How to make a better justice-based argument for conducting CRISPR/Cas9 research to cure Sickle Cell Disease (pre-refereed print)

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Post-refereed version accepted in *Bioethics*, forthcoming. Article DOI: 10.1111/BIOE.12690

1 | Introduction

Sickle cell disease (SCD) is caused by a genetic abnormality resulting in defective red blood cells, mostly afflicting patients of African (or Mediterranean) descent. SCD is held to be a promising candidate for genetic-therapy research using CRISPR/Cas9, a biotechnology with genome editing capabilities. In a recent article, Marilyn Baffoe-Bonnie makes an ethical case to pursue this SCD genetic-therapy research.[1] She offers three justice-based arguments that the research would help address historical and current injustices in SCD research and care. The first argument is that it would promote distributive justice in research. The second argument is that the research would help repair the healthcare system's relationship with SCD patients. The third is that it would benefit even those who are not research participants. I will grant that the first argument is sound, but show that the second and third arguments suffer from roughly the same defect. A better justice-based argument for conducting SCD CRISPR/Cas9 research will use only Baffoe-Bonnie's first argument.

[1] Baffoe-Bonnie, M. S. (2019). A justice‐based argument for including sickle cell disease in CRISPR/Cas9 clinical research. *Bioethics*.

2 | Baffoe-Bonnie's second argument

For convenience I will use 'genetic-therapy' to refer to CRISPR/Cas9 therapy. Baffoe-Bonnie's second argument is basically this: Because blacks in the USA have often not been treated with dignity and respect by healthcare providers, blacks have historically been distrustful of the healthcare system. Baffoe-Bonnie argues that pursuing SCD genetic-therapy research would help repair the relationship between healthcare providers and SCD patients, and therefore we should conduct such research. She writes that providers should understand the historical reasons why SCD patients may mistrust them. Further, "[i]f health care providers have historically sensitive conversations with their patients with SCD about CRISPR/Cas9 research, greater trust could be built between them and their patients."[2] Such conversations "would make it more visible to patients with SCD that many different actors understand that more needs to be done to treat and cure their illness."[3] So, conducting research in genetic-therapy for SCD will give healthcare providers a chance to repair trust and show they understand a cure is needed.

However, this argument is defective because the benefits it points to are not the results of doing research in SCD genetic-therapy, but the results of sensitive and concerned attitudes on the part of healthcare providers. So, those benefits are not reasons to conduct that research but reasons for providers to be sensitive and to show concern. For instance, suppose that the research is indeed conducted. It is nevertheless possible that healthcare providers inform SCD patients about this emerging research in a demeaning or unconcerned manner. It is even possible that they do not inform SCD patients at all. So, pursuing SCD genetic-therapy research is compatible with

[2] Ibid., p. 5.
[3] Ibid.

the relationship remaining poor. Hence, conducting that research is not sufficient for repairing the patient-provider relationship.

Nor is it necessary for repairing it. Baffoe-Bonnie points out that the patient-provider relationship has often been poor for two major reasons: First, black patients often feel unwelcome in emergency rooms, and their physical pain is often undertreated. Second, in educating patients and their parents about SCD, providers have sometimes communicated in a manner perceived as antagonistic or suspicious.[4] However, these two causes for the poor relationship can be addressed without pursuing genetic-therapy research; providers can repair the relationship by treating patients with dignity and genuine concern as they provide the current conventional therapies for SCD, regardless of whether genetic-therapy research is done. Healthcare providers could communicate to patients a genuine wish that there were a cure for SCD and even relay the need to government agencies, thereby improving the patient-provider relationship. Thus, pursuing SCD genetic-therapy research is neither necessary nor sufficient to rebuild patient-provider trust. Indeed, these reflections show that the actual determinant to repairing trust is the providers' attitudes.[5] So, what Baffoe-Bonnie offers is actually an argument for providers to treat SCD patients with dignity and concern, rather than an argument to conduct SCD genetic-therapy research.

Now if SCD genetic-therapy research were actually done, one might think it must be effective to some degree to improve the patient-provider relationship. Perhaps hearing about the research may cause the patient to then expect that providers would administer the future cure, and this helps the relationship, regardless of whether providers have a concerned and respectful

[4] Ibid.
[5] Viz. the healthcare sector's responsibility here; patient attitudes are also a factor.

attitude. But this factor seems to be negligible in impact (to the relationship) compared to whether providers actually show respect and concern. Furthermore, after hearing of the research, the patient is far more likely to simply be grateful to the researchers, than to think ahead to the providers who would administer any future cure. Thus, providers' attitudes are the primary determinant to repairing trust.

3 | Baffoe-Bonnie's third argument

The third argument Baffoe-Bonnie offers is that SCD genetic-therapy research should be conducted since benefits from that research would impact more than just those subjects participating in the research. This is an argument from "benefit-sharing". Benefit-sharing "is connected to the principle of distributive justice and ensures that there is an ethical and fair distribution of new biotechnologies."[6] She identifies three ways that SCD genetic-therapy research would promote benefit-sharing.

The first is that the "larger population of SCD sufferers, whether in the States or abroad, should stand to gain" from the research, not just the research participants.[7] However, this is merely an argument to conduct SCD therapy research *of any kind*, not an argument to conduct genetic-therapy research in particular, since it is plausible that research for any SCD therapy would potentially benefit all SCD sufferers.[8] Baffoe-Bonnie gives no reason that the benefit of genetic-therapy research to the larger population of SCD sufferers, relative to its benefit to

[6] Ibid.
[7] Ibid.
[8] Suppose the benefit in view is a cure, which genetic-therapy alone provides. However, recall that the benefit-sharing argument turns on the *sharing* of the benefit, not the type of benefit.

research participants, is greater than the corresponding relative benefit associated with some other kind of SCD therapy research, such as new bone-marrow transplant research.

The second way is that healthcare providers of SCD patients who are not research participants could nonetheless tell those patients about the genetic-therapy research. She adds: "In so doing, other patients would have the benefit of feeling included in clinical research and feeling that the gravity of their illness is acknowledged by the clinical and research community."[9] However, the defect identified in the previous paragraph (and indeed Section 2) plagues this argument, since it really argues for something besides genetic-therapy research *per se*: it argues for researchers and clinicians to genuinely acknowledge the gravity of SCD and convey that to patients appropriately and inclusively. This could be occasioned by discussing even current research of any SCD therapy, not necessarily genetic-therapy.[10] Thus this argument fails to argue for that research.

The third way Baffoe-Bonnie argues that genetic-therapy research would bring about benefit-sharing is on grounds of financial accessibility. She reasons that if genetic-therapy for SCD is inexpensive in the long run, SCD treatment would be more accessible to SCD patients. Instead, "[i]f CRISPR/Cas9 is expensive, adequate benefit-sharing would encourage measures to reduce financial barriers for SCD patients"[11] However, in this case there would be nothing about genetic-therapy that promotes benefit-sharing, since genetic-therapy's high cost would instead prevent patients from obtaining the benefit. Thus, her reasoning here is actually an argument, in spite of this, for those more well-off to practice benefit-sharing by subsidizing SCD patients,

[9] Ibid.
[10]Genetic-therapy research might be evidence they truly acknowledge SCD's gravity, but as Section 2 showed, researchers and providers could still be demeaning toward patients, and so it is the acknowledgement which is the primary determinant of the benefit here.
[11] Ibid., p.6.

rather than an argument for doing SCD genetic-therapy research. But perhaps, as Baffoe-Bonnie had suggested, SCD genetic-therapy may be inexpensive overall. However, this is merely an assumption. And without justification for it, this third version of the benefit-sharing argument fails. Indeed, there is evidence to doubt the assumption, from an article that Baffoe-Bonnie cites but does not quote: "The ease, cost, and permanency of CRISPR therapies do not necessarily mean they will be cheaper than companion therapies, especially where patents are involved." [12] Thus, neither of the three versions of the benefit-sharing argument succeeds.

4 | Conclusion

We saw that Baffoe-Bonnie's second and third arguments for pursuing SCD genetic-therapy research are defective. However, I grant that her first pro-argument is sound.[13] She states that the only significant objection is participant-risk in genetic-therapy research. She responds that if research participants suffer severe SCD and are properly informed about research risks, they should decide if the risks are warranted. She adds, "[i]n doing so, patients with SCD have the dignity to engage in their health-care decisions."[14] So, respecting patient-autonomy makes this risky research permissible, and I think this is an effective response. Therefore, a better justice-based argument for conducting SCD genetic-therapy research will use only Baffoe-Bonnie's first pro-argument while retaining the patient-autonomy response to defend its permissibility.

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[12]Sherkow, J. S. (2017). Focus: Genome Editing: CRISPR, Patents, and the Public Health. *The Yale journal of biology and medicine*, *90*(4), 667-672, p. 668. This quotation appears in the context of comparing costs in the long run.

[13] This is a persuasive distributive justice argument that the historical neglect of SCD research is grounds for research not merely into management/transplant therapies but a cure, which presently only genetic-therapy has a chance of providing. Ibid., p.4-5.

[14] Ibid., p. 7.