releases/nih-launch-genome-editing-research-program [https://perma.cc/HV63-GWXD].

62. Francis Collins, *Accelerating Cures in the Genomic Age: The Sickle Cell Example*, NIH: DIRECTOR'S BLOG (Dec. 11, 2018), https://directorsblog.nih.gov/2018/12/11/accelerating-cures-in-the-genomic-age-the-sickle-cell-example/ [https://perma.cc/T8TE-58YH].

63. *Id.*

64. News Release, Nat'l Insts. of Health, NIH Launches Initiative to Accelerate Genetic Therapies to Cure Sickle Cell Disease (Sept. 13, 2018), https://www.nih.gov/news-events/news-releases/nih-launches-initiative-accelerate-genetic-therapies-cure-sickle-cell-disease [https://perma.cc/564H-YYJ9].

65. *Id.*

watershed moment for those living with this debilitating illness, especially in light of SCD's long history of neglect.[66] Though the disease was first described over a century ago,[67] very little progress has been made to advance affordable, accessible treatment for those affected by SCD.[68]

Persaud, Bonham, and colleagues conducted a qualitative study between April and December 2017 to engage the SCD community and ascertain its views on gene-editing therapies.[69] The study[70] consisted of fifteen focus groups: six patient, six parent, and three physician groups. Participants answered survey questions about their views on gene editing and participation in future clinical trials.

The study examined the views of patients, parents, and physicians within the SCD community and found that, broadly, all three stakeholder groups expressed enthusiasm over a seemingly overdue treatment that carries the potential to completely eradicate SCD. One patient stated, "With me sitting here in pain right now . . . if there's something that can be done to heal that, then I'm for it." Another said, "I'm very optimistic. It's another possible option for sickle cell patients and unfortunately we don't have many." Despite the community's overall optimism, a number of reservations regarding gene editing were reported, especially relating to equitable access. "To have the sickle cell population move this forward and then not have this available for them equally, would be extremely traumatic to the community," said one physician, especially when examining the SCD community's history of discrimination.

III. SCD AND SCT: A LEGACY OF DISCRIMINATION

The legacy of discrimination against the SCD community provides a backdrop for understanding current attitudes and apprehensions regarding inequitable access to a potential cure. After providing some general thoughts on the value-harm tradeoff inherent in knowing one's sickle cell status, this part provides an overview of the history of discrimination against those living with SCD and SCT

66. Collins, *supra* note 62.

67. Herrick, *supra* note 2, at 179 & cmt. a.

68. Keith Wailoo, *Sickle Cell Disease – A History of Progress and Peril*, 376 NEW ENG. J. MED. 805, 805 (2017).

69. Anitra Persaud et al., *A CRISPR Focus on Attitudes and Beliefs Towards Somatic Genome Editing from Stakeholders Within the Sickle Cell Disease Community*, GENETICS MED. 1 (Dec. 24, 2019), https://www.nature.com/articles/s41436-018-0409-6.pdf [https://perma.cc/BZ2M-HRW2].

70. For the remainder of this section, the study discussed is referring to the Persaud and Bonham study.

and spotlights three especially striking examples of that discrimination: in the U.S. military, the workplace, and the provision of medical care. It then considers how the potential for discrimination continues.

A. The Clinical Benefit and Harm in Knowing One's Sickle Cell Carrier Status

SCT, the heterozygous inheritance for sickle hemoglobin,[71] has evolutionarily persisted throughout the world due to its protection against severe malaria syndromes.[72] "In the United States, between 2.5 to 3 million people live with SCT including an estimated 6% to 9% of the African American population and 0.01% to 0.07% of the remaining population, primarily those of Arab, Southeast Asian, Hispanic, and Mediterranean descent."[73] SCT affects an estimated 300 million individuals worldwide, "with a prevalence ranging from 2% to 30% in more than 40 countries."[74] Because of its prevalence, SCT reproductive counseling has been identified as an important public health campaign and testing has been suggested in various settings.[75] SCT carriers can have children who are homozygous SCD, compound heterozygous SCT, or not affected at all.[76] Although SCT is generally an asymptomatic carrier state and most individuals never have complications, studies have reported potential clinical manifestations of SCT.[77]

There are instances where screening and knowledge of one's SCT status are important for reproductive decisions and can help one to take potentially life-saving measures, e.g., preventing dehydration and overexertion in circumstances involving extremely challenging

71. Jelili Ojodu et al., *Incidence of Sickle Cell Trait—United States, 2010*, 63 MORBIDITY & MORTALITY WKLY. REP. 1155, 1155 (2014).

72. Steve M. Taylor, Christian M. Parobek & Rick M. Fairhurst, *Haemoglobinopathies and the Clinical Epidemiology of Malaria: A Systematic Review and Meta-Analysis*, 12 LANCET INFECTIOUS DISEASES 457, 457 (2012) ("Haemoglobin AS, CC, and AC genotypes and homozygous and heterozygous α-thalassaemia provide significant protection from severe malaria syndromes . . . .").

73. Rakhi P. Naik et al., *Clinical Outcomes Associated with Sickle Cell Trait*, 169 ANNALS INTERNAL MED. 619, 619 (2018).

74. *Id.*

75. REG'L OFFICE FOR AFR., WORLD HEALTH ORG., SICKLE-CELL DISEASE: A STRATEGY FOR THE WHO AFRICAN REGION 1 (2010), https://apps.who.int/iris/bitstream/10665/1682/1/AFR-RC60-8.pdf [https://perma.cc/KF5L-YAMQ]; *see also* Althea M. Grant et al., *Public Health Implications of Sickle Cell Trait: A Report of the CDC Meeting*, 41 AM. J. PREVENTATIVE MED. S435, S438 (2011).

76. REG'L OFFICE FOR AFR., WORLD HEALTH ORG., *supra* note 75, at 1.

77. Chika Duru, *Out for Blood: Employment Discrimination, Sickle Cell Trait, and the NFL*, 9 HASTINGS RACE & POVERTY L.J. 265, 269–72 (2012).

physical activity.[78] In a controversial decision, the National Collegiate Athletic Association ("NCAA") decided in 2010 that Division I student-athletes must be screened for SCT after a number of college football players with SCT died, resulting in lawsuits against the NCAA and the student-athletes' universities.[79] NCAA-mandated testing was extended to Division II schools in 2012 and Division III schools in the 2014–2015 academic year.[80] A team of hematologists and experts in SCD conducted a systematic review of the literature from 1970 to 2018, finding only moderate evidence of risk of exertional rhabdomyolysis[81] in those with SCT in high-exertional exercise settings but no sufficient evidence supporting the risk of

78. Vence L. Bonham, George J. Dover & Lawrence C. Brody, *Screening Student Athletes for Sickle Cell Trait — A Social and Clinical Experiment*, 363 NEW ENG. J. MED. 997, 998 (2010).

79. *Id.* at 997. *See generally* Verdict and Settlement Summary, Lloyd v. William March Rice Univ., No. C-2008-56506, 2009 WL 2462617 (Tex. Dist. Ct. June 29, 2009) (detailing the settlement reached between parents of a deceased nineteen-year-old football player, the university, and the NCAA after the player experienced a fatal acute exertional rhabdomyolysis event associated with his SCT). In the *Lloyd* settlement, the NCAA agreed to recommend SCT testing during all routine mandatory physicals for student-athletes at Division I institutions. *Id.*; Heather R. Quick, Note, *Privacy for Safety: The NCAA Sickle-Cell Trait Testing Policy and the Potential for Future Discrimination*, 97 IOWA L. REV. 665, 667 (2012).

A Pennsylvania appellate court noted that failing to test athletes can create a significant risk. *See* Hill v. Slippery Rock Univ., 138 A.3d 673, 680 (Pa. Super. Ct. 2016). The *Hill* court considered a negligence claim brought by a deceased student-athlete's parents. *Id.* The parents in *Hill* claimed that "the university should have tested for SCT before allowing students to join in athletics and that the NCAA's failure to require Division II schools to screen for SCT was negligent." *Id.*; Matt Fair, *Pa. Justices Snub Appeal Over NCAA's Place in Death Suit*, LAW360.COM, https://www.law360.com/articles/877516/pa-justices-snub-appeal-over-ncaa-s-place-in-death-suit [https://perma.cc/RQY7-SWDB (dark archive)]. The *Hill* court held that an increased risk of harm significant enough to support a negligence action can occur through a failure to act or a "sin of omission," and thus the parents sufficiently pleaded a negligence claim when they alleged that the NCAA's failure to test a student for SCT increased the risk of harm to that student. *Hill*, 138 A.3d at 680. The Supreme Court of Pennsylvania denied the NCAA's Petition for Allowance of Appeal. Hill v. Slippery Rock Univ., 640 Pa. 598 (2017).

80. Susan L. Smith & Miriam Shuchman, *Sickle Cell Screening of College Athletes: Legal Obligations Fulfilled, Moral Obligations Lacking*, 92 OR. L. REV. 1127, 1128 (2014). Smith and Shuchman note that the American Society of Hematology does not support the mandatory testing. *Id.* (citing *Statement on Screening for Sickle Cell Trait and Athletic Participation*, AM. SOC'Y HEMATOLOGY (Jan. 26, 2012), https://www.hematology.org/news/2012/7703.aspx [https://perma.cc/2NS4-U4NV]).

81. "Exertional rhabdomyolysis, a syndrome characterized by skeletal muscle degeneration and muscle enzyme leakage, has been shown to occur in normal, healthy individuals following strenuous exercise. In severe cases, this syndrome can result in renal failure and sudden death." Gary L. Harrelson, A. Louise Fincher & James B. Robinson, *Acute Exertional Rhabdomyolysis and Its Relationship to Sickle Cell Trait*, 30 J. ATHLETIC TRAINING 309, 309 (1995).

sudden death.[82] There is a continuing debate regarding the clinical utility of testing student-athletes to prevent risk of clinical complications.[83]

While testing and knowledge may be quite helpful to some with SCT, both SCD and SCT have a long and complicated history with health-care delivery and the law. A legacy of discrimination, a lack of health-care resources, and a lack of research support are all a part of the history of this disease. This past may impact the sickle cell community's willingness to embrace new advances in addressing the disease and offer up their own bodies for research to solidify such advances.

B. Discrimination Against People Living with SCD and SCT

Since its discovery, SCD has "emerged and reemerged at the intersection of a variety of medical, genetic, serological, anthropological, personal, and administrative discourses on whiteness, hybridity, tribes, and citizenship."[84] After his research "transform[ed SCD] into the 'first molecular disease,'" Dr. Linus Pauling also astoundingly suggested a public health campaign whereby SCT carriers would be tattooed on their foreheads so they would be readily recognizable to one another "and avoid falling in love, thereby reducing the incidence of the disease."[85] In 1959, physician Lydia A. DeVilbiss advocated for "managing" SCD by means of mandatory premarital blood testing, as was done at the time for venereal diseases, implying "that both conditions fall within the realm of governance and must be addressed not only at the level of the individual sick body . . . but also at the level of the citizen, that is, through government programs and with respect to its implications for the society as a whole."[86]

Some scholars assert that SCT—not the actual disease, SCD—has served historically as a pretext for state government surveillance of reproductive decisions of African Americans.[87] For example, in the 1960s and 1970s, some community members contended that because

82. Naik et al., *supra* note 73, at 624–25.

83. Charlotte Baker et al., *Implementation of the NCAA Sickle Cell Trait Screening Policy: A Survey of Athletic Staff and Student-Athletes*, 110 J. NAT'L MED. ASS'N 564, 565 (2018); *see also* Duru, *supra* note 77, at 271.

84. MELBOURNE TAPPER, IN THE BLOOD: SICKLE CELL ANEMIA AND THE POLITICS OF RACE 3 (1999).

85. KEITH WAILOO, DYING IN THE CITY OF THE BLUES: SICKLE CELL ANEMIA AND THE POLITICS OF RACE AND HEALTH 228 (2001).

86. TAPPER, *supra* note 84, at 92–93.

87. *Id.* at 106.

medical professionals at government-sponsored genetic counseling programs "work[ed] at the behest of the state, [they] were committed more to eliminating blacks than to eradicating the disease."[88]

By the 1970s, SCT carriers were denied educational opportunities,[89] as well as jobs with commercial airlines[90] and chemical companies,[91] and were disqualified from entrance into military academies.[92] Carriers also faced challenges in obtaining insurance.[93] Throughout the United States, states enacted laws that invaded the privacy of African Americans by mandating sickle cell testing in a paternalistic and intrusive manner. In 1971, the Massachusetts state legislature enacted a law that required blood tests for both SCT and SCD before a child could attend school.[94] Even more invasive, the California legislature passed a law in 1971 permitting the state's Public Health Department to require testing of black citizens "whenever appropriate."[95] Instead of promoting education and research for treatments, the laws passed brought

88. ALONDRA NELSON, BODY AND SOUL: THE BLACK PANTHER PARTY AND THE FIGHT AGAINST MEDICAL DISCRIMINATION 133 (2011).

89. *See, e.g.*, *id.* at 136 (describing the experience of a woman with sickle cell anemia who was denied admission to a nursing program after administrators learned of her medical condition).

90. TROY DUSTER, BACKDOOR TO EUGENICS 28 (2d ed. 2003) ("[A]lmost all of the major airlines grounded or fired their employees with sickle-cell trait in the early and mid-1970s."). As of 2014, "the Federal Aviation Administration (FAA) does not require screening for SCT, nor is SCT disqualifying for any class of FAA certificate." Bryant J. Webber & Catherine T. Witkop, Commentary, *Screening for Sickle-Cell Trait at Accession to the United States Military*, 179 MIL. MED. 1184, 1186 (2014). Additionally, in the 2008 clinical practice guideline, the Aerospace Medical Association did not recommend a universal screening for SCT for aviators. AM. SOC'Y OF AEROSPACE MED. SPECIALISTS, CLINICAL PRACTICE GUIDELINE FOR SICKLE CELL DISEASE/TRAIT (2008), http://www.asams.org/guidelines/Completed/NEW%20Sickle%20cell%20anemia.htm [https://perma.cc/5MGE-RJJ4].

91. In 1980, the DuPont Company admitted to "routinely" conducting preemployment blood screening of black candidates to determine SCT carrier status. Richard Severo, *Air Academy to Drop Its Ban on Applicants with Sickle-Cell Gene*, N.Y. TIMES (Feb. 4, 1981), https://www.nytimes.com/1981/02/04/us/air-academy-to-drop-its-ban-on-applicants-with-sickle-cell-gene.html [https://perma.cc/G2UM-M2JL]. While no data showed that carriers were at special risk in the chemical workplace, DuPont maintained that its screening was a service to employees, not a means for barring them from working. *Id.*

92. TAPPER, *supra* note 84, at 121–22.

93. *See* Severo, *supra* note 91. In a report commissioned by the National Academy of Sciences, the Committee for the Study of Inborn Errors of Metabolism stated "that although [SCT] carriers paid more for insurance with nine out of twelve companies, their mortality rates did not differ from those of blacks without the trait." *Id.*

94. DUSTER, *supra* note 90, at 41.

95. *Id.* at 51. A California state regulation mandated sickle cell screening of all blacks admitted to hospitals, regardless of reason for admission. *Id.* at 42.

"minimal health implications, capricious targeting of youthful carriers, and the associated stigmatization without treatment or counseling."[96] These laws thus provided no benefit and allowed great intrusion into the private lives of black Americans.

The October 1970 *Journal of the American Medical Association* ("*JAMA*") article authored by a white physician at Virginia Commonwealth University, Robert B. Scott, "boosted sickle cell anemia's visibility" in mainstream medicine and brought national attention to the disease.[97] The article highlighted striking disparities that existed in funding among genetic diseases.[98] For example, data from 1967 showed that diseases such as cystic fibrosis and muscular dystrophy, found predominately in populations of European descent, received nonpublic volunteer funding amounting to millions of dollars, whereas sickle cell anemia received only $100,000, even though all three diseases shared similar rates of incidence.[99] Further, at that time NIH-funded grants were reported to be less common for SCD than other rare genetic conditions.[100] Scott's widely read *JAMA* article is stated to have played a pivotal role in spurring politicians who vied to be credited with meeting the neglected health needs of black communities.[101] In 1972, Congress passed and President Nixon signed into law the National Sickle Cell Anemia Control Act, the first major U.S. law focused on SCD.[102] The law increased federal funding exponentially to expand SCD programs that developed research and educational materials relating to SCD;[103] it also made receipt of federal funding to states contingent upon sickle cell testing being voluntary.[104] In 1976, Congress passed a law requiring Veterans

96. *Id.* at 41.

97. NELSON, *supra* note 88, at 121.

98. Robert B. Scott, *Health Care Priority and Sickle Cell Anemia*, 214 JAMA 731, 731 (1970).

99. NELSON, *supra* note 88, at 124; Scott, *supra* note 98, at 731.

100. *Id.*

101. *Id.* at 123–25.

102. National Sickle Cell Anemia Control Act, Pub. L. No. 92-294, 86 Stat. 136 (1972) (codified as amended in scattered sections of 29 and 42 U.S.C.).

103. *Id.* at 138.

104. 42 U.S.C. § 300(a) (2012). The law was enacted in response to widespread genetic screening in the United States, purportedly aimed at exposing "poor health care systems by identifying carriers of sickle cell anemia" and designed to identify individuals who possessed the SCT, as well as SCD. Melinda B. Kaufmann, *Genetic Discrimination in the Workplace: An Overview of Existing Protections*, 30 LOY. U. CHI. L.J. 393, 402 (1999); *see also id.* at 402 n.65 ("[T]hese programs began with the best intentions, and were supported by African American leaders until they realized that such measures 'would be used to stereotype and disadvantage the very people they sought to help.'").

Administration hospitals to maintain the confidentiality of records relating to sickle cell anemia.[105]

In the 1970s, the African American community and organizations, such as the Black Panthers, embraced a complex agenda for genetic testing, prevention, care, and alleviation of the disease.[106] While stakeholders affiliated with the SCD and SCT community had separate and sometimes divergent political agendas,[107] alleviating human suffering appears to have been the common driving purpose behind efforts to bring recognition, funding, and progress to treatment of SCD.[108]

By the 1990s, however, many SCD patients experienced barriers to accessing comprehensive care and pain management.[109] For example, staff at hospital emergency rooms questioned the authenticity of pain associated with SCD, some arguing that providing pain relief for SCD community members would reward "drug-seeking" behavior.[110] This attitude enabled the narrative that those suffering from SCD were "a variant of the inner city drug addict stereotype."[111]

The year 1995 marked the first year of many where federal genetic discrimination legislation was introduced, and then languished, in Congress.[112] In 2000, testifying before the Senate Committee on Health, Education, Labor, and Pensions, then Director

105. Veterans Omnibus Health Care Act of 1976, Pub. L. No. 94-581, § 111(a)(1), 90 Stat. 2842, 2849 (codified as amended at 38 U.S.C. § 7332(a)(1) (2012)).

106. NELSON, *supra* note 88, at 118–19. Founded in Oakland, California, in 1966, the Black Panther Party's primary mission included community service and health promotion within the African American community. *Id.* at 1, 49.

107. *Id.* at 116, 148. Nelson argues that the Nixon administration's interest in SCD was "a calculated political strategy," motivated by a desire for black American votes. *Id.* at 148. Nelson also asserts that the Black Panther Party used SCD as a proxy to spotlight "the inequities of a profit-driven U.S. healthcare system sustained by publicly funded biomedical research" and as a "powerful symbol of [the Party's] affiliation with and service to African American communities." *Id.* at 116.

108. WAILOO, *supra* note 85, at 23 (contrasting the "compassion and awareness" the political campaigns of the 1970s brought with the stigmatization of the disease in 1990s politics); Roland B. Scott, *Reflections on the Current Status of the National Sickle Cell Disease Program in the United States*, 71 J. NAT'L MED. ASS'N 679, 679 (1979) (describing advances in sickle cell treatment as related to politics and pointing out that, as of the late 1970s, the advances were already at risk as sickle cell centers were already closing down).

109. Vani A. Mathur et al., *Multiple Levels of Suffering: Discrimination in Health-Care Settings Is Associated with Enhanced Laboratory Pain Sensitivity in Sickle Cell Disease*, 32 CLINICAL J. PAIN 1076, 1076–77 (2016).

110. WAILOO, *supra* note 85, at 23.

111. *Id.*

112. *See* Rep. Louise Slaughter, Essay, *Genetic Information Non-Discrimination Act*, 50 HARV. J. ON LEGIS. 41, 49–55 (2013).

of the National Human Genome Research Institute, Francis S. Collins, warned of the potential for "insidious discrimination" that, without protections in place, would undoubtedly grow from the Human Genome Project's successful decoding of 3.2 billion chemical letters that make up the human genome.[113] The African American community already had suffered discrimination and neglect in matters relating to work, health insurance, and the provision of medical care on numerous bases, including SCD and SCT status.[114] Community members had legitimate concerns that population genetic testing may expand discrimination.[115]

In 2003, President George W. Bush signed the Sickle Cell Treatment Act ("SCTA") into law as an amendment to the American Jobs Creation Act.[116] This law expanded community-based research and treatment grants for SCD, including the SCD Treatment Demonstration Program;[117] in 2009, however, authorization for the SCTA expired and there were no immediate laws enacted to reauthorize funding for programs established under the SCTA.[118]

For decades there has been an ebb and flow of commitment to the cause of those suffering from SCD. As noted earlier, in the late 1960s, when compared with private funding for diseases occurring at rates comparable to SCD but primarily affecting white communities—e.g., cystic fibrosis and muscular dystrophy—those diseases garnered greater funding than what was raised for SCD.[119] Laws and policies ostensibly intended to support research and treatment of those affected by SCD often encountered, and continue to encounter, obstruction from various fronts.[120] While these actions

113. *Genetic Information in the Workplace: Hearing before the S. Comm. on Health, Educ., Labor, & Pensions*, 106th Cong. (2000) (statement of Dr. Francis S. Collins, Director of the National Human Genome Research Institute), 2000 WL 1115522.

114. *See supra* notes 90–93 and accompanying text.

115. Dorothy E. Roberts, *The Nature of Blacks' Skepticism About Genetic Testing*, 27 SETON HALL L. REV. 971, 971–72 (1997).

116. American Jobs Creation Act of 2004, Pub. L. No. 108-357, § 712, 118 Stat. 1418, 1558–61 (codified as amended in scattered sections of 42 U.S.C.); *see also Examining Legislation to Improve Public Health: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 114th Cong. 32 (2016) (prepared statement of Sonja L. Banks, President, Sickle Cell Disease Association of America) [hereinafter *Examining Legislation to Improve Public Health*].

117. American Jobs Creation Act of 2004, § 712, 118 Stat. at 1558–61.

118. *Examining Legislation to Improve Public Health*, *supra* note 116, at 2.

119. Scott, *supra* note 98, at 731; *see also* NELSON, *supra* note 88, at 124 (outlining the obvious racial implications of underfunding for SCD).

120. DUSTER, *supra* note 90, at 61–62. Over the years, other groups began demanding federal funding for their own diseases, while others argued successfully for a single comprehensive bill covering all disorders. *Id.* at 62.

may not be deliberately aimed at marginalizing the SCD community, the effect may be experienced as such. For example, passage of the Sickle Cell Disease and Other Heritable Blood Disorders Research, Surveillance, Prevention, and Treatment Act of 2018 highlights Congress's commitment to push forward with research that will increase understanding of the "prevalence, distribution, outcomes, and treatments associated with SCD."[121] This law was originally drafted to exclusively focus on SCD; however, it was expanded before passage to include other blood disorders.[122] Still, the new law is beneficial in that "[i]t also reauthorizes SCD prevention and treatment grants awarded by the Health Resources and Service Administration (HRSA), and it authorizes the Centers for Disease Control and Prevention [('CDC')] to award SCD surveillance grants to states, academic institutions and nonprofit organizations."[123]

Though progress has been made at the federal level, some state laws specifically applicable to SCD remain on the books, and some of these laws invade genetic privacy rights of patients and the parents of those patients who have SCD or SCT.[124] In other instances, laws not

121. *The President Signs the Sickle Cell Treatment Act of 2018!*, SICKLE CELL DISEASE ASS'N AM., INC. (Dec. 19, 2018), https://www.sicklecelldisease.org/2018/12/19/the-president-signs-the-sickle-cell-treatment-act-of-2018/ [https://perma.cc/WV5J-NQFK].

122. *Compare* Sickle Cell Disease Research, Surveillance, Prevention, and Treatment Act of 2018, S. 2465, 115th Cong. (2018) (as proposed in Senate, Feb. 28, 2018), *with* Sickle Cell Disease and Other Heritable Blood Disorders Research, Surveillance, Prevention, and Treatment Act of 2018, S. 2465, 115th Cong. (2018) (proposed as an amendment in the nature of a substitute in Senate, Aug. 15, 2018) (amending the bill to, in effect, reduce the funds and available resources for SCD). The latter version was signed into law on December 18, 2018. *The President Signs the Sickle Cell Treatment Act of 2018!*, *supra* note 121.

123. *Id.*

124. DUSTER, *supra* note 90, at 62 ("While the federal law eliminated compulsion, it has also brought mass genetic screening into the sphere of routine public health activities. Given the fact that many screening laws have not actually been repealed and that compulsory screening programs might survive a court test, it is not frivolous to suggest that the current popularity of voluntary laws is no guarantee that mandatory programs will not someday be resumed."). By 1987, newborn screening was again mandatory in seven states. *Id.* As of 2007, routine state screening of newborns was universal throughout the United States, and as of 2025, "nearly all individuals enlisting in the military should have been previously screened." KENNETH LIN & MARY B. BARTON, U.S. DEP'T OF HEALTH & HUMAN SERVS., SCREENING FOR HEMOGLOBINOPATHIES IN NEWBORNS: REAFFIRMATION UPDATE FOR THE U.S. PREVENTIVE SERVICES TASK FORCE 1 (2007), https://www.ahrq.gov/downloads/pub/prevent/pdfser/sicklecelles.pdf [https://perma.cc/5647-LXN9]; *see also* SEC'Y'S ADVISORY COMM. ON HERITABLE DISORDERS IN NEWBORNS & CHILDREN, U.S. DEP'T OF HEALTH & HUMAN SERVS., SCREENING U.S. COLLEGE ATHLETES FOR THEIR SICKLE CELL DISEASE CARRIER STATUS 11–13 (2010), https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/reports/college-athletes-sickle-cell.pdf [https://perma.cc/Z5SN-9D6B]; Webber & Witkop, *supra* note 90, at 1188.

specifically focused on genetic information still play a critical role in protecting individuals with manifested or diagnosed medical conditions such as SCD.[125] As discussed later in this Article, for these individuals, federal protections under the Genetic Information Nondiscrimination Act of 2008 ("GINA") do not cover manifested or diagnosed genetic diseases.[126] Thus, case law specifically addressing the rights of those with SCD—even cases dating back to the 1980s—can be instructive and relevant in understanding current rights under the law.

C. Discrimination in the Military

Although the 1972 National Sickle Cell Anemia Control Act curtailed *state*-ordered mandatory testing, controversial practices based upon disputed scientific evidence continued to inform U.S. military policies that discriminated against SCT carriers. Such policies held that recruits with SCT would be barred from submarine service in the U.S. Navy and from serving as air crew members in the U.S. Army.[127] The death of four black Army recruits out of approximately four thousand between March 1968 and February 1969 at a moderate altitude (>4060) training camp led the National Academy of Sciences and National Research Council to request, and the U.S. Department of Defense ("DoD") to organize, a committee to investigate and make recommendations.[128] In 1970, the Military Aviation Safety Subcommittee determined that data on clinical outcomes associated with SCT carrier status were inadequate but nevertheless recommended screening for both the trait and disease in all recruits "regardless of race."[129] Additionally, the committee recommended limitations on SCT carriers' military activities, such as in "aviation, diving, special forces [assignments] and high-altitude parachuting."[130] However well intentioned the committee's recommendations were,

125. For examples of discrimination in the workplace and the use of ADA and section 504 of the Rehabilitation Act where the Genetic Information Nondiscrimination Act of 2008 would otherwise not have provided protection against discrimination of a manifested genetic condition, see *infra* Section III.D.

126. *See infra* Section V.B.2.

127. Severo, *supra* note 91.

128. DUSTER, *supra* note 90, at 26–27; Mauricio De Castro et al., *Genomic Medicine in the Military*, 1 GENOMIC MED., no. 15008, Jan. 13, 2016, at 1, 1; V.M. Voge, N.R. Rosado & J.J. Contiguglia, *Sickle Cell Anemia Trait in the Military Aircrew Population: A Report from the Military Aviation Safety Subcommittee of the Aviation Safety Committee, AsMA*, 62 AVIATION, SPACE & ENVTL. MED. 1099, 1100 (1991).

129. DUSTER, *supra* note 90, at 27; De Castro et al., *supra* note 128, at 2.

130. De Castro et al., *supra* note 128, at 2.

the investigation lacked "essential controls and comparisons."[131] Though largely based on mere observation of frequencies—inviting the hazard "of spurious relations and false conclusions"[132]—the committee's recommendations were implemented "by all branches of the U.S. military in 1973."[133] At the time, many scientists and physicians believed that restrictions relating to those carrying SCT are "a senseless stigma and an unscientific suggestion that their genes are somehow inferior."[134]

1. U.S. Air Force Academy Prohibitions and Successful Challenge

Following the committee's recommendations, the U.S. Air Force ("USAF") Academy adopted a policy of excluding blacks who carried SCT.[135] This policy was applied only to the elite Air Force Academy—the Air Force Reserve Officers' Training Corps ("ROTC") scholarship program did "not disqualify blacks from general enlistment or from being commissioned."[136]

Stephen Pullens, a former state champion high hurdler and four-sport star athlete and mountain climber, passed the Air Force Academy's pilot qualifying exam, including a physical examination, before reporting to the school in July 1979.[137] After a blood test revealed Pullens's SCT carrier status, he was forced to leave the Academy.[138] The Air Force argued that it had legitimate interests in screening future and current pilots for health problems.[139] Sociologist Troy Duster contends that the Air Force's position that SCT-carrying pilots would pose potential risks to others or would themselves experience heightened risks indicates that Pullens's dismissal presented yet another instance of "appropriated genetic explanation"

131. DUSTER, *supra* note 90, at 27.

132. *Id.*

133. Voge et al., *supra* note 128, at 1100.

134. Severo, *supra* note 91.

135. DUSTER, *supra* note 90, at 28.

136. *Air Force Academy Sued over Sickle Cell Policy*, N.Y. TIMES (Jan. 4, 1981), https://www.nytimes.com/1981/01/04/us/air-force-academy-sued-over-sickle-cell-policy.html [https://perma.cc/9CMY-3624].

137. *Id.* The complaint cited to then-General Air Force Regulation 60-43, 5-11, which stated that SCT carrier status would not disqualify an individual from entering military service because those with the trait show no handicapping symptoms at altitudes above 10,000 feet or under physical stress, and rarely experience complications. *Id.* The complaint alleged that Pullens was never tested to ascertain if he could handle such stresses and that the Academy's and Air Force's regulations conflicted and denied due process and equal protection of the law. *Id.*

138. *Id.*; *see also* DUSTER, *supra* note 90, at 28.

139. Severo, *supra* note 91.

unsupported by research.[140] In the context of numerous discriminatory and stigmatizing actions taken in the name of unproven dangers of SCT, the Air Force Academy screening policy appeared to be "set up only to block, not to provide the grounds for further empirical investigation."[141]

In 1980, with support from the NAACP, Pullens sued the U.S. Air Force in the U.S. District Court for the District of Minnesota.[142] By early 1981, the case was settled, and the Air Force Academy eliminated its ban on SCT-carrying airmen.[143] A new policy made "[c]andidates for the Air Force Academy who [had SCT] . . . eligible for admission, provided they [were] otherwise medically qualified and [met] the standard entrance requirements."[144] Pullens met all of the requirements.[145]

2. Different Branches, Different Practices

In 1981, all U.S. military services permitted those with SCT to be assigned to aviation duties with only limited restrictions.[146] During this time, the DoD required screening of all new service members but only restricted the activities of those servicemen who tested as greater than 41% sickle hemoglobin ("HbS").[147] Under the DoD directive, the various branches undertook a number of different initiatives to gather information, monitor, study, and compile and compare data regarding SCT-carrying service members and control individuals.[148] By 1985, "the DoD eliminated the [>41% HbS] cutoff," removing all restrictions for SCT carriers in occupational specialties.[149]

Again in the 1990s, after three USAF recruit deaths, the Armed Forces Epidemiology Board revisited the possibility of specialty restrictions for SCT carriers, recommended against SCT screening, and instead recommended heat injury prevention.[150] In 1996, the DoD

140. DUSTER, *supra* note 90, at 28.

141. *Id.* at 30.

142. Pullens v. U.S.A.F., No. 4-80 Civil 595 (D. Minn. July 21, 1981) (on file with the North Carolina Law Review).

143. Severo, *supra* note 91.

144. *Id.* (reporting statements made by the Air Force Surgeon General, Lieutenant General Paul W. Myers); *see also* Webber & Witkop, *supra* note 90, at 1185 (describing the DoD's policy that dropped the occupational restrictions on SCT service members and also mandated SCT screening).

145. *See* Severo, *supra* note 91.

146. Voge et al., *supra* note 128, at 1100.

147. Webber & Witkop, *supra* note 90, at 1185.

148. Voge et al., *supra* note 128, at 1100–01.

149. Webber & Witkop, *supra* note 90, at 1185.

150. *Id.*

updated Instruction 6465.1 to eliminate the mandated Hemoglobin S testing for SCT in all military accessions.[151] And yet, as of 2014, the Air Force, Navy, and Marine Corps continued to "screen all accessions for disqualifying hemoglobin disorders and mandat[ed] dismissal of all individuals whose HbS concentration exceed[ed] 45%[, and although t]he Army selectively screen[ed] individuals entering certain military occupational specialties (e.g., aviation, diving, and special operations)," the Army did not "consider SCT a disqualifying condition."[152] Practices at service academies have continued to vary with no cohesive policies in place.[153]

The U.S. military's approach to addressing SCT in recruits clearly remains unsettled.[154] A 1987 study found that SCT was associated with a higher risk of exercise-related sudden death.[155] A 2016 study of military recruits did not find an association between a higher risk of exercise-related sudden death for those with SCT as opposed to other recruits; it did find a significantly higher risk of exertional rhabdomyolysis in recruits with the trait.[156] A 2018 systematic review of the clinical literature found moderate evidence that in high-exertional exercise settings there is a risk of exertional rhabdomyolysis in those with SCT, but there is insufficient evidence to support a risk of sudden death.[157] The study stated that prospective large-scale research studies to understand the clinical risk associated with SCT are needed.[158] Today, the need persists for research to protect the safety of recruits with SCT and the development of uniform service-wide policies based on rigorous empirical studies. As reported in 2014,

> [t]he USAF, Navy, and Marine Corps provid[ed] group-based counseling for SCT+ recruits early in basic training, but interventions differ[ed]: USAF recruits [would] wear a white armband at all times throughout training; Navy recruits [would] wear a red belt or red dog tag during exercise; and Marine Corps recruits [were] not publicly identified.[159]

151. *Id.*
152. *Id.*
153. *Id.*
154. *See* De Castro et al., *supra* note 128, at 4.
155. John A. Kark et al., *Sickle-Cell Trait as a Risk Factor for Sudden Death in Physical Training*, 317 NEW ENG. J. MED. 781, 781 (1987).
156. D. Alan Nelson et al., *Sickle Cell Trait, Rhabdomyolysis, and Mortality Among U.S. Army Soldiers*, 375 NEW ENG. J. MED. 435, 436 (2016).
157. Naik et al., *supra* note 73, at 625.
158. *Id.*
159. Webber & Witkop, *supra* note 90, at 1185.

While the military has a significant interest in quickly identifying genetic traits of recruits for health and safety purposes,[160] the branches should be cognizant of potential discrimination.

D. Discrimination in the Workplace

Employees affected by discrimination or stigma based on actual or perceived sickle cell status have attempted to assert their legal rights. A few standout sickle cell cases have helped to raise awareness of discriminatory practices and have been elevated to the national stage for use in informing and shaping federal law and policy.

A seminal genetic discrimination case, *Norman-Bloodsaw v. Lawrence Berkeley Laboratory*,[161] considered whether an employee "may, without [his/her] knowledge [or consent], be tested for highly private and sensitive medical and genetic information," such as SCT, during a general employee physical.[162] This case is frequently cited in genetic discrimination literature and was specifically referenced in the "Findings" section of GINA.[163] As the first class action case alleging discrimination and invasion of privacy in relation to genetic testing in the workplace, *Norman-Bloodsaw* represents the reality of everyday genetic discrimination in the workplace before passage of GINA, the federal legislation intended to protect employees.[164] The case is still influential in circumstances where genetics protections under federal and state law are lacking.[165]

In *Norman-Bloodsaw*, the employer was a federal contractor with the U.S. Department of Energy, and the named defendants were sued in both their official and individual capacities.[166] All but one of

160. "The military has a legitimate interest in obtaining information about warfighters' physical and mental abilities, including genomic information, but only if the genomic test is a valid indicator of what it purports to show and the information is necessary in order to carry out the mission." De Castro et al., *supra* note 128, at 3.

161. 135 F.3d 1260 (9th Cir. 1998).

162. *Id.* at 1264.

163. 42 U.S.C. § 2000ff cmt. 4 (2012) (Legislative Findings) ("Congress has been informed of examples of genetic discrimination in the workplace. These include the use of pre-employment genetic screening at Lawrence Berkeley Laboratory, which led to a court decision in favor of the employees in that case[.] Norman-Bloodsaw v. Lawrence Berkeley Laboratory (135 F.3d 1260, 1269 (9th Cir. 1998)). Congress clearly has a compelling public interest in relieving the fear of discrimination and in prohibiting its actual practice in employment and health insurance.").

164. Elizabeth Pendo, *Race, Sex, and Genes at Work: Uncovering the Lessons of* Norman-Bloodsaw, 10 HOUS. J. HEALTH L. & POL'Y 227, 230 (2010).

165. *Id.* at 229 ("[G]enetic testing of workers occurs and is likely to continue even after GINA, and the gathering and use of genetic information in the workplace is not neutral and often exacerbates long-standing patterns of discrimination based on race and sex.").

166. *Norman-Bloodsaw*, 135 F.3d at 1264.

the plaintiffs were individuals who had "received written offers of employment expressly conditioned upon a 'medical examination,' 'medical approval,' or 'health evaluation.'"[167] In the process of completing medical history questionnaires and providing blood and urine samples, the plaintiffs were asked if they had any of sixty-one medical conditions, including sickle cell anemia.[168] Thereafter, blood samples were tested for SCT, without notice or consent, and allegedly this testing was only conducted on samples from black employees.[169]

In 1995 the plaintiffs obtained an Equal Employment Opportunity Commission ("EEOC") right-to-sue letter on behalf of both past and present employees who were at any time subjected to the testing at issue.[170] Specifically, the plaintiffs alleged that the defendants violated: (1) the Americans with Disabilities Act of 1990 ("ADA") by "requiring, encouraging, or assisting in medical testing that was neither job-related nor consistent with business necessity"; (2) the constitutional right to privacy under both federal and California law; and (3) "Title VII by singling out black employees for [SCT] testing."[171] After the district court dismissed all claims, the plaintiffs filed an appeal in the Ninth Circuit.[172] Ultimately, the appellate court affirmed the dismissal of the ADA claims but reversed on the Title VII and the federal and state privacy claims under the U.S. and California Constitutions.[173]

With regard to SCT, the appellate court stated that carrier status pertains to "sensitive information about family history and reproductive decision making," and these were "aspects of one's health in which one enjoys the highest expectations of privacy."[174] The appellate court further found that the alleged discrimination fell "neatly into a Title VII framework," namely that the plaintiffs had alleged "that black . . . employees were singled out for additional nonconsensual testing and that defendants thus selectively invaded

167. *Id.* at 1264–65. The employer represented that the program's objectives were "to protect employees from possible health hazards in their work environment; to assure placement in work that can be performed in a reliable and safe manner; to promote early detection, treatment and rehabilitation; and to apply preventative medical measures toward the maintenance of good physical and mental health . . . ." Pendo, *supra* note 164, at 232 (quoting Brief of Defendants–Appellees, Norman–Bloodsaw v. Lawrence Berkeley Lab., 135 F.3d 1260 (9th Cir. 1998) (No. 96-16526), 1997 WL 33633545, at *9–10).

168. *Norman-Bloodsaw*, 135 F.3d at 1265.

169. *Id.*

170. *Id.*

171. *Norman-Bloodsaw*, 135 F.3d at 1265–66.

172. *Id.* at 1266.

173. *Id.* at 1275.

174. *Id.* at 1270.

the privacy of certain employees on the basis of race."[175] Although the district court held that the tests were not a condition of employment, the Ninth Circuit found that, since "the preplacement exams were, literally, a condition of employment," the fact that the preplacement exam tested black employees for SCT made it a condition of employment.[176]

The parties reached a settlement in this case under which Lawrence Laboratories paid $2.2 million to the plaintiffs.[177] Further, Lawrence Laboratories agreed to implement new procedures that would prohibit employee testing without informed consent and provide employees opportunities to review their medical records.[178] Lawrence Laboratories also offered to expunge from the medical records any testing information—positive or negative—relating to SCT.[179]

Additionally, in *Fleming v. State University of New York*,[180] a plaintiff's SCD became the center of employment litigation involving an aspiring young doctor. Dr. Lester Fleming, an anesthesiologist, had recently completed his residency at the State University of New York ("SUNY") and was seeking permanent employment at the Yuma Regional Medical Center in Arizona ("Yuma").[181] After Yuma and Dr. Fleming entered into an employment contract, Yuma began a credentialing process that included inquiries with Dr. Fleming's former employers.[182] During this process, the SUNY residency program director disclosed Dr. Fleming's SCD to Yuma.[183] After confirming this diagnosis with Dr. Fleming's hematologist, Yuma informed Dr. Fleming that he should seek employment elsewhere.[184] Yuma modified Dr. Fleming's employment offer, adding the requirement that he sign an acknowledgement stating that, if he were to fall ill, Yuma was not able to provide him a reasonable accommodation for his operating room and call schedules.[185] Dr.

175. *Id.* at 1272.
176. *Id.*
177. Pendo, *supra* note 164, at 246.
178. *Id.*
179. *Id.*
180. 502 F. Supp. 2d 324 (E.D.N.Y. 2007).
181. *Id.* at 327.
182. *Id.*
183. *Id.*
184. *Id.*
185. *Id.*

Fleming refused to sign the contract addendum and characterized the added requirement as constructive termination in his lawsuit.[186]

The district court found merit in Dr. Fleming's claim under section 504(d) of the Rehabilitation Act because section 504 adopts the ADA's Title I provision that declares: "No covered entity shall discriminate against a qualified individual with a disability because of the disability of such individual in regard to job application procedures, the hiring, advancement, or discharge of employees, employee compensation, job training, and other terms, conditions, and privileges of employment."[187] The defendants—Dr. Fleming's former employers—had described Dr. Fleming as a person suffering from sickle cell anemia, thus classifying him as a person with a disability; this classification, in turn, adversely affected his opportunities to work as an anesthesiologist.[188]

Further, citing Second Circuit precedent, the district court asserted that an individual's constitutional right to privacy in his health status protects information about "'serious medical condition[s],' especially those that are likely to provoke . . . 'discrimination and intolerance.'"[189] Finding that sickle cell anemia is such a disease with "the potential to provoke intolerance and discrimination," the court rejected SUNY's contention that sickle cell anemia "falls far short of the 'excruciatingly private and intimate' medical conditions that inevitably provoke 'hostility and intolerance from others.'"[190] The court noted that, while there are few reported cases of discrimination based on sickle cell anemia, "a history of such discrimination exists"[191] and found that Dr. Fleming's Fourteenth Amendment right to privacy in health information did, indeed, entitle him to confidentiality regarding his sickle cell anemia.[192]

Two years later, Dr. Fleming was before the Ninth Circuit in his lawsuit against Yuma.[193] There, and in the underlying case, he alleged

186. *Id.*

187. *Id.* at 336.

188. *Id.* at 337.

189. *Id.* at 342 (first alteration in original) (quoting Doe v. City of New York, 15 F.3d 264, 267 (2d Cir. 1994)). While *Doe* involved the confidentiality of HIV status, the *Fleming* court stated: "The holding of *Doe* thus plainly applies to [SCD], which, while arguably less likely than HIV to provoke discrimination and intolerance, nonetheless may do so, and indeed has done so in the past." *Id.* at 345. The *Fleming* court also noted that malice or bad intent in the disclosure of such private information was not a prerequisite to establishing an actionable claim. *Id.*

190. *Id.*

191. *Id.* at 343.

192. *Id.*

193. Fleming v. Yuma Reg'l Med. Ctr., 587 F.3d 938 (9th Cir. 2009).

that Yuma's refusal to accommodate his operating and call schedules due to his sickle cell anemia constituted a breach of employment contract and disability discrimination in violation of the Rehabilitation Act of 1973.[194] The district court had granted Yuma's motion for summary judgment, finding that the Rehabilitation Act was inapplicable.[195] The Ninth Circuit reversed,[196] and the Supreme Court denied Yuma's petition for writ of certiorari.[197]

E. Discrimination in Provision of Medical Care

Avery v. County of Burke[198] is an important example of how status as a sickle cell carrier has been used to justify extreme, unnecessary, and ill-informed decisionmaking in the provision of medical care. In this case, the Fourth Circuit vacated the lower court's entry of summary judgment against a fifteen-year-old woman, Virginia Ann Avery, who was told by state employees that she had SCT and was then advised to undergo a sterilization procedure.[199] The state clinic's nurses and doctor "told Avery and her mother that because Avery had [SCT], childbirth would either immediately endanger her life" or shorten it by "two or three years,"[200] and that pregnant women with SCT are more "susceptible to numerous diseases."[201] Based on these representations, Virginia Avery and her

194. *Id.* at 940. Section 504(a) of the Rehabilitation Act of 1973 creates a private right of action for individuals subjected to disability discrimination by any program or activity receiving federal financial assistance. 29 U.S.C. § 794a(a)(2) (2012).

195. *See Fleming*, 587 F.3d at 940. Yuma had argued that it was not subject to requirements of the Rehabilitation Act because the anesthesiologist position at issue was that of an independent contractor. *See id.*

196. *See id.* at 939 (holding that section 504 of "the Rehabilitation Act [does in fact] cover[] discrimination claims by an independent contractor"). Furthermore, the Ninth Circuit found "[t]he Rehabilitation Act covers any 'otherwise qualified individual' who has been 'excluded from the participation in, or denied the benefits of, or . . . subjected to discrimination under any program or activity receiving Federal financial assistance.'" *Id.* at 941–42 (second alteration in original) (quoting 29 U.S.C. § 794(a) (2012)). Thus, the Act "covers 'all of the operations' of covered entities, not only those related to employment." *Id.* at 942 (quoting 29 U.S.C. § 794(b) (2012)).

197. Fleming v. Yuma Reg'l Med. Ctr., 561 U.S. 1006 (2010). As of 2019, Doctor Fleming is a successful anesthesiologist practicing in the state of Virginia. *Dr. Lester Fleming*, U.S. NEWS & WORLD REP., https://health.usnews.com/doctors/lester-fleming-191363 [https://perma.cc/H298-8QU9 (staff-uploaded archive)].

198. 660 F.2d 111 (4th Cir. 1981).

199. *Id.* at 113.

200. *Id.* The Fourth Circuit observed that SCT "is the carrier gene state of sickle cell syndrome which *exclusively* affects black people." *Id.* (emphasis added). Additionally, both nurses involved in "Avery's sterilization testified that they had no special training in handling sickle cell cases." *Id.* at 115.

201. *Id.* at 113.

mother consented to sterilization and a North Carolina state court authorized the procedure.[202] Subsequent to her sterilization,[203] Avery underwent additional testing that showed she did *not* have SCT.[204] This case represents an example of paternalism, fear tactics, and possibly deliberate malfeasance in order to control a black woman's reproductive choices.

Under 42 U.S.C. § 1983, Avery brought suit against the County Board of Health and County Board of Social Services, alleging violations of her Fourteenth Amendment rights of privacy and procreation.[205] She argued that "she was wrongfully sterilized because she did not have [SCT] and because sterilization is not medically recommended or proper, even when there has been a correct diagnosis of the trait."[206] After having been pressured into submitting to the sterilization procedure so she could not bear children, Avery's claims were dismissed by the U.S. District Court for the Western District of North Carolina.[207] The Fourth Circuit Court of Appeals revived the case, stating, "It is not essential . . . [to] show that all persons suspected of having [SCT] have been mistreated [by the county]. It is enough that an identifiable group of people . . . is subject to constitutional deprivations through the inaction of the boards."[208] The *Avery* case is just one more example of the legacy of discrimination against those in the SCD and SCT community, as well as those perceived as belonging to that community.

IV. COMMUNITY ENGAGEMENT IS VITAL IN PREVENTING PERPETUAL HEALTH INEQUITIES

While SCT and SCD community members remain optimistic, the legacy of discrimination informs and heightens their uneasiness and apprehension about inequitable access to curative genetic treatments that the community, by participating in human genome-editing technology research, will have brought to fruition. As seen in the

202. *Id.*
203. *Id.* at 112.
204. *Id.*
205. *Id.*
206. *Id.*
207. *Id.*
208. *Id.* at 114 (citing Withers v. Levine, 615 F.2d 158, 161 (4th Cir. 1980), *abrogated by* Moore v. Winebrenner, 927 F.2d 1312 (4th Cir. 1991)) ("North Carolina law required both [the health and social services] boards to supervise their employees and to promulgate guidelines and policies to protect the health and well-being of the citizens of the county.").

Persaud-Bonham study,[209] members of the SCD community, their families, and their physicians have voiced a concern that the SCD community may participate in the clinical trials and then not benefit equitably from advances in gene-editing technology.[210] The National Academies of Sciences, Engineering, and Medicine 2017 Report on Human Genome Editing concluded that "extensive and inclusive public participation should precede clinical trials for any extension of human genome editing *beyond treatment or prevention of disease or disability*."[211] The report further stated that "[p]ublic participation should be incorporated into policy-making process[es] for human genome editing and should include ongoing monitoring of public attitudes, informational deficits, and emerging concerns about issues surrounding 'enhancement.'"[212] This Article contends that public engagement and opinions are required not just for use of genome editing for enhancement and germline alterations but for treatment to prevent or cure disease and lessen disabling consequences of disease.

Due in part to the uncertainty related to the long-term impact of gene editing, and the legacy of discrimination experienced by the SCD community, participants in the Persaud-Bonham study emphasized the need for absolute transparency by government and biomedical researchers with respect to the development of clinical trials. Study participants all wanted the government and researchers to respect the community's views and to meaningfully engage the community in the development of clinical trials. A patient in the study articulated this point, stating: "We need a seat at the table. When this clinical trial is going on and you've got the researchers setting up protocols, setting up how it is going to work—advocacy, [Community Based Organization] . . . people that have sickle cell, need to be involved in every aspect of the trial."

In some respects, the study participants provided strategies for how these goals could be met, including (1) partnerships with brokers of trust within the community, (2) development of clear and effective educational tools, (3) dissemination of information relevant to the prospective participants through social media and other commonly used communication platforms, and (4) a commitment to dedicating resources to advance the treatment and care of SCD patients

209. Persaud et al., *supra* note 69, at 7. In this section, further discussion of "the study" also refers to the Persaud-Bonham study. *See supra* Section II.C.

210. *See supra* Section II.C.

211. *See* NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 5, at 178 (emphasis added).

212. *Id.*

regardless of whether the fruits of gene editing come to bear. Physicians, on the other hand, stressed being clear about the limitations of gene editing, avoiding both explicit and implicit coercion, and walking the path carefully to prevent further alienation of the community. One physician offered the following comments:

> I would say don't mess it up . . . if you are really talking about it impacting the sickle cell population, you have to be very careful that the other rare diseases that have more resources don't take it over and the sickle cell population gets left in the dust. [Sickle cell patients] have been left in the dust with so many other things that they already are skeptics.

All three stakeholders—patients, parents, and physicians—were concerned that access to gene-editing treatments in the future would comprise a huge impediment to care and warned against using the community as a means to an end.

Systematic public engagement of the disease communities in developing gene-editing clinical trials and public education resources is necessary. This engagement should not be limited to the most controversial uses of the new technology, e.g., germline gene editing or genetic enhancement; it is equally essential for uses related to somatic gene editing for treatment and prevention of disease. The equitable access to curative genetic therapies—like gene therapy and gene editing—requires public input to guide public policy. Especially when the disease—like SCD—is surrounded by a history of abuse and neglect.

V. LEGAL PROTECTIONS OF INDIVIDUALS' GENETIC INFORMATION

Though the SCD and SCT community has experienced ongoing discrimination, Congress has endeavored to create meaningful protections. This section considers GINA and the protections, and lack thereof, which it provides to the historically undermined and marginalized SCD and SCT community. Prior to GINA's enactment, there were up to 500 documented cases of genetic discrimination in the United States.[213] Without a law specifically guarding against this discrimination, laws such as Title VII of the Civil Rights Act of 1964,[214] the Americans with Disabilities Act of 1990,[215] section 504 of

213. Ifeoma Ajunwa, *Genetic Data and Civil Rights*, 51 HARV. C.R.-C.L. L. REV. 75, 77–78 (2016).

214. With all the protections Title VII affords, this law makes no mention of genetic information or health information. *See* Slaughter, *supra* note 112, at 47.

the Rehabilitation Act of 1973, and the Health Insurance Portability and Accountability Act of 1996 ("HIPAA")[216] sometimes provided recourse and remedies for those suffering from discrimination based on genetic information or disease. However, when these earlier federal employment, antidiscrimination, and health-care privacy laws were enacted, the potential for genetic knowledge and the discriminatory implications and ramifications of genetic testing could

215. Carriers of genetic mutations who do not have or exhibit a symptomatic disorder are not explicitly covered by the ADA. Slaughter, *supra* note 112, at 47–48. A 1995 Guidance issued by EEOC advised employers to refrain from taking action against otherwise healthy employees and applicants based on the presence of genetic mutations that may have predisposed the employee or applicant to disease. *Id.* at 48. But guidance is just that—guidance, not law. *See id.* Still, guidelines do "constitute a body of experience and informed judgment to which courts and litigants may properly resort for guidance." Skidmore v. Swift & Co., 323 U.S. 134, 140 (1944).

Unlike Title VII and the ADA, GINA lacks a disparate impact liability provision. *See* 42 U.S.C. § 2000ff-7(a)–(b) (2012) (recognizing that allegations of disparate impact on the basis of genetic information does not establish cause of action under GINA); 29 C.F.R. § 1635.5(b) (2018); Ajunwa, *supra* note 213, at 84. However, this could change because, though GINA was not intended to address specific protected classes, under 42 U.S.C. § 2000ff-7(b), GINA requires that

> [o]n the date that is 6 years after May 21, 2008, there shall be established a commission, to be known as the Genetic Nondiscrimination Study Commission (referred to in this section as the "Commission") to review the developing science of genetics and to make recommendations to Congress regarding whether to provide a disparate impact cause of action under this Act.

§ 2000ff-7(b). This should have occurred in May 2014, but it still has not. Ajunwa, *supra* note 213, at 86–87, 87 n.74. Ajunwa suggests that the increased protection afforded by disparate impact theory is needed to extend GINA's reach where a plaintiff is unable to obtain "actual evidence of genetic discrimination." *Id.* at 105. Ajunwa offers the following four reasons that support addition of a disparate impact clause to GINA:

> (1) [the] theory . . . is in line with the precedent set by prior employment discrimination laws; (2) the EEOC has declared that proof of deliberate acquisition of genetic information is not necessary to establish a violation of GINA, and proof of intent to discriminate likewise should not be required to demonstrate genetic discrimination; (3) ease of access to genetic testing and the insecurity of genetic information has increased the likelihood of genetic discrimination in employment; and (4) real world instances of genetic testing have shown that facially neutral testing may result in racial disparities.

Id. at 100.

216. HIPAA prohibits health insurance companies from assessing higher premiums for unwell individuals within an employer-sponsored group policy, or from excluding preexisting conditions; however, the group *as a whole* can be charged higher premiums. *See* Slaughter, *supra* note 112, at 48. Therefore, there is a disincentive for employers to hire potential employees who might be perceived as more likely to need medical care and/or to be carrying genetic mutations. *See* Ajunwa, *supra* note 213, at 89. This disincentive may work against women of childbearing age, older workers, and those who fit race-based assumptions about health conditions such as SCT and SCD.

not be fully envisioned.[217] GINA's drafters incorporated instructions to close certain gaps in protections.[218] For example, as required by GINA, 2013 revisions to the HIPAA Privacy Rule added that genetic information is Protected Health Information ("PHI") covered by the Privacy Rule, to the extent that such information is individually identifiable.[219] Further, HIPAA-covered entities may not use or disclose protected genetic information for underwriting purposes.[220] The Patient Protection and Affordable Care Act of 2010 ("ACA") filled additional gaps, and as of January 1, 2014, patients with preexisting conditions, like SCD, could no longer be denied health insurance coverage.[221] In addition, prophylactic measures such as pneumonia and influenza vaccinations—which are important for people living with SCD—are currently covered as preventative services.[222] However, if successful, recent attempts to dismantle the ACA will undo the law's preexisting conditions protections.[223]

A. The Need for Protections Spurs GINA

In the 1990s, genomic science was growing exponentially. As scientists, policymakers, and legislators realized the obvious clinical relevance of genomic medicine, they also understood that research participation by individuals to benefit our collective health would be met by fear that genetic research study participants would subsequently encounter genetic discrimination in the health insurance

217. Slaughter, *supra* note 112, at 42.

218. *Id.* at 42, 48.

219. 45 C.F.R. § 164.502(a)(5)(i) (2018).

220. *Privacy in Genomics*, NIH: NAT'L HUM. GENOME RES. INST. (Apr. 21, 2015), https://www.genome.gov/27561246/privacy-in-genomics/ [https://perma.cc/5Q98-SABK]. No such restrictions attach to the use or disclosure of PHI that has been de-identified. *Id.* De-identification is often impermanent, due to insufficient proactive protections, and the documented ability of computer science hackers to re-identify previously de-identified information. Mats G. Hansson et al., *The Risk of Re-Identification Versus the Need to Identify Individuals in Rare Disease Research*, 24 EUR. J. HUM. GENETICS 1553, 1553 (2016).

221. Patient Protection and Affordable Care Act, 42 U.S.C. § 18001(a), (d) (2012).

222. Cara V. James, *On the Path to Health Equity: Improving the Quality of Sickle Cell Disease Care*, CMS.GOV: CMS HEALTH EQUITY BLOG (Sept. 22, 2016), https://www.cms.gov/About-CMS/Agency-Information/OMH/about-cms-omh/blog/sickle-cell-disease-care.html [https://perma.cc/FVV4-CA5Z].

223. Laura Hercher & Anya E.R. Prince, *Gene Therapy's Field of Dreams: If You Build It, Will We Pay?*, 97 N.C. L. REV. 1463, 1491 (2019). A recent victory for those who oppose the ACA came in *Texas v. United States*, 340 F. Supp. 3d 579 (N.D. Tex. 2018), when the Northern District of Texas issued a decision declaring the ACA unconstitutional. *Id.* at 619. Sixteen states and the District of Columbia, intervenors in the action, have appealed and continue to defend the ACA. Notice of Appeal at 1–2, Texas v. United States, 340 F. Supp. 3d. 579 (N.D. Tex. 2018) (No. 4:18-CV-00167-O).

sector and the workplace.[224] In fact, 92% of Americans were concerned that results of genetic testing might be used for harmful purposes.[225] Despite the uncertainty and complexity of genetic testing, some employers and health insurers perceived a benefit from obtaining genetic information.[226] Reforms were urgently needed to address citizens' concerns about the real threats of workplace and health insurance discrimination.[227] Senator Edward Kennedy, a GINA cosponsor in the Senate, aptly stated: "Discrimination in health insurance and the fear of potential discrimination threaten both society's ability to use new genetic technologies to improve human health and the ability to conduct the very research we need to understand, treat, and prevent genetic disease."[228]

As researchers worked to harness the potential of genetic medicine to improve understanding of diseases and develop new, personalized treatments, legislators began efforts to craft protections against genetic discrimination.[229] In deliberating the need for a federal law that would protect private citizens from genetic discrimination, Congress considered evidence of targeted genetic discrimination against individuals in minority populations who carried genes associated with a specific genetic disease or risk; SCD among African Americans was one such disease.[230] After years of diligence and

224. *See* Kathy L. Hudson, M.K. Holohan & Francis S. Collins, *Keeping Pace with the Times – The Genetic Information Nondiscrimination Act of 2008*, 358 NEW ENG. J. MED. 2661, 2661, 2663 (2008); *see also Protecting Workers from Genetic Discrimination: Hearing Before the Subcomm. on Health, Emp't, Labor & Pensions of the H. Comm. on Educ. & Labor*, 110th Cong. 33 (2007) [hereinafter *Protecting Workers from Genetic Discrimination*] (prepared statement of Karen H. Rothenberg, Dean and Marjorie Cook Professor of Law, University of Maryland School of Law) ("The tremendous promise of genomics is hamstrung by fear."); Kathy L. Hudson, *Prohibiting Genetic Discrimination*, 356 NEW ENG. J. MED. 2021, 2022 (2007) (explaining that fear of genetic discrimination also stymied patients' willingness to undergo genetic tests recommended by their physicians or have results of such tests included in their medical records).

225. *Protecting Workers from Genetic Discrimination*, *supra* note 224, at 11 (prepared statement of the Hon. Louise McIntosh Slaughter).

226. Slaughter, *supra* note 112, at 44; *see also Genetic Non-Discrimination: Examining the Implications for Workers and Employers: Hearing Before the Subcomm. on Emp'r-Emp. Relations of the H. Comm. on Educ. & the Workforce*, 108th Cong. 71 (2004) [hereinafter *Genetic Non-Discrimination*] (statement of National Workrights Institute) ("In a 2001 survey of U.S. firms almost 2% were currently conducting genetic tests for Sickle Cell and Huntington's Disease, 14% were acquiring genetic information during workplace susceptibility testing and 20% reported requesting family medical histories containing information on the likelihood of disease.").

227. *See* Hudson et al., *supra* note 224, at 2661.

228. *Id.* at 2662.

229. *See id.*

230. Expert Report of Paul A. Lombardo at 4, Lowe v. Atlas Logistics Grp. Retail Servs., No. 1:13-cv-02425-AT (N.D. Ga. June 5, 2015), ECF No. 70.

determination, GINA was signed into law by President George W. Bush.[231] Senator Edward Kennedy proclaimed GINA "the first major new civil rights bill of the new century."[232]

B. GINA's Protections

GINA's purpose is to "'establish[] a . . . uniform . . . standard' of *un*acceptable use of genetic information . . . 'to fully protect the public from discrimination and allay their concerns about the potential for discrimination, thereby allowing individuals to take advantage of genetic testing, technologies, research, and new therapies.'"[233] GINA has two major parts. Title I, which prohibits genetic discrimination in health insurance, applies to employer-sponsored group health plans, health insurance issuers in group and individual marketplaces, Medigap insurance, and state and local nonfederal government plans.[234] Title I expressly bans use or disclosure of genetic information for underwriting purposes but does not mandate coverage of any particular genetic test or treatment and does not prohibit medical underwriting based on current health status.[235] Title II of GINA

231. Prior to GINA's passage, by Executive Order signed by President Clinton, federal agencies were prohibited from discriminating against job applicants and employees based on genetic information. *See generally* Exec. Order No. 13,145, 65 Fed. Reg. 6877 (Feb. 10, 2000). Dating back at least to 2001, President George W. Bush also supported legislation to end unfair genetic discrimination, stating:

> Genetic discrimination is unfair to workers and their families. It is unjustified—among other reasons, because it involves little more than medical speculation. A genetic predisposition toward cancer or heart disease does not mean the condition will develop. To deny employment or insurance to a healthy person based only on a predisposition violates our country's belief in equal treatment and individual merit.

The President's Radio Address, 37 WEEKLY COMP. PRES. DOC. 963 (June 23, 2001).

232. Ben Feller, *Bush Signs Anti-Discrimination Bill [GINA]*, CTR. FOR GENETICS & SOC'Y (May 21, 2008), https://www.geneticsandsociety.org/article.php?id=4096 [https://perma.cc/SLY6-GN2S].

233. Lowe v. Atlas Logistics Grp. Retail Servs. (Atlanta), LLC, 102 F. Supp. 3d 1360, 1367 (N.D. Ga. 2015) (first alteration in original) (emphasis added).

234. Slaughter, *supra* note 112, at 56.

235. *Id.* HHS Standards for Privacy of Individually Identifiable Health Information, known as medical privacy regulations, provide protections against use and disclosure of all individually identifiable genetic information, but those regulations allow "use" of health information for insurance underwriting purposes. 45 C.F.R. §§ 160.103, 164.502 (2018). GINA also amended the Employee Retirement Income Security Act of 1974. 29 U.S.C. § 1191b(d)(6)(B) (2012) (clarifying that protected genetic information includes "requests for, or receipt of genetic services, or participation in clinical research that includes genetic services by [an employee] or any family member [of the employee]"). The Public Health Service Act, Internal Revenue Code of 1986, and Title XVIII of the Social Security Act are also amended by GINA. Slaughter, *supra* note 112, at 56. Under GINA, health

makes it illegal to discriminate against employees or job applicants based on genetic information.[236] The Department of Labor, the Department of Health and Human Services ("HHS"), and the Treasury Department have joint power to promulgate and enforce regulations relating to health insurance under GINA's Title I.[237] The EEOC oversees GINA's Title II, which relates to employment discrimination.[238] Under 42 U.S.C. § 2000ff-10, the EEOC promulgated a rule codified at 29 C.F.R. § 1635;[239] the GINA rule defines "genetic test" with the exact language from the statute.[240] The regulation goes further, though, and provides specific examples of genetic testing, including: "[c]arrier screening for adults using genetic analysis to determine the risk of conditions such as . . . *sickle cell anemia*."[241] The regulation notes that the list is not intended to be exhaustive.[242]

1. GINA and SCD

As stated earlier, sickle cell anemia was among the first single-gene mutations identified.[243] In the 1970s, African Americans had been targeted for genetic testing for SCD and SCT. Their test results were not held in confidence, and stigmatization and discrimination in employment and health insurance coverage ensued.[244] SCD has become a "racialized" genetic disease in that it has been cast as

insurance issuers are prohibited from adjusting premiums or contribution amounts for group coverage on the basis of genetic information. 29 U.S.C. § 1182(b)(3)(A) (2012). And group health plans and health insurers are prohibited from denying coverage to a healthy individual or charging that individual higher premiums based solely on a genetic predisposition to specific diseases. *Id.* § 1182(b)(1). Further, Title I applies to data relating to genetic information in the context of family history and prohibits a health insurer from requesting or requiring participants to undergo genetic testing. 42 U.S.C. § 2000ff-1 (2012).

236. *Id.* Hiring, firing, job assignments, and promotions are examples of areas where genetic information discrimination is prohibited, and the bill extends beyond employers to include unions, employment agencies, and labor-management training programs. Slaughter, *supra* note 112, at 57.

237. *See* Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, § 106, 122 Stat. 881, 905 (codified as amended in scattered sections of 42 U.S.C.).

238. *See* 42 U.S.C. § 2000ff-10 (2012).

239. *See* 29 C.F.R. § 1635.3(f)(1) (2018).

240. "[G]enetic test" is defined as "an analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detects genotypes, mutations, or chromosomal changes." 42 U.S.C. § 2000ff(7)(A) (2012); § 1635.3(f)(1).

241. 29 C.F.R. § 1635.3(f)(2) (2018) (emphasis added).

242. *Id.*

243. *See* Slaughter, *supra* note 112, at 43.

244. *See Hearing: Genetic Non-Discrimination*, *supra* note 226, at 107–08 (statement of Karen H. Rothenberg, Dean and Marjorie Cook Professor of Law, University of Maryland School of Law); *see also* Slaughter, *supra* note 112, at 45.

belonging to a particular race, contrary to fact and science.[245] Therefore, with genetic variants like those present in SCT and SCD, concerns about discrimination are heightened. For this reason, GINA specifically names carriers for sickle cell anemia in its "Findings" section:

> [M]embers of a particular group may be stigmatized or discriminated against as a result of that genetic information. *This form of discrimination was evident in the 1970s, which saw the advent of programs to screen and identify carriers of sickle cell anemia* . . . . State legislatures [enacted] discriminatory laws . . . and in the early 1970s began mandating genetic screening of all African Americans for sickle cell anemia, leading to discrimination and unnecessary fear.[246]

2. GINA's Limitations

As noted above, GINA has been described as the first civil rights legislation of the twenty-first century. Yet concern continues that genetic information will be used to "violate the privacy that surrounds familial relationships and medical care."[247] A number of studies document that underrepresented groups in research still have heightened concerns regarding privacy, including control over their genetic information.[248]

Despite the "Findings" section's reference to the SCD and SCT community's experienced legacy of discrimination, GINA does not provide protection to those with genetic diseases, including SCD. For example, an individual's diagnosed disease, disorder, or pathological condition, or any signs or symptoms of such conditions, are *not* covered genetic information under GINA, even if that condition has a genetic basis.[249] GINA restricts its definition of "genetic test" to

245. Ajunwa, *supra* note 213, at 86.

246. 42 U.S.C. § 2000ff cmt. 3 (Legislative Findings) (emphasis added).

247. Expert Report of Paul A. Lombardo, *supra* note 230, at 3.

248. Ellen W. Clayton et al., *A Systematic Literature Review of Individuals' Perspectives on Privacy and Genetic information in the United States*, 13 PLOS ONE, no. e0204417, Oct. 31, 2018, at 1, 12.

249. *See* 42 U.S.C. § 2000ff-9 (2012); 29 C.F.R. § 1635.12(a) (2018); Ajunwa, *supra* note 213, at 94. A disease, disorder, or pathological condition is considered "manifested" if the individual "has been or could reasonably be diagnosed with the disease, disorder, or pathological condition by a healthcare professional." 29 C.F.R. § 1635.3(g) (2018). A disease, disorder or pathological condition is not considered manifested "if the diagnosis is based principally on genetic information." *Id.* Health insurance regulations similarly have defined "manifestation." Anya E.R. Prince & Benjamin E. Berkman, *When Does an Illness Begin: Genetic Discrimination and Disease Manifestation*, 40 J.L. MED. & ETHICS 655, 661 (2012). Though GINA does not cover a condition's diagnosis or signs or

analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detect genotypes, mutations, or chromosomal changes.[250] However, it does not prohibit other widely used tests, for example, those that measure complete blood counts, cholesterol, or liver function.[251] This creates a "gray area for discrimination," as a simple blood test may be used to detect genetic diseases like SCD.[252] Furthermore, GINA does not protect "analys[e]s of proteins or metabolites that are directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved."[253] Also, an employer does not violate GINA by using, acquiring, or disclosing medical information "that is *not* genetic information about a manifested disease, disorder, or pathological condition of an employee or member," even if the disease, disorder, or pathological condition has or may have a genetic basis or component.[254] These deficiencies give rise to calls by some scholars for a disparate impact theory of protection under GINA, which "would allow plaintiffs to show a pattern of employers turning away individuals known [or believed] to carry such genetic diseases from employment," even if the employer had not subjected the potential employee to testing deemed to be "genetic testing" under GINA's stringent definition.[255]

One of its principal sponsors in the House viewed GINA as "an important step towards freedom from insidious discrimination," but the effort is by no means finished.[256] And "[j]ust as access to all civil

symptoms of that diagnosis, the EEOC has made clear that such information is still subject to other laws that regulate the acquisition and use of medical information, such as Title I of the ADA. *Id.* at 661.

250. 29 C.F.R. § 1635.3(f)(3) (2018).

251. *Id.*; Ajunwa, *supra* note 213, at 94.

252. Ajunwa, *supra* note 213, at 94. These holes in protection expose individuals to "covert genetic discrimination." *Id.*

253. *Id.* (alteration in original).

254. 29 C.F.R. § 1635.12(a) (2018) (emphasis added).

255. Ajunwa, *supra* note 213, at 94. *But see* Duru, *supra* note 77, at 286–87 ("M]any judges remain hostile towards the disparate impact theory of liability, which is unlikely to survive many more court challenges.").

256. Slaughter, *supra* note 112, at 59. One notable limitation is that GINA provides no protection against genetic discrimination by insurers selling policies for life, disability, or long-term care insurance, or discrimination by creditors based on genetic information. Hudson et al., *supra* note 224, at 2662. "This [was] not the result of oversight: a strategic decision was made early on to recognize the very distinct markets, social purposes, risks of adverse selection, and bodies of relevant law governing these types of insurance." *Id.* at 2663. As of 2017, forty-eight states and the District of Columbia have instituted their own laws prohibiting genetic discrimination by health insurance providers, and thirty-five states and the District of Columbia have prohibitions against genetic discrimination in

rights developed in stages," GINA represents "only a first step" toward protecting the American people from discrimination based on genetic information.[257] The law is imperfect and does not provide as much protection as some organizations and families may have hoped,[258] and even with GINA in place the risk of a "genetic underclass" persists.[259] Gaps in legal protections make equitable access to gene-editing treatments all the more important, as GINA will not protect individuals with SCD against discrimination in the workplace or in obtaining insurance. This, and the tenuous status of ACA preexisting condition protections, leaves the SCD community with a pressing need for not only a cure but a cure that is affordable. Being blocked from workplace participation and affordable health care (which often is obtained through one's workplace), the community experiences a heightened vulnerability and need for solutions.

Perhaps the most striking of GINA's limitations is that once an individual's genetic condition manifests or is diagnosed, that person no longer qualifies for GINA protections.[260] So, for example, in the

employment. *Genetic Discrimination and Other Laws*, NIH: NAT'L HUM. GENOME RES. INST. (Apr. 17, 2017), https://www.genome.gov/27568503/genetic-discrimination-and-other-laws [https://perma.cc/8VTT-TVG8]. Mississippi and Washington are the only two states that have not passed laws prohibiting genetic discrimination in health insurance. *Id.* Some states have bolstered GINA protections by including prohibitions against genetic discrimination in "other insurances," including those for life, disability, and long-term care policies. *Id.* As of 2017, seventeen states have additional laws restricting the use of genetic information in determining coverage for life insurance, seventeen states for disability insurance, and eight states for long-term care insurance. *Id.* Three years after GINA's passage, the state of California passed the California Genetic Information Nondiscrimination Act ("CalGINA"), which expands GINA's protections by prohibiting genetic discrimination in emergency medical services, housing, mortgage lending, education, state-funded services, and public accommodation and also lowers the employee amount to five (from the more permissive fifteen-employee threshold under GINA). CAL. GOV'T CODE §§ 1135, 12920 (West 2018); *see also* Slaughter, *supra* note 112, at 63. In 2016, Maryland imposed restrictions on life insurance companies, prohibiting unfair discrimination between individuals of the same class and equal life expectancy, and made specific mention of SCT. MD. CODE ANN., INS. § 27-208 (Westlaw through legis. effective Apr. 30, 2019, from the 2019 Reg. Sess.).

257. Slaughter, *supra* note 112, at 59.

258. Hudson et al., *supra* note 224, at 2662. For example, it is argued that if diagnosed genetic illnesses had been included within GINA's protections, this would have caused economic disruption in the individual health insurance market which, at that time, underwrote on the basis of diagnosed diseases. *Id.* at 2662–63. Further, from an ethics standpoint, it would have been "fundamentally unjust to treat people with genetic diseases differently from those whose diseases are nongenetic or have unknown causes." *Id.* at 2663.

259. Ajunwa, *supra* note 213, at 90.

260. *See supra* note 249 and accompanying text.

context of the SCD and SCT community, an infant testing positive for SCT is a carrier of a genetic variant but does not have the disease and, thus, is protected by GINA.[261] By contrast, an infant who tests positive at birth for SCD seems to be stripped of GINA's protections because he or she has a diagnosed genetic condition. As Keith Wailoo states, "[T]he experience of the illness varies greatly from one person to the next. In some, pain and infection are overwhelming and recurrent, and in others such symptoms are barely discernible."[262] But this fact is irrelevant under GINA, which appears to draw bright, unyielding lines.

Currently, individuals facing discrimination based on SCD must rely on clever combinations of federal and state laws, other than GINA, to assert their rights.[263] Legislation specifically extending protections to those with genetic diseases—manifested and/or diagnosed—is needed to meaningfully advance the cause of members of the SCD community who suffer discrimination in the workplace and in obtaining insurance, especially if ACA protections are eliminated. If federal legislators are unable or unwilling to implement changes, state legislators and governors can play a substantial role in bringing forth change. While GINA provides a baseline of protection at the national level, some states have crafted even broader safeguards to supplement those provided under GINA, although these state laws vary widely in scope, applicability, and degree of protection.[264] GINA sets a floor of minimum protection against genetic discrimination; state laws with stricter protections are not preempted.[265]

The law's response when CRISPR technology successfully cures genetic disease will be noteworthy. Unless clarified through new legislation or regulations, the courts will need to address reconciling GINA's approach to the manifested genetic disease with an outcome GINA did not anticipate: the cured genetic disease. What type of

261. *See supra* note 249 and accompanying text. As we learn more about sickle cell carrier status and other diseases with a recessive pattern of inheritance, in rare circumstances, having one allele may have clinical complications. Should this be considered "manifested disease" for purposes of GINA? We assert carrier status is not clinical manifestation of a genetic disease.

262. WAILOO, *supra* note 85, at 9.

263. For case law describing the legacy of discrimination and recognized patients' rights, see *supra* Part III.

264. *Genetic Discrimination and Other Laws*, *supra* note 256. Some of these laws predated GINA, and some were enacted subsequent to GINA. *Id.*

265. *Id.*; *see also* Hudson et al., *supra* note 224, at 2662. For a discussion of more extensive state law protections, see text accompanying *supra* note 256.

proof will be necessary to restore an individual's protection under GINA? These are among the questions the law will need to contemplate. But first, there are more salient questions regarding how best to achieve and ensure equitable access to SCD cures. For the SCD community, which historically has experienced health inequities, this is a critical concern.

VI. EQUITY AND GENOME EDITING

Thus far, the Article has highlighted how gene editing is a source of hope for the SCD community, explored the community's skepticism and fear in embracing that hope and examined reasons why the community might be distrustful of government agencies, researchers, and some health-care providers. The Article spotlighted instances of this community's experienced history of discrimination and described the inadequacy of current legal protections. This part highlights additional concerns surrounding equitable access to gene editing in the context of SCD. It concludes by summarizing why equity concerns should be paramount in treatment and research efforts surrounding gene editing in SCD and then offers initial thoughts on how such equity concerns can remain central to future work.

A. Disparity Diseases and Civil Rights

SCD adversely impacts U.S. populations that already experience significant health disparities.[266] Congress defined health disparities as "a significant disparity in the overall rate of disease incidence, prevalence, morbidity, mortality, or survival rates in the population as compared to the health status of the general population" in the Minority Health and Health Disparities Research and Education Act of 2000.[267] Healthy People 2020 defines a health disparity as

> a particular type of health difference that is closely linked with social or economic disadvantage. Health disparities adversely affect groups of people who have systematically experienced greater social or economic obstacles to health based on their racial or ethnic group, religion, socioeconomic status, gender, mental health, cognitive, sensory, or physical disability, sexual

266. Michele Goodwin, *Revisiting Death: Implicit Bias and the Case of Jahi McMath*, HASTINGS CTR. REP., Nov.–Dec. 2018, S77, S78–S79.

267. 42 U.S.C. § 285t(d)(1) (2012).

> orientation, geographic location, or other characteristics historically linked to discrimination or exclusion.[268]

As stated earlier, African ancestral populations have the highest rates of SCD in the United States and, overall, also experience greater health inequities and health disparities.[269] Although SCD is far more prevalent than other rare genetic diseases, historically, less funding, research, and overall attention has been allocated for SCD treatment.[270]

Addressing health disparities is a civil rights issue. "Civil rights laws and their enforcement are social determinants of health because they affect other social determinants of health . . . such as education, housing, transportation, employment, and the system of justice . . . ."[271] As such, civil rights laws "causally affect the societal distribution of resources that in turn affect disease, injury, and health."[272] Health equity is the principle to address disparities in health, striving for the highest possible standard of health for all.[273]

The disparities that exist in the treatment of SCD must be contextualized in the development of the human genome-editing technology aimed at the disease's treatment and prevention. If researchers, biotechnology firms, and policymakers are not mindful of this context, we are concerned that this disease, burdened with the legacy of neglect, will not benefit equally in genetic editing.

268. U.S. DEP'T OF HEALTH & HUM. SERVS., THE SECRETARY'S ADVISORY COMMITTEE ON NATIONAL HEALTH PROMOTION AND DISEASE PREVENTION OBJECTIVES FOR 2020, at 28 (2008), https://healthypeople.gov/sites/default/files/PhaseI_0.pdf [https://perma.cc/PJN2-LTP4].

269. *CDC Health Disparities & Inequalities Report*, CENTERS FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/minorityhealth/CHDIReport.html [https://perma.cc/J7RX-JY7A].

270. Scott, *supra* note 98, at 731.

271. R.A. Hahn, B.I. Truman & D.R. Williams, *Civil Rights as Determinants of Public Health and Racial and Ethnic Health Equality: Health Care, Education, Employment, and Housing in the United States*, 4 SSM POPULATION HEALTH 17, 17–18 (2018).

272. *Id.*

273. Paula Braveman, *What Are Health Disparities and Health Equity? We Need to Be Clear*, 129 PUB. HEALTH REP. 5, 6, 7 (2014) ("Health equity and health disparities are intertwined. Health equity means social justice in health (i.e., no one is denied the possibility to be healthy for belonging to a group that has historically been economically/socially disadvantaged). Health disparities are the metric we use to measure progress toward achieving health equity. A reduction in health disparities (in absolute and relative terms) is evidence that we are moving toward greater health equity.").

B. Ensuring Equitable Access Globally and the Legal and Economic Obstacles

Equity and fairness in access to new curative genetic therapies is not limited to the United States and Europe. It is important to note the extensive burden of SCD outside of high-income countries. Estimates of infants born with sickle cell anemia annually range from 300,000 to 400,000.[274] The vast majority of these births occur in three countries: Nigeria, the Democratic Republic of the Congo, and India.[275] Approximately 1000 babies are born with SCD in Africa every day and more than half will die before their fifth birthday.[276] Piel and colleagues report that the global burden is increasing and highlight the need for low- and middle-income countries to develop national policies for newborn screening, public health planning, and treatment.[277] Researchers contemplating the potential of human genome editing as a genetic curative strategy for SCD must also question the impact for low- and middle-income countries experiencing the greatest burden of this disease. Low- and middle-income countries are even less equipped to conduct (*ex vivo*) human genome editing, especially when considering the unsustainable cost anticipated in high-income countries.[278]

However, leaders in global health and development are looking to use CRISPR and other genome-editing technologies to help humanity overcome some of its biggest and most persistent challenges.[279] For example, the director of the NIH, Francis Collins,

274. Piel et al., *Sickle Cell Disease*, *supra* note 25, at 1561.

275. *Id.*

276. *World Sickle Cell Day*, SICKLE CELL DISEASE COALITION, http://www.scdcoalition.org/priorities/global.html [https://perma.cc/S9QP-YGGJ].

277. Piel et al., *Global Burden*, *supra* note 30, at 9.

278. "Currently, most gene therapy trials for [SCD] are *ex vivo*. However, *ex vivo* gene therapy is a complicated, multi-step process that takes weeks and requires hospitalization." Alice Dickow, *The Gates Foundation Backs Gene Editing Research to Treat a Devastating Disease*, INSIDE PHILANTHROPY (Mar. 2, 2019), https://www.insidephilanthropy.com/home/2019/3/3/the-gates-foundation-backs-gene-editing-research-to-treat-a-devastating-disease [https://perma.cc/RU9M-Q7H5]. Researchers are developing methods that allow *in vivo* gene-therapy applications for SCD in areas of the world where health-care systems are less developed than in the United States and Europe. *Id.*

279. *See, e.g.*, Bill Gates, *Gene Editing for Good: How CRISPR Could Transform Global Development*, FOREIGN AFF. (Apr. 10, 2018), https://www.foreignaffairs.com/articles/2018-04-10/gene-editing-good [https://perma.cc/FSQ5-BKJC] ("The technology is making it much easier for scientists to discover better diagnostics, treatments, and other tools to fight diseases that still kill and disable millions of people every year, primarily the poor. It is also accelerating research that could help end extreme poverty by enabling millions of farmers in the developing world to grow crops and raise livestock that are more

discussed how genome editing may accelerate a cure for SCD, noting that

> [t]he complicated, high-tech procedures . . . may not be practical for a very long time in places like sub-Saharan Africa. That's one reason why NIH recently launched a new effort to speed the development of safe, effective genome-editing approaches that could be delivered directly into a patient's body (*in vivo*), perhaps by infusion of the CRISPR gene editing apparatus.[280]

Moreover, at the end of 2018, the Bill and Melinda Gates Foundation awarded a $1.5 million grant to Boston Children's Hospital to research and develop gene-therapy treatment for SCD with the long-term goal of making the treatment available to patients in developing countries.[281]

Exploring the legal, policy, and social implications of genome editing includes grappling with this question of whether low- and middle-income countries and their citizens will benefit from this new technology. If the goal is truly to benefit those suffering from SCD, the scientific agenda must develop and implement an international framework for somatic human genome editing that is accessible to the millions of sub-Saharan African and Indian people with this disease.

However, patent disputes and the projected exorbitant costs of treatment may hinder progress with respect to developing and perfecting CRISPR biotechnology.

1. Legal Disputes Could Slow Clinical Trials and Treatment

While there is optimism about the scientific community's commitment to finding a cure, patent litigation between leaders[282] in

productive, more nutritious, and hardier. New technologies are often met with skepticism. But if the world is to continue the remarkable progress of the past few decades, it is vital that scientists, subject to safety and ethics guidelines, be encouraged to continue taking advantage of such promising tools as CRISPR.").

280. Collins, *supra* note 62.

281. David A. Williams, *Boston Children's Hospital Receives Grant for Sickle Cell Disease Research*, HEALIO (Dec. 30, 2018), https://www.healio.com/hematology-oncology/hematology/news/online/%7B9ba22126-f234-457d-bfd7-23fef382e43c%7D/boston-childrens-hospital-receives-grant-for-sickle-cell-disease-research [https://perma.cc/8P9K-29DT] ("While gene therapies are currently confined to a few research hospitals in the U.S. and other developed countries, our long-term goal is to make this treatment available to patients in developing countries—and we have already begun to think about how to translate this specialized, potentially curative therapy.").

282. The University of California, Berkeley ("UC Berkeley"), with the University of Vienna and Emmanuelle Charpentier, and the Broad Institute, with MIT and Harvard, are parties involved in the litigation over patent rights to the CRISPR-Cas9 gene-editing technology. *See* Univ. of Cal. v. Broad Inst. Inc., 903 F.3d 1286, 1286 (Fed. Cir. 2018).

the CRISPR-Cas9 field has complicated matters in the United States[283] and in Europe.[284] Final outcomes of these matters are critically important because they determine who holds which rights, who may decide on and implement future research with the biotechnology, and who may grant licenses for its use. Most importantly, patent litigation could potentially stall development of curative genetic therapies.

However, forward momentum is evident in clinical trials. For example, in April 2018, sponsor CRISPR Therapeutics and collaborator Vertex submitted an Investigational New Drug ("IND") Application to the FDA for the treatment of adults with SCD using CTX001 CRISPR technology.[285] In late May 2018, the FDA placed a

283. *See id.* On September 10, 2018, the Federal Circuit upheld the U.S. Patent & Trademark Patent Trial and Appeal Board ("PTAB") determination in favor of the Broad Institute. *Id.* at 1296. The Federal Circuit held that though Doudna (of UC Berkeley) and Charpentier (of the University of Vienna) were first to publish their CRISPR-Cas9 findings, Doudna & Charpentier, *supra* note 22, demonstrating that the isolated elements of the CRISPR-Cas9 system could be used in vitro in a *noncellular experimental environment*, the Broad researchers' February 2013 article described use of CRISPR-Cas9 in a *human cell line*. *Id.* at 1289. A distinction made by the PTAB is that CRISPR-Cas systems occur naturally in prokaryotes such as bacteria but have not been found to naturally exist in eukaryotes, such as plants and animals. *Id.* The court found that substantial evidence supported the PTAB's determination that, given the differences in eukaryotic cells and prokaryotic systems, a person of ordinary skill in the art would not have had a reasonable expectation of success in applying the CRISPR-Cas9 system in eukaryotic cells. *Id.* at 1290, 1296. The court agreed with the PTAB that UC Berkeley's claims to the use of CRISPR-Cas9 did not "render obvious" Broad's claims to its use in eukaryotes. *Id.* The Federal Circuit noted that this position could be supported in the record. *Id.* at 1294. "The prior art contained a number of techniques that had been used for adapting prokaryotic systems for use in eukaryotic cells, obstacles adopting other prokaryotic systems had been overcome, and [the UC Berkeley team] suggested using those techniques to implement CRISPR-Cas9 in eukaryotes." *Id.* The court, however, went on to note that its function was appellate in nature and that it was not at liberty to reweigh the evidence. *Id.* "It is not our role to ask whether substantial evidence supports fact-findings not made by the Board, but instead whether such evidence supports the findings that were in fact made." *Id.* For an excellent update on the *Broad Institute* litigation, see Sharon Begley, *University of California to be Granted Long-Sought CRISPR Patent, Possibly Reviving Dispute with the Broad Institute*, STAT: BIOTECH (Feb. 8, 2019), https://www.statnews.com/2019/02/08/the-university-of-california-gets-its-key-crispr-patent [https://perma.cc/4JHD-XMBJ].

284. *See EP2800811 – Methods and Compositions for RNA-Directed Target DNA Modification and for RNA-Directed Modulation of Transcription*, EUR. PAT. REG. (Dec. 26, 2018), https://register.epo.org/application?number=EP13793997&lng=en&tab=main [https://perma.cc/8977-6BU4]. The same plaintiffs that were unsuccessful in the *Broad Institute* litigation prevailed in their European patent challenge against the same defendants before the European Patent Office and were granted a broad European patent for CRISPR-Cas9. *Id.*; *see also Broad Inst.*, 903 F.3d at 1286.

285. *CRISPR Therapeutics and Vertex Provide Update on FDA Review of Investigational New Drug Application for CTX001 for the Treatment of Sickle Cell Disease*,

hold on the proposed clinical trial, but that hold was lifted by October 2018.[286] The FDA had certain questions that it required the sponsors to resolve before approval of the Phase I-II trial but has now accepted the IND Application and will allow the early-phase clinical trial to proceed.[287] The sponsors also have obtained approvals of clinical trial applications in multiple countries for both β-thalassemia and SCD.[288] At the December 2018 American Society of Hematology Annual Meeting, a team of scientists reported that the CRISPR technology data shows that the "*BCL11A* enhancer editing approach[] . . . is a practicable therapeutic strategy to produce durable HbF induction in SCD and β-thalassemia."[289] Genome editing to increase HbF has the potential to alleviate transfusion requirements for β-thalassemia patients and painful and debilitating sickle crises for sickle cell patients.[290]

2. Costs and Who Will Pay?

Affordability is a key consideration when making decisions about advancing genetic science. Particularly, is it worth it to invest in converting the science into therapies for which we will have to pay significant sums of money?[291] This is a major concern of the SCD community. It is also a worry of legislators in states concerned about

CRISPR THERAPEUTICS (May 30, 2018), https://globenewswire.com/news-release/2018/05/30/1514301/0/en/CRISPR-Therapeutics-and-Vertex-Provide-Update-on-FDA-Review-of-Investigational-New-Drug-Application-for-CTX001-for-the-Treatment-of-Sickle-Cell-Disease.html [https://perma.cc/6FEU-SVY8] [hereinafter *Update on FDA Review*].

286. *Id.*; *CRISPR Therapeutics and Vertex Announce FDA Has Lifted the Clinical Hold on the Investigational New Drug Application for CTX001 for the Treatment of Sickle Cell Disease*, CRISPR THERAPEUTICS (Oct. 10, 2018), https://globenewswire.com/news-release/2018/10/10/1619581/0/en/CRISPR-Therapeutics-and-Vertex-Announce-FDA-Has-Lifted-the-Clinical-Hold-on-the-Investigational-New-Drug-Application-for-CTX001-for-the-Treatment-of-Sickle-Cell-Disease.html [https://perma.cc/SD4C-ETAX] [hereinafter *CRISPR Therapeutics*]; Alex Keown, *FDA Lifts Clinical Hold; Green-Lights Vertex and CRISPR's Sickle Cell Gene Therapy Trial*, BIOSPACE (Oct. 11, 2018), https://www.biospace.com/article/fda-lifts-clinical-hold-green-lights-vertex-and-crispr-s-sickle-cell-gene-therapy-trial/ [https://perma.cc/Z2A3-TSP9].

287. *CRISPR Therapeutics*, *supra* note 286.

288. *See Pipeline: Tackling a Range of Diseases with Different Approaches*, CRISPR THERAPEUTICS, http://www.crisprtx.com/programs/pipeline [https://perma.cc/2PVE-JCVY].

289. Am. Soc'y of Hematology, *3482 Highly Efficient Therapeutic Gene Editing of* BCL11A *Enhancer in Human Hematopoietic Stem Cells from β-Hemoglobinopathy Patients for Fetal Hemoglobin Induction*, ASH HOME (Dec. 2, 2018), https://ash.confex.com/ash/2018/webprogram/Paper119365.html [https://perma.cc/SF3G-5TNX].

290. *Update on FDA Review*, *supra* note 285.

291. Erika Check Hayden, *Gene Therapies Pose Million-Dollar Conundrum*, 534 NATURE 305, 305 (2016).

an inability to cover costs of available treatments.[292] While new treatments for SCD and other serious diseases are great news for patients, even called "a Renaissance for treatments of long-untreatable illnesses," states may have some very difficult decisions to make.[293] One cost-covering solution on the rise is a deal brokered between drug companies and insurers, known as "pay for performance," whereby insurer payments are tied to a medicine's actual performance; if patients fail to reach some pre-agreed-upon therapeutic response or the insurer ends up paying more than it has budgeted, the pharmaceuticals manufacturer refunds money to the insurer.[294] Such deals are estimated to be in play in fourteen countries, mostly in the United States and Europe but also in middle-income countries, including Brazil.[295]

Some scientists are exuberant about the potential for CRISPR in treating classic genetic diseases like SCD, believing that CRISPR not only will be transformative but also will make gene editing "cheap, easy and accessible, and therefore more common."[296] According to bioethicist Mildred Cho, however, even if CRISPR proves successful in clinical trials, the actual treatment will be cost prohibitive for many patients.[297] Emphasizing the significant differences between undergoing gene-therapy treatment and taking a pill from a pharmacy, Cho states: "It's more like getting an organ transplant. It's a very complex procedure. Cancer immunotherapy already costs in the hundreds of thousands of dollars per year. There's no way that gene-edited treatments are going to be any less expensive."[298]

With any CRISPR technology approved for use in treating SCD, there will be no existing approved drugs that work similarly, thus there may be little competition or incentive for companies to keep prices affordable.[299] This is a major reason why there should be some type of agreement, understanding, or bargain between the SCD community and pharmaceutical companies that study CRISPR technology in clinical trials using volunteers from the sickle cell

292. Michael Booth, *Effective But Very Expensive Drugs Are Forcing State Medicaid Directors to Make Some Tough Decisions*, NAT'L CONF. ST. LEGISLATURES (Feb. 1, 2017), http://www.ncsl.org/bookstore/state-legislatures-magazine/effective-but-expensive-drugs-are-beyond-the-reach-of-many.aspx [https://perma.cc/BNG3-E7KV].

293. *Id.*

294. Hayden, *supra* note 291, at 306.

295. *Id.* Data gathering and sharing centers are part of these arrangements. *See id.*

296. Shwartz, *supra* note 11, at 27.

297. *Id.* at 26.

298. *Id.*

299. Hayden, *supra* note 291, at 306.

community. These patients, and those in their community, must reap lasting benefits from any positive discoveries in research that they help to move forward.

One option that may foster equitable access can be seen in public-private partnerships. Through public-private partnerships, philanthropic foundations commit resources to diseases or causes and act as facilitators in brokering agreements and negotiating promises of affordability and access.[300] Recently, the Duke Charitable Foundation has funded the Critical Path Institute ("C-Path") for development of advances in therapies for SCD.[301] C-Path has a public-private partnership with the FDA and an established record of building consortia to speed development of novel medical therapies for patients suffering from various diseases and conditions.[302] The Duke Charitable Foundation lists sickle cell patient advocacy groups as stakeholders that will be part of the conversation.[303] Hopefully, affordability and access—both initially and long-term—will be central to the discussion.

Another, more mature C-Path endeavor, in collaboration with The Bill & Melinda Gates Foundation, is an initiative to develop effective treatments for Tuberculosis.[304] That program specifically addresses concerns about the "dire need for faster-acting drugs to treat TB in all its forms that are effective, affordable, and accessible."[305] Other disease-specific initiatives are the ACT Initiative of the National Hemophilia Foundation[306] and the Kidney Innovation

300. *See, e.g.*, Press Release, Critical Path Inst., Doris Duke Charitable Foundation Awards Grant to Critical Path Institute to Advance Therapies for Sickle Cell Disease (Sept. 6, 2018), https://c-path.org/doris-duke-charitable-foundation-awards-grant-to-critical-path-institute-to-advance-therapies-for-sickle-cell-disease/ [https://perma.cc/8BN3-E2KH].

301. *Id.*

302. *Id.*

303. *Id.*

304. *Critical Path to TB Drug Regimens*, CRITICAL PATH INST., https://c-path.org/programs/cptr/ [https://perma.cc/LUT4-SRYG].

305. *Id.*

306. The National Hemophilia Foundation implemented the ACT initiative with numerous partners from the biopharmaceuticals industry "to meet the imperative need to build [the] national capacity to maintain, and achieve where lacking, access to care for people with bleeding disorders." *The ACT Initiative*, NAT'L HEMOPHILIA FOUND., https://www.hemophilia.org/About-Us/Access-to-Care-Today-Achieving-Cures-Tomorrow [https://perma.cc/HDK9-N8ZH]. The National Hemophilia Foundation defines access as follows: "[a]dherence to state-of-the-art standards of care, [a]ccess to hemophilia treatment centers (HTCs), [a]ccess to treatment products appropriate for the individual, and [a]dequate reimbursement for these life-saving therapies." *Id.*

Accelerator ("KidneyX").[307] These more established programs and their emphasis on affordability and access can serve as examples as the newer SCD C-Path moves forward.

CONCLUSION

The promise of genome editing to address the burden of SCD is profound. The possibility that it will cause harm and will not equitably benefit those living with SCD in high-income countries, such as the United States, is real. With an eye toward ensuring equitable access, scientists, ethicists, economists, lawyers, and policymakers must develop new approaches to implement this new and expensive treatment in a population recognized to have been underserved.

The stakes are high. The challenge is to foresee obstacles to access and affordability now, as Phase I clinical trials are being conducted, so that the SCD community is not left with a solution and no means of using it to solve this life-and-death problem. Currently, in low-income countries with the highest burden of SCD, the potential to benefit from genetic curative therapies and genome editing is unrealistic when those countries do not even have resources to implement newborn screening and preventive care.[308] If the United States and other scientifically advanced countries are able to get the science right, we can and must share our knowledge and resources with low-income countries carrying the highest burdens of the disease.

The National Academies of Sciences 2017 Report identified seven principles that should undergird the oversight systems, research on, and eventual clinical uses of human genome editing: (1) promoting well-being, (2) transparency, (3) due care, (4) responsible science, (5) respect for persons, (6) fairness, and (7) transnational

307. The Kidney Innovation Accelerator (KidneyX) is a public-private partnership designed to accelerate innovation in prevention, diagnosis, and treatment of kidney disease. *HHS Announces Kidney Innovation Accelerator at ASN Kidney Week 2017*, ASN (Jan. 9, 2018), https://www.asn-online.org/news/item.aspx?ID=144 [https://perma.cc/RBX6-8TYY]. "The Accelerator will establish a public-private innovation fund capable of seeding and accelerating not just incremental improvements in treating kidney disease, but will foster real breakthroughs in dialysis and other treatments for kidney disease." *Id.* In order to ensure that the path to commercialization is "straight and clear," the Accelerator will bring together key components of HHS, notably the FDA, CMS, and the NIH. *Id.*

308. Lewis Hsu et al., *White Paper: Pathways to Progress in Newborn Screening for Sickle Cell Disease in Sub-Saharan Africa*, 6 J. TROPICAL DISEASES, no. 1000260, July 10, 2018, at 1, 5; Bertin Tshimanga Kadima et al., *High Rate of Sickle Cell Anaemia in Sub-Saharan Africa Underlines the Need to Screen All Children with Severe Anaemia for the Disease*, 104 ACTA PAEDIATRICA 1269, 1272 (2015).

cooperation.[309] Each principle is essential to implementation of genome editing for SCD. The first five reflect requirements or aspirations clearly articulated in existing U.S. laws and policies relating to human subjects research. The last two, fairness and transnational cooperation, more easily have been bypassed in the race to develop new treatments for ailments in high-income countries.

> The future will be bright for those who carry the burden of SCD as an everyday life experience . . . provided that we prioritize the development of strategies to equitably integrate these new curative genetic therapies. With commitment, cooperation, and careful planning, we could forever reduce the burden of this disease.

309. NAT'L ACADS. SCI., ENG'G, & MED., *supra* note 5, at 11–12.