

Biomedical research's unpaid debt

NIH's initiative to support and implement fairer competition for minority students is a welcome step to redress the exploitation of African Americans by science

Winston E Thompson^{1,2}, Roland A Pattillo², Jonathan K Stiles³ & Gerald Schatten⁴

Louis Agassiz, a Swiss-born American naturalist, was a leading and influential scientist in the 19th century. He was Professor of Zoology and Geology at Harvard University, the first foreign secretary of the US National Academy of Sciences, President of the American Association for the Advancement of Science, and the founding director of Harvard's Museum of Comparative Zoology. In a letter to his mother, written in 1846, he wrote: "It was in Philadelphia that I first found myself in prolonged contact with negroes; all the domestics in my hotel were men of color. I can scarcely express to you the painful impression that I received, especially since the feeling that they inspired in me is contrary to all our ideas about the confraternity of the human type and the unique origin of our species. But truth before all. Nevertheless, I experienced pity at the sight of this degraded and degenerate race, and their lot inspired compassion in me in thinking that they are really men. Nonetheless, it is impossible for me to reprocess the feeling that they are not of the same blood as us. In seeing their black faces with their thick lips and grimacing teeth, the wool on their head, their bent knees, their elongated hands, their large curved nails, and especially the livid color of the palm of their hands, I could not take my eyes off their face in order to tell them to stay far away. And when they advanced that hideous hand towards my plate in order to serve me, I wished I were able to depart in order to eat a piece of bread elsewhere, rather than dine with such service. What unhappiness for the white

race—to have tied their existence so closely with that of negroes in certain countries! God preserve us from such a contact!" Although the vast majority of scientists today would be shocked by Agassiz's words, such views were published widely and presented in prominent lectures, 16 years before US President Abraham Lincoln formally abolished slavery.

While the Emancipation Proclamation and the victory of the North in the American Civil War ended slavery in the USA, they did not prevent scientists from continuing to exploit African Americans throughout the following centuries. Surgical advances were first tested on black people before they were deemed sufficiently safe to be performed on white patients, and white doctors deliberately mistreated or refused to treat black patients in order to study disease progression. Moreover, much of molecular biology, cell biology, and cancer research was founded upon cells and tissues "donated" by an unsuspecting African American woman.

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And yet, while the "contributions" of African Americans have advanced biomedical research and health care, black people still suffer from healthcare inequities from

before the cradle and into the grave. Moreover, 151 years after the Emancipation Proclamation and 51 years after Martin Luther King's "I Have a Dream" speech, discrimination and prejudice continue even in research. A 2011 study found that African American applicants for NIH research grants are 10–13% less likely to get funded [1], that there is a notable paucity of African Americans as NIH principal investigators (PIs, Fig 1), and that there is persistent discrimination in the anonymous review of NIH grants (Fig 2). The NIH Advisory Committee on Diversity in the Biomedical Research Workforce under Lawrence Tabak noted that: "while Blacks or African Americans comprised 12.6% of the U.S. population in 2010, they only accounted for 1.1 percent of NIH PIs receiving research project grants (compared to 72.4 percent and 71 percent, respectively, for Whites)" [2]. In response, NIH leaders launched the Building Infrastructure Leading to Diversity (BUILD) initiative that will invest US\$500 million over 10 years to encourage minority students to pursue a research career and improve their chances of getting funded. While this is worthwhile and commendable initiative, is it sufficient to help black scientists and what else could be done to pay back the debt?

The exploitation of African Americans in the name of science began in the early days of medical research in the USA. "When the practice of hands-on anatomical dissection became popular in United States medical education in the late 18th and early 19th centuries, demand for

1 Mentoring Academy, Morehouse School of Medicine, Atlanta, GA, USA

2 Department of Obstetrics and Gynecology, Morehouse School of Medicine, Atlanta, GA, USA

3 Department of Microbiology, Biochemistry & Immunology, Morehouse School of Medicine, Atlanta, GA, USA

4 Departments of Cell Biology, Bioengineering, OB/GYN and Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA.

E-mail: gschatte@pdc.magee.edu

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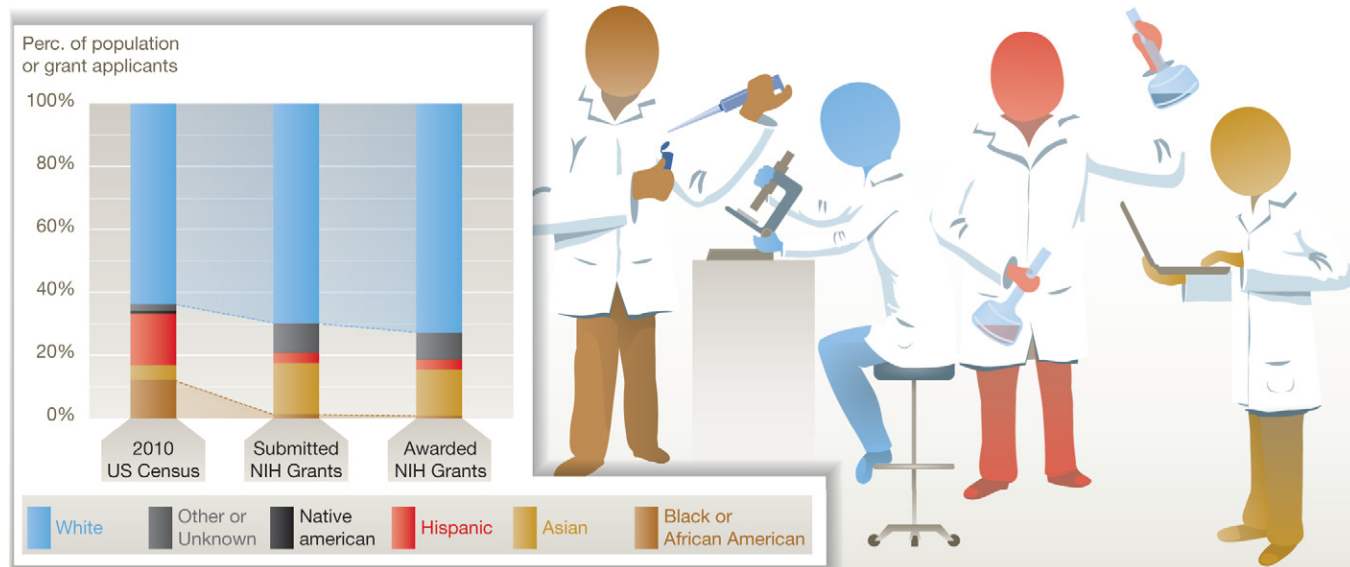


Figure 1. Diversity in the NIH-Funded Research Workforce.

While African Americans represent 12.6% of the U.S. population, only 1.1% of Principal Investigators are African American. Discordance is also worrisome for Hispanic Americans (16.3% versus 3.5% PIs), Native Americans (0.9% versus 0.2%), and Native Hawaiians (0.2% versus 0.1%).

cadavers exceeded the supply. Slave bodies and thefts by grave robbers met this demand. [...] Slave owners sold the bodies of their deceased chattel to medical schools for anatomic dissection. Stories of the ‘night doctors’ buying and stealing bodies became part of African American folklore traditions. The physical and documentary evidence demonstrates the disproportionate use of the bodies of the poor, the Black, and the

marginalized in furthering the medical education of white elites” [3].

In the same vein, Henrietta Lacks, an African American woman, unwillingly made her enormous contribution to molecular and cell biology in 1951 when, while she was undergoing treatment for cervical cancer at Johns Hopkins University Hospital in Baltimore, doctors removed samples from her tumor without her permission. Johns Hopkins researcher George Gey discovered that her cells could be kept alive to grow in culture indefinitely. His discovery became the basis for the first immortal human cell line, HeLa, variations of which are used in research all over the world, resulting in more than 70,000 publications and enormous economic and health benefits (Fig 3). Yet, scientists and the public only recently became aware of Henrietta Lacks’s contribution to science through Rebecca Skloot’s 2010 book *The Immortal Life of Henrietta Lacks* [4]. Even Lacks’s own family had been left in the dark for decades about the important role of her cancer cells.

while all American’s were donating to the March of Dimes foundation to fight polio [5,6]. HeLa cells were ideal for growing the poliovirus, and huge quantities were required for vaccine production. The contracts were granted to the Tuskegee Institute, associated with the historically black Tuskegee University in Alabama. Tuskegee scientists, many of them African Americans, grew mass quantities of HeLa cells to produce sufficient poliovirus to vaccinate all Americans regardless of the color of their skin.

It was also at Tuskegee where an infamous syphilis study treated African American men like guinea pigs, chronicling their decline and death from the ravages of untreated infection, until it finally was stopped in 1972. Susan Reverby, in her comprehensive monograph, notes that approximately 600 impoverished men, two-thirds of whom were previously infected with syphilis, were treated merely as subjects, some of whom went on to infect their wives and children [7].

J. Marion Sims (1813–1883) is lionized as the “Father of Gynecology” for his invention of the speculum and the development of a successful surgical intervention against fistulas. His achievements, however, were the result of experiments on enslaved African American women with their owner’s consent, but certainly not theirs [8]. Some of these

Poignantly, HeLa cells played an essential role in the development of polio vaccines, even when racial inequities were prominent. US President Franklin D. Roosevelt, himself a polio-survivor, established the Georgia Warm Springs Foundation in 1927 for children to recuperate from the disease. Yet, segregationists prevented children of African Americans from benefitting, even

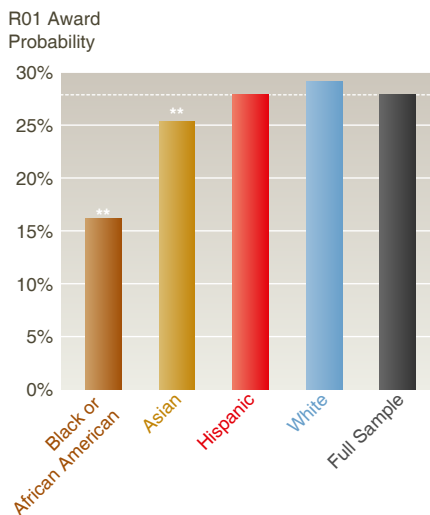


Figure 2. Unequal distribution of NIH Research Grants.

African American applicants for NIH research grants are funded at 10–13% lower rates compared to white researchers [1].

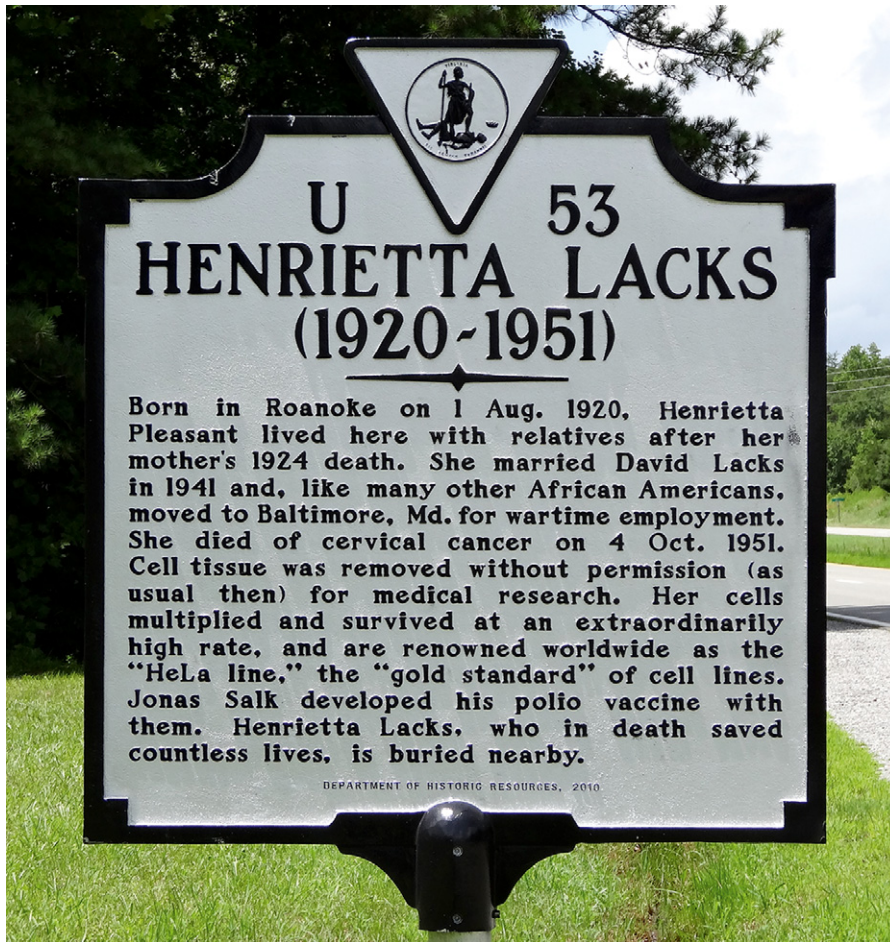


Figure 3. In memory of Henrietta Lacks' contribution to biomedical research.

Henrietta Lacks historical marker, located about 15 m west of the intersection of James D. Hagood Highway (US 360) and Clover Road (SR 92)/Guill Town Road (SR 720). Wikimedia Commons/This image is reproduced under the GNU Free Documentation License.

women underwent up to 30 operations without anesthesia, though anesthesia was administered to white women, as Sims did not think that they could endure the pain suffered by African Americans. “The Woman’s Hospital was instituted for the same reason that Sims gathered diseased black women into his backyard—to provide guinea pigs for his self-education, before he and others could convincingly offer care to the wives of the wealthy” [9].

More than a decade into the 21st century, this legacy of injustice still persists. The EMBL press release about the publication of the HeLa cell line genome was titled “Havoc in biology’s most-used human cell line.” The headline was probably intended to comment on the genomic havoc of the HeLa cell line, rather than the ethical havoc that resulted from sequencing the HeLa cell genome

without informing the Lacks family. Hank Greely and Mildred Cho have commented in this journal on the ongoing discussions and agreements between the NIH and the Lacks family [10].

The National Institute for Child Health and Human Development, in its 2012 Scientific Vision, called for the establishment of “biorepositories that capture the diversity of the US population” (https://www.nichd.nih.gov/publications/pubs/Documents/NICHD_scientific_vision_120412.pdf). African Americans remain under-represented in global embryonic stem cell banks, including the NIHs. These banks obtain their cells from surplus embryos after infertility treatment, and socio-economic factors limit the access of many African Americans to expensive assisted reproductive

technologies, which are not usually covered by health insurance in the USA.

Properly established biorepositories might enable insights into the genetic heterogeneity of people of African descent. Africa remains the birthplace of our species and harbors enormous genetic heterogeneity. Exacerbated by centuries of abductions, enslavement and human trafficking, and compounded by white male abuse of enslaved women, the genetic and epigenetic diversity of African Americans presents a worthy scientific challenge. Studies delving into the African diaspora in the USA might well illuminate some of the biological causes of disease prevalence.

Repaying the debts of more than a century of exploitation will also mean addressing the fact that African American biomedical researchers are rare. Rather than the encouragement, incentives, and resources they are entitled to, they instead often encounter bruising experiences and, as mentioned above, less NIH funding, ostensibly because many of them are applying from historically black colleges and universities (HBCUs). In fact, the NIH already sponsors career development at institutions that serve minorities, so perhaps reviewers have the impression that such applicants are already well supported by NIH programs and do not need traditional research funding. Alternatively, perhaps reviewers share a biased belief that the research environment and capacity at minority institutions is inferior to those at major research institutes. Few in the research community have ever been to minority institutions, and the training mechanisms are largely designed to bring majority insights to the minorities and not *vice versa*.

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There is certainly more that could be done to guarantee fair competition among biomedical scientists. The triage system, through which more than half of the submitted applications are never reviewed, is already relaxed for new applicants; perhaps

colleagues from under-represented minorities should similarly benefit from the more detailed consideration and critiques afforded to new applicants. Maybe NIH Study Sections should hold their meetings at HBCUs or Hispanic-serving institutions.

During and after World War II, the USA benefitted enormously from embracing European scientists displaced by the war and the Holocaust. Will the NIH Building Infrastructure Leading to Diversity (BUILD) initiative be a sufficient strategy to address the prevailing inequalities in research?

Beyond the shameful statistic that only 1.1 percent of NIH PIs are African American, there are stunning fiscal inequities. Given that the NIH budget in 2013 was around US\$30.3 billion, and assuming proportional *per capita* taxation, African Americans contribute annually around US\$3.8 billion to the NIH. If only 1.1 percent of the budget goes to support the research of African American PIs, only US \$333 million went back to their community versus US\$3.8 billion in taxes. Needless to say, there are many assumptions and confounding factors intrinsic in this short calculation, but the fact remains that African Americans are contributing to the NIH and are not benefitting proportionally. While BUILD's US\$50 million per year appears to be a generous sum to rectify historic and current inequities, it is still a tiny amount—only 1.3 percent—relative to the US\$3.8 billion or so collected for the NIH in taxes from black citizens.

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According to Ginther *et al*, [1] of the 40,069 PIs working at the NIH from 2000 to 2006, 1,149 were African American. Of these, 337 would be expected to obtain NIH awards based on the average success rate of NIH applicants. However, only 185 NIH grants were actually awarded to African American PIs between 2000–2006, meaning

that 152 PIs and their graduate, postdoctoral, and undergraduate trainees were potentially deprived of vital funding. A straightforward strategy for addressing these inequities would be for each of the 27 NIH institutes or centers to offer an annual award to a competitive African American PI who just missed the funding cutoff. Moreover, we propose that the NIH should convene a Reconciliation Commission to investigate why potentially 152 African Americans were not funded and to discuss mechanisms for restorative justice. The message conveyed by such a commission might help to overcome lingering notions of racial inequalities and relegate the outrageous discrimination of the past to history. Failing to properly address NIH's past discrimination will discourage promising trainees and encourage expensive and ineffective compensatory over-recruitment.

As part of BUILD, NIH suggests to enlist more mentors for minority students, which is an encouraging and helpful step. Recent evidence shows that intensive mentoring and partnered research experiences are constructive [11] and that partnerships between minority and majority institutions should be encouraged for research, training, resource repositories, and especially mentoring. Yet, beyond the NIH, African Americans in biomedical research still encounter a multitude of problems. As the NIH implements its plans, it should consider these larger problems that must be addressed to create a more diverse research community. For many scientists, science is a passion and not a mere job. How can we instill this sense of wonder and curiosity in the next generation of young people of color? Notwithstanding the commendable strategies put in place to support minority students, there are many good reasons for devoting even greater attention to improve the career outcomes of our current and future biomedical workforce, to provide experiences and attractive options beyond the academic laboratory and to better integrate a diverse population into the research community.

Considering the analogy of a leaky biomedical research pipeline resulting in high attrition rates for African Americans, it is imperative to capture and train the current cohort of African Americans as well as Hispanics, Native Americans, and other underrepresented groups through mentoring

programs, which will train mentors to become role models for the next generation. Fixing the leaky pipe will require true partnerships between majority and URM (underrepresented minority) institutions that go beyond the BUILD program. Evidence from successful mentoring programs at various institutions, including the visiting professors program at the American Society for Cell Biology (ASCB) Minority Affairs Committee [11] and the Mentoring Academy at Morehouse School of Medicine, indicates that effective mentoring works and should be supported and expanded nationwide.

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In summary, we commend NIH officials and their advisors for their leadership to address these difficult issues, particularly at a time of fiscal contraction and sequestration. It is the right thing to do: justice delayed is justice denied. This re-energized push to create representative diversity in the US research workforce by coordinated and sustained improvements in the biomedical infrastructure benefits all Americans. The rectification of the currently shameful situation is timely, urgent, and important.

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Conflict of interest

The authors declare that they have no conflict of interest.

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