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'Editing the gene-editing debate: re-assessing the normative discussions on emerging genetic technologies'

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Abstract

The revolutionary potential of the CRISPR-Cas9 gene-editing technique has created a resurgence in enthusiasm and concern in genetic research perhaps not seen since the mapping of the human genome at the turn of the century. Some such concerns and anxieties revolve around crossing lines between somatic and germline interventions as well as treatment and enhancement applications. Underpinning these concerns, there are familiar concepts of safety, unintended consequences, damage to genetic identity and the creation of designer children through pursuing human enhancement and eugenics. In the policy realm, these morally-laden distinctions and anxieties are emerging as the basis for making important and applied measures to respond to fast-evolving scientific developments. This paper argues that the dominant normative framing for such responses is insufficient for this task. This paper illustrates this insufficiency as arising from a continued reliance on misleading genetic essentialist assumptions that generate groundless speculation and over-reactionary normative responses. This phenomenon is explicit with regard to prospective human (germline) genetic enhancements. While many normative theorists and state-of-the-art reports continue to gesture toward the influence of environmental and social influences on a person and their traits and capacities, this recognition does not extend to the substance of the arguments themselves which tend to revert to the debunked genetic determinist framework. Given the above, this paper argues that there is a pressing need for a more central role for sociological input into particular aspects of this enhancement myth in order to give added weight, detail and substance to these environmental influences and influence from social structures.

INTRODUCTION

The revolutionary potential of the CRISPR-Cas9 gene-editing technique has created a resurgence in enthusiasm in genetic research perhaps not seen since the mapping of the human genome at the turn of the century. Understandably, it has also seen a resurgence in various concerns and caution. In particular, concern is most evident when certain familiar moral red-lines are, or are at risk of being, crossed, such as when genetic interventions move beyond somatic to the germline and therapeutic interventions move to enhancement. Underpinning these red-lines, there are equally familiar anxieties expressed over such issues from safety and unintended consequences to perceptions of damage to genetic identity and the creation of designer children through pursuing human enhancement and eugenics. In the policy realm, these morally-laden distinctions and anxieties are emerging as the basis for making important and applied measures to respond to fast-evolving scientific developments. The news of the gene-edited Chinese twins underlies this rapid progress as well as the pressing issue of developing adequate ELSI responses. However, while it is vital to develop guidance that is adapted to these rapid developments, it is also vital to ensure this guidance is robust and its supporting normative arguments are themselves critically scrutinised. In short, the focus should not just be on evaluating new technologies, but also continuously re-assessing the normative arguments themselves – particularly when those arguments are both pervasive and highly reputable.

This paper argues that the dominant normative framing for such arguments is insufficient for this task. As will be outlined below, it requires a crucial – oft noted yet oft ignored – revision for two interconnected reasons: to generate plausible empirically-grounded speculation of gene-editing technological possibilities in order to generate the appropriate and proportional ELSI and normative responses. This paper illustrates this insufficiency as arising from a continued reliance on misleading genetic essentialist assumptions that generate groundless speculation and over-reactionary normative responses.[1] This phenomenon is particularly

[1] Habermas, Jürgen (2003) *The Future of Human Nature* ; Sandel, Michael J. (2007) *The Case Against Perfection: Ethics in the Age of Genetic Engineering*. Cambridge, Massachusetts: Belknap Press of Harvard University Press; Greenfield, Andy et al. (2016) *Genome editing: an ethical review.* Nuffield Council on Bioethics; Charo, R. Alta, Hynes, Richard O. et al. (2017) *Human Genome Editing: Science, Ethics, And Governance.* Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations. A Report of National Academy of Sciences and National Academy of Medicine. Washington, DC: The National Academies Press; European Academies Science Advisory Council (2017) *Genome editing: scientific opportunities, public*

explicit in the normative responses with regard to prospective human (germline) genetic enhancement and therefore this will be the focus of the paper.[2] While many normative theorists and state-of-the-art reports continue to gesture toward the influence of environmental and social influences on a person and their traits and capacities, this recognition does not extend to the substance of the arguments themselves which tend to revert to the debunked genetic determinist framework. While it will be noted that there are recent moves in this direction, it will be noted that such moves have yet to reframe this normative debate.[3] Given the above, this paper argues that there is a pressing need for a more central role for sociological input into particular aspects of this enhancement debate in order to give added weight, detail and substance to these environmental influences and influence from social structures.

THE 'PROBLEM' OF ENHANCEMENTS

From the Human Genome Project to the immediately prior to the discovery of the improved CRISPR method of gene-editing, there has been much work done in terms of genetic sequencing and genetic testing, particularly due to the emergence and expansion of direct-to-customer testing companies.[4] On the other hand, there has been less success in terms of successful and viable genetic interventions and applications, particularly in the context of human therapeutics.[5] The two dominant methods of gene-editing during this period consisted of finger nucleases2 (ZFNs) and Transcription activator-like effector nucleases (TALENS)[6]. In both cases, the processes have been complex, expensive, inefficient, time-consuming and generating low success in results.[7] The progress since Emmanuelle Charpentier and Jennifer

interests and policy options in the European Union. EASAC Policy Report 31. German National Academy of Sciences Leopoldina.

[2] Other potential applications of genetic or genome editing technologies would be relevant for a wider focus.

[3] Yeung, Karen (2018) *Genome editing and human reproduction: social and ethical issues*. Nuffield Council on Bioethics; Freese, Jeremy & Shostak, Sara (2009) 'Genetics and Social Inquiry' *Annual Review of Sociology*, Vol. 35:107-128 (August 2009).

[4] Borry, Pascal, Cornel Martina C. & Howard, Heidi C. (2010) 'Where are you going, where have you been: a recent history of the direct-to-consumer genetic testing market'. *Journal of Community Genetics* 1:101–106

[5] Emmert-Streib, Frank, Dehmer, Matthias & Yli-Harja, Olli (2017) 'Lessons from the Human Genome Project: Modesty, Honesty, and Realism.' *Frontiers in genetics* Vol. 8 184. (Nov. 2017).

[6] Gaj, Thomas., Gersbach, Charles A. & Barbas, Carlos F., 3rd (2013). 'ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering'. *Trends in biotechnology*, *31*(7), 397–405.

[7] ibid

Doudna's 2012 publication on the possibility of reprogramming the viral defence mechanism of bacteria to create precise changes to any sequence of DNA, in any cell, has been significant.[8] CRISPR (clustered regularly interspaced short palindromic repeats), or rather CRISPR-Cas9, has raised the possibility of making genetic changes to human and non-human targets a much more realistic, and immediate, goal. In short, it is cheaper, easier, more accurate, efficient than previous methods (although such previous methods are still being further developed) and can be directed toward making any changes, to any sequence of DNA – whether to delete or silence an existing sequence or to insert a new one.[9] The method can be applied to making somatic changes but also germline changes, which raises the increased prospect of affecting future generations.[10] To underlie this revolutionary advance in technical capacities, it only took less than six more years to come to a point where the first confirmed cases of humans were born with their heritable genetic constitution gene-edited using CRISPR-Cas9.[11] Dr Jiankui He's germ-line reproductive gene-editing of twin girls (with a HIV-infected father and unaffected mother) consisted of inserting a variant of the CCR5 gene to confer immunity to HIV. The case was significant for a number of reasons and not just because of the apparent technical feat that it represented.[12] While technical limitations regarding the possibility of successfully intervening on the germline with successful births was one factor, the more fundamental factors were the ethical and legal safeguards that were ignored in the process.[13] It may be some months or years before it can be known what possible side-effects will face the twin girls from a variety of unknown – and currently unknowable – changes that may have been caused and have yet to manifest.

Initial reactions to the He-Case

Directly upon the announcement, there were a number of reactions from the academic, scientific, policy-making and wider communities. These reactions could be broadly divided

[8] Jinek, Martin, Chylinski, Krzysztof, Fonfara, Ines, Hauer, Michael, Doudna, Jennifer A. & Charpentier, Emmanuelle (2012) 'A Programmable Dual-RNA–Guided DNA Endonuclease in Adaptive Bacterial Immunity' Science, Vol. 337 (August 2012).
[9] ibid
[10] Lanphier, Edward, Urnov, Fyodor, Haecker, Sarah E., Werner, Michael, Smolenski, Joanna (2015) 'Don't edit the human germ line' *Nature* Vol. 519 (March 2015).
[11] Cyranoski, David (2019) 'The CRISPR-baby scandal: what's next for human gene-editing' Nature 566 (February 2019), 440-442.
[12] ibid
[13] ibid

into two distinct types. Firstly, there were, what I call, general bioethical reactions (A), some of which were along the following lines:

I. 'safety concerns'
II. 'lack of medical necessity'
III. 'possibility of off-target mutations and mosaicism'
IV. 'reckless experimentation'
V. 'questionable informed consent process'
VI. 'lack of transparency'
VII. 'inadequate regulation and oversight'[14]

In addition to the above reactions, there was another important aspect to the case that generated another series of enhancement-specific reactions. While the germline intervention was ostensibly health-related, it was not, strictly-speaking, a treatment, but rather an enhancement. While there is a variant of the CCR5 gene that provides the bearer with resistance to HIV infection, this is rare in the human population under normal circumstances. As it was not present in the case of the twins that He intervened on, it was a case of making a modification that brought about something that was beyond the normal state. The intended enhancement was to bring about disease prevention that does not commonly exist. In many cases, such disease-preventing enhancements would inhabit a grey area between treatments and enhancements usually understood. For greater precision, it could be stated that there are two concepts of enhancement. Disease preventing enhancements are, what Stephen Wilkinson calls, 'super-normality' enhancements because they improve upon what is normal while still focussed on the broad medical goal of preventing disease.[15] These would be distinct from 'non-disease avoidance' enhancements which would be focussed on improvements that are unrelated to disease, focussing on traits already within the normal range.[16]. Ultimately,

[14] Park, Alice (2018) '"They Will Be Studied for the Rest of Their Lives." How China's Gene-Edited Twins Could Be Forever Changed By Controversial CRISPR Work' *TIME* 29 Nov. 2018. Available at: http://time.com/5466967/crispr-twins-lives/ [last accessed – 29/03/19]; Cyranoski, David & Ledford, Heidi (2018) 'Genome-edited baby claim provokes international outcry' *Nature* 26 Nov. 2018. Available at: https://www.nature.com/articles/d41586-018-07545-0 [last accessed – 29/03/19]; Davies, Kevin (2018) 'Under Fire, He Jiankui Defends Germline Editing Study' *GEN: Genetic Engineering & Biotechnology News* 28 Nov. 2018. Available at: https://www.genengnews.com/insights/under-fire-he-jiankui-defends-germline-editing-study/ [Last accessed: 29/03/2019].

[15] See Wilkinson, Stephen. 2010. Choosing Tomorrow's Children: The Ethics of Selective Reproduction. Oxford: Clarendon Press, pp187-190.

[16] ibid

while at the less controversial end of the enhancement spectrum, super-normality interventions that are disease-related are enhancements. As a consequence, in addition to – and distinct from – the above reactions, there was a number of other 'enhancement-specific' responses that I call reactions (B), which would be held by some in addition to reactions (A). Some of these were as follows:

I. Arthur Caplan: "taking a step down the road of eugenics"[17]
II. Marcy Darnovsky: "Throwing open the door to a society of genetic haves and have-nots [that] undermines our chances for a fair and just future."[18]
III. Craig Klugman: "The film GATTACA turned 20 years old this year...a couple visits their local neighborhood geneticist and orders up their child, choosing the most favorable genes as well as some tweaks to avoid common diseases. That scene took one step closer to reality..."[19]

While any mention of enhancement seems to increase moral unease for some, it should be noted that there could also be a further unintended enhancement that is much deeper into the controversial end of enhancements. It has been observed that CCR5-edited mice are correlated with enhanced cognitive functioning.[20] While observations in mice does not simply translate to humans, there is still a possibility that the twin-girls will have had a modification that is, at least possibly, a cognitive enhancement of some degree, or a step in that direction. Taking this onboard, it would further sharpen the criticisms and concerns already expressed in the reactions (B) and would be subject to negative assessments from a number of conventions, declarations, guidelines and regulations. For instance, in 2015, the UNESCO's International Bioethics Committee (IBC) noted that:

[17] See: https://www.theverge.com/2018/11/26/18112970/crispr-china-babies-embryos-genetic-engineering-bioethics-policy [Last accessed: 29/03/2019].
[18] See: https://www.geneticsandsociety.org/press-statement/claim-genetically-modified-babies-if-true-grave-abuse-human-rights [Last accessed: 29/03/2019].
[19] See: http://www.bioethics.net/2018/11/birth-of-twins-from-embryo-editing-raise-ethical-legal-and-social-issues/ [Last accessed: 29/03/2019].
[20] Cyranoski, D (2018) 'Baby gene edits could affect a range of traits' Nature. Available at: https://www.nature.com/articles/d41586-018-07713-2

> rapid advances in genetics are making “designer babies” an increasing possibility [with] the power of science to modify genetically human embryos in the laboratory, so as to control inherited traits, such as appearance and intelligence.[21]

The case of the possible unintended enhancement here can be related to some potentially unavoidable problems facing any stance that seeks to permit and promote interventions that can be classified as treatments (or even *disease-preventing* enhancements) while seeking to prohibit interventions that can be classified as unambiguous enhancements. The notion of the effective unavoidability of enhancement has been raised by Eric T. Juengst et al. in a paper on the issue of ‘incidental enhancements’.[22] This is where a treatment for a given disease or disability can also be an intervention that brings about enhancing side-effects. For instance, there may be enhanced cognition 'side-effects' from Alzheimer's disease research. In such cases, the treatment (or 'prevention to disease' focus) "would raise the same worries about competitive advantages, equality of access, authentic agency..." and so on.[23] One particular area where this would seem prevalent is in the case of aging-related interventions. A key concern noted here would be the possible regulatory restrictions that may affect interventions for treatments (that are themselves uncontroversial and valuable), when these treatments could also bring about enhancements, or have enhancing effects.

Council of Europe’s Recommendation as an Example

For instance, this risk can be seen if we look at the wording of the Council of Europe’s Recommendation 2115 (2017) on the use of new genetic – specifically including genome editing – technologies in human beings where it reaffirmed the opposition to deliberate germline editing as expressed in the ‘Oviedo Convention’ as crossing “a line viewed as ethically inviolable”.[24] While it is unlikely that they expected ‘quite soon’ to be as soon as it was, the authors of the Recommendation recognised that:

> recent advances in genome editing are bound to result in germline interventions in human beings quite soon, for example with the birth of children whose genome has

[21] https://en.unesco.org/news/unesco-panel-experts-calls-ban-editing-human-dna-avoid-unethical-tampering-hereditary-traits
[22] Juengst Eric T. Henderson Gail E. Walker Rebecca L. Conley John M. MacKay Douglas Meagher Karen M. Saylor Katherine Waltz Margaret Kuczynski Kristine J. Cadigan R. Jean (2018) ‘Is Enhancement the Price of Prevention in Human Gene Editing?’ *The CRISPR Journal* 1(6) Dec. 2018.
[23] ibid
[24] http://assembly.coe.int/nw/xml/XRef/Xref-XML2HTML-EN.asp?fileid=24228&lang=en

> been altered with some unforeseeable consequences in such a way that their descendants are also affected.[25]

In other words, while not universally supported, germline interventions were increasingly perceived to be sufficiently realisable to be of imminent concern. As can be seen in the following passage, it is not only germline, but enhancements that come in for specific concern:

> Recent discoveries related to the human genome [...] raises complex ethical and human rights questions, including – but not limited to – unintended harm which may result from the techniques used, access and consent to such techniques, and their potential abuse for enhancement or eugenic purposes.[26]

The final sentence is very telling: the 'potential abuse *for enhancement* or eugenic purposes' of such gene-editing techniques. To highlight this, compare the following two sentences: "*their potential abuse for enhancement or eugenic purposes*" (CoE original) and '*the potential for enhancement purposes, including potential abuse for risky, or unsafe, or uncertain, or controversial, or harmful enhancement purposes'* (my alternative wording). In 'my alternative wording', there *can* be abuse for enhancement purposes, but it is not necessarily, not intrinsically, the case. In the original sentence that the Council of Europe uses, the abuse is *intrinsic to any* application for enhancement purposes, no matter what. It is also notable that the concept of 'enhancement' is grouped so closely to the concept of 'eugenics'. This normative overreaction is something that needs to be firmly addressed by proponents of a properly regulated application of enhancements. In a similar sense, the concern over disease prevention research efforts being penalised by policy concerns about enhancement or 'incidental enhancements' would seem to be set to become a crucial focus on enhancement discussion in the years ahead.

Accordingly, the issue of how 'enhancement' has been seen, and how it should be seen, in terms of the general bioethical issues normally raised and as noted in such reactions (B) above, will be the focus of the rest of the paper. The reactions (A) noted above are related to more basic and self-evident issues that are not in question and are accepted throughout the rest of this discussion. What is important is the normative framing underlying reactions (B) as

[25] ibid
[26] ibid

some of the force of concern that they exhibit may have at least some basis in a persisting normative misunderstanding of the science of genetics. When the potential of genetic interventions was more modest, the potential of enhancements largely remained the stuff of science fiction, useful as a though-experiment for various normative arguments, but unlikely to have any real impact given the actual slow progress of genetic interventions. CRISPR-Cas9 has enabled a dramatic increase in the pace of discovery and of the potential of future genetic interventions. In turn, normative arguments and their underlying framing of how genetic interventions (such as enhancements) work, will increasingly have real-world impacts.

THE MYTH OF ENHANCEMENT

Over the last number of decades, there has been a growing literature on the potential ethical and social justice concerns of the use of new genetic technologies for enhancement purposes, particularly with regard to germline enhancements (e.g. Kass, Habermas, Sandel and Melmann). Throughout most of this time, the prospect of enhancement as a technical possibility seemed remote and, to some extent, close to – or fully within – the realm of science fiction. While the technical prospects have changed considerably in recent years, the dominant normative arguments still rely upon the same quasi-scientific genetic essentialist assumptions which remain central to the formation of the normative framework in which the assessment of enhancements still takes place. In other words, to borrow a phrase from comparative literature, there has been a *myth* built up over the years in the normative literature about what enhancements will entail in terms of the likely type and degree of changes to the individual, the family and to broader society. This has consequences for the degree of ethical concerns that arise and the ELSI responses that emerge. Using the term 'myth' is not to suggest that enhancements themselves are not real and would not have significant individual and social impact. The term 'myth' is used against the image of enhancements that has been built with a debunked genetic determinist framework. I call it a myth as it is an *overly* constructed fiction without sufficient empirical basis. This is not a criticism of bioethical speculation nor is it a criticism of approaches in anticipatory governance

or forecasting.[27] Those are important and necessary approaches when dealing with novel emerging technologies with uncertain technical and ELSI trajectories. Indeed, this is what is advocated in this paper. However, it is important to note that these approaches usefully speculate upon what *might* be, by basing their starting point from what is already known to be. What is empirically known offers a framework for the speculation of the 'more plausible' unknowns and for the associated ELSI and normative recommendations to be more appropriate, proportional and responsible. For instance, to take a fanciful example, if a pill instantly made someone immortal, all-powerful and easily morally corruptible, it would be appropriate to target this form of intervention, and proportional to prohibit all research to this end and it would be acting responsibly to ethically support (for instance) prohibition even if many other possible goods were thereby forgone in the cessation of associated research. On the contrary, it would be irresponsible to permit such research and such applications if an evil Übermensch was the likely consequence.[28] While the myth of enhancement does not necessarily, or always, go to such extremes, I contend that many of the prominent normative approaches have an unhelpful tendency in that direction. This is also not just a case of it arising in literature that is on the fringes of academia and scientific commentary. It can be seen arising in a number of high-level reports that have been drafted to respond to the advent of CRISPR-Cas9 gene-editing.

Before examining this issue in more detail below, it may be useful to give a brief summary of the main concepts and arguments arising in three recent and major reports on genome editing, with a focus here on human (germline) enhancements. In the 2016 Nuffield Council on Bioethics 'Genome editing: an ethical review' Report, it is noted that "[m]any of the questions that arise in respect of the use of genome editing beyond treatment and (arguably also) prevention of disease [i.e. enhancement] are not new and have been raised in relation to gene therapy and embryo selection following PGD".[29] The key issues raised include the standard treatment/enhancement distinction, slippery slope concerns, consumerisation of human biology, liberal eugenics, problematic interference with personal identity as well as

[27] Scott, Christopher Thomas & Selin, Cynthia (2019) 'What to Expect When Expecting CRISPR Baby Number Four', *The American Journal of Bioethics*, 19:3, 7-9,
[28] Friedrich Nietzsche (1883) *Thus Spoke Zarathustra*
[29] Greenfield, Andy et al. (2016) *Genome editing: an ethical review*. Nuffield Council on Bioethics, p.51

other well-known concepts and arguments from the established normative literature.[30] In each case, these key issues, and underlying normative arguments, rest on the assumption that the genetic is playing a crucial, dominant role, without highlighting what the equivalent environmental or social role would be.[31] While noting some issues of exceptionalism of genetic choices and also what counts as 'normal', there is considerably less focus on this as opposed to the aforementioned arguments.[32] Throughout, there is very little focus on any pro-enhancement positions (apart from briefly noting arguments from transhumanists or from approaches that see future enhancements as potentially necessary to respond to environment/climate change).[33] Overall, the enhancement discussion remains relatively intact from the pre-CRISPR normative literature where, in the main, enhancement is seen as particularly 'special' with regard to the type and degree of impact and associated normative concerns and responses.

Similarly, the National Academies of Sciences, Engineering and Medicine's 2017 'Human Genome Editing: Science, Ethics & Governance' Report notes that enhancements are characterised as spanning a normative spectrum from the 'mundane to the dangerous and problematic'.[34] This disposition is reflected in the 2016 Pew study of surveys where they observe that enhancements generate 'more anxiety than enthusiasm'.[35] Throughout, familiar pre-CRISPR concerns from unfairness, inauthenticity, eugenics and mastery are raised on the assumption of the crucial, dominant role genetic interventions would make, above what equivalent interventions (to the same or similar ends) would do in the environmental or social context.[36] The treatment/enhancement distinction is supported as being fundamentally sound, albeit not perfect, and useful, with modifications to include vaccine-like interventions.[37] While they note that, if safety and other similar concerns are overcome, there

[30] ibid, pp. 28, 51-53.
[31] In terms of the basic science elsewhere in the report, the environment is discussed with regard to the relationship between genome and phenotype. However, this basic assumption is not applied to the normative discussion.
[32] ibid, p.28
[33] ibid, p.51
[34] Charo, R. Alta, Hynes, Richard O. et al. (2017) *Human Genome Editing: Science, Ethics, And Governance. Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations.* A Report of National Academy of Sciences and National Academy of Medicine. Washington, DC: The National Academies Press. Ch. 6
[35] ibid
[36] ibid
[37] ibid

could be less objection to the application of the technology for enhancement purposes, the aforementioned societal concerns (from unfairness to mastery) would still remain to be overcome.[38] In this report, there is also scant attention devoted to any pro-enhancement positions (again, briefly noting transhumanists & environment/climate change).[39]

Finally, in the 2017 European Academies' Science Advisory Council Report, human application is only one of the many applications evaluated (the rest including agricultural applications, gene-drives and so on).[40] Nevertheless, it is still notable that the only mentions of enhancement applications are related to a fear of increasing social inequalities and an unclear statement on how they be used coercively (whether this means people would be coerced into using enhancements due to social or other pressures, or that future generations would be coerced by having interventions done upon them, prior to their ability to give consent).[41] In this report, the Genetic Alliance UK survey is referred to in highlighting that most respondents continue to rely on the treatment-enhancement distinction, while not favouring the enhancement side.[42] Overall, there is no pro-enhancement stance taken.

None of the three Reports contain anything much by way of positive discussion of enhancement but many negative points, influenced by the now very familiar normative discussions (as cited throughout the reports).[43] This is not necessarily calling for a pro-enhancement position from such reports, all things considered. Nor, of course given the focus of the reports, is it to question the obvious emphasis on the role of genetics and the normative assessment of *genetic* interventions. However, as will be detailed in the following section, the issue of imbalance arises where this genetic emphasis does not include, at its core, the

[38] ibid
[39] ibid
[40] European Academies Science Advisory Council (2017) *Genome editing: scientific opportunities, public interests and policy options in the European Union*. EASAC Policy Report 31. German National Academy of Sciences Leopoldina. Ch.5.
[41] ibid
[42] ibid
[43] In discussions of enhancements, it should be noted that there can be different interpretations on what is meant by 'enhancement' – some modest improvements in certain capabilities, while others can be more extensive. A more nuanced approach – as this paper seeks to move the debate toward – would not seek to approve or prohibit 'enhancements' per se, but would give different normative assessments to different forms of enhancement depending on the effects on the resulting people and on society in general.

equivalent emphasis of environmental or social influences in its normative assessment of genetic interventions, such as (germline) enhancement.

CHARTING NEW WATERS WITH OLD SHIPS?

A key influence from earlier normative discussions, that continues to be significantly highlighted in such reports, is the treatment-enhancement distinction that, with some minor 'disease prevention' modifications, remains pretty much as noted by Kass et al. in the 2003 Beyond Therapy, Biotechnology and the Pursuit of Happiness report:

> Where the goal is restoring health, the doctor's discretion is guided by an agreed-upon and recognizable target. But a physician prescribing for goals beyond therapy is in uncharted waters. Although fully armed with the means, he has no special expertise regarding the end—neither what it is nor whether it is desirable [and is] ungoverned by any deep ethical norms (304).[44]

Other key concerns raised in the reports also have links to earlier discussions that have highlighted various ways that enhancements are problematic in a way that treatments are not. Habermas (2003) for instance, is particularly concerned over the unfreedom that any enhanced offspring will experience due to the (irreversible) design by third parties and the prevention of being the undivided author of one's own life.[45] Sandel (2007) focus is on the motivations and character of parents who would seek enhancements for their future offspring.[46] It would, he argues, be the result of a negative character trait that strives for total mastery over one's offspring.[47] The problem is that these, and the many other normative arguments, share an underlying genetic essentialist, or genetic determinist, assumption that frames the entire normative discussion.[48] While the science of genetics, and genetic interventions, does not subscribe to any such assumption, the downplaying of the role of the

[44] Kass, Leon R., et al. (2003), *Beyond Therapy, Biotechnology and the Pursuit of Happiness* (Washington DC: Report by the President's Council on Bioethics).
[45] Habermas, Jürgen (2003) *The Future of Human Nature.* Cambridge: Polity Press.
[46] Sandel Michael J. (2007) *The Case Against Perfection: Ethics in the Age of Genetic Engineering*. Cambridge (MA): Belknap Press.
[47] ibid
[48] Resnik, D & Vorhaus D (2006) 'Genetic modification and genetic determinism' *Philosophy, Ethics, and Humanities in Medicine* 1:9

environment as an essential and equally important factor in the formation of the human (and more so, the social environment formation of the socialised human) is a puzzling but common theme in the normative discussions that dominated the pre-CRISPR context. This underlying framing takes the following form:

> Natural pre-child genetic 'potential' followed by the ('in the world') guidance of the child's lived experience (pre-genetic intervention context)

which is replaced with:

> Natural pre-child genetic 'potential' [*and then unprecedented artificial outside (genetic) influence instead of person's own negotiation of the world and its opportunities and obstacles (family, peers, schooling, etc)]* followed by the ('in the world') guidance of the child's lived experience (with whatever range of options remain) (traditional genetic enhancement context)

A seemingly obvious point seems oddly missed regarding the fundamental influence that the environment – specifically the social and parental environment – has, or should have, in the above equation. It is well established from an interactionist perspective, as Susan C. South & Robert F. Krueger note, that the so-called nature versus nurture debate has been replaced with the wider appreciation on how both influences make fundamental contributions to variation in human personality.[49] More broadly, epigenetics has also highlighted 'an important bridge' between life experiences and phenotypes by the environmental influences on gene expression.[50] More broadly still, Allen Buchanan dismisses objections that argue that genetic enhancements causing changes 'in us' are fundamentally different from 'external' or 'environmental' enhancements. It would be, he continues, "tantamount to denying that culture plays a significant role in our individual and collective identities".[51] These external or environmental enhancements are not avoidable, nor are they less profound than our genetic

[49] South, S. C., & Krueger, R. F. (2008). An interactionist perspective on genetic and environmental contributions to personality. *Social and Personality Psychology Compass*, *2*(2), 929-948. http://dx.doi.org/10.1111/j.1751-9004.2007.00062.x

[50] Tammen, Stephanie. A., Friso, Simonetta., & Choi, Sang-Woon. W. (2013). Epigenetics: the link between nature and nurture. *Molecular aspects of medicine*, *34*(4), 753–764. doi:10.1016/j.mam.2012.07.018

[51] Buchanan, Allen (2011) *Beyond Humanity?: The Ethics of Biomedical Enhancement* OUP: Oxford. p.39

influences.[52] We do not just emerge into social structures but we emerge out of them, for instance the physical social environment (urban environment, school)[53]; the cultural social environment (socialisation of norms, values[54]); the learning social environment (degree and type of sensory stimulation promotes and shapes cognitive development, creating and shaping neural pathways in the brain[55]); the emotional social environment (shapes identity, personality[56]) and combinations of all the above and more.[57] If we speak of the issue of irreversible effects of genetic design, this is not just a feature of genetic interventions but socio-environmental ones too. While the effects of a particular social intervention or influence may be reversible, does not mean that they all can. At least, not without the person essentially becoming a different person (although numerically continuous).[58] Nor need the effects (as opposed to the changes to the DNA itself) of genetic design be less irreversible. Like environmental and social design, some may and some may not.[59] The problem facing such normative discussions that rely on assumptions that downplay this artificial environmental influence is that it thereby treats as entirely unprecedented the artificial genetic influences that may be possible with interventions termed as enhancements. This is not a new criticism, rather one that has, hitherto, not been sufficiently heeded. Resnik and

[52] Bearman, Peter (eds)(2008) 'Exploring Genetics and Social Structure' *American Journal of Sociology*, Vol. 114, supplement; Giddens, Anthony, (1984). *The constitution of society: Outline of the theory of structuration*. Cambridge: Polity Press.

[53] Macionis, John J. (2013). *Sociology* (15th ed.). Boston: Pearson

[54] Bouissou, Christine & Tap, Pierre (1998). Parental education and socialisation of the child: internality, valorisation and self-positioning. European Journal of Psychology of Education, Springer Verlag, vol XIII (n°4), pp.475-484.

[55] Woollett, Katherine, & Maguire, Eleanor. A. (2011). 'Acquiring "the Knowledge" of London's layout drives structural brain changes'. *Current biology* 21(24), 2109–2114.

[56] Macionis, John J. (2013). *Sociology* (15th ed.). Boston: Pearson; Bouissou, Christine & Tap, Pierre (1998). Parental education and socialisation of the child: internality, valorisation and self-positioning. European Journal of Psychology of Education, Springer Verlag, vol. XIII (n°4), pp.475-484; Hertzman C. Putting the concept of biological embedding in historical perspective. Proceedings of the National Academy of Sciences of the United States of America. 2012;109(Suppl. 2):17160–17167

[57] Macionis, John J. (2013). *Sociology* (15th ed.). Boston: Pearson; Macionis, John J., & Gerber, Linda M. (2011) *Sociology*. Toronto: Pearson Canada.

[58] Parfit, Derek, (1984) *Reasons and Persons*. Oxford: Clarendon Press.

[59] It should be noted that none of this is to suggest that genetic factors can never have an impact independently from the social environment. For instance, the disease caused by the autosomal dominant mutation in the Huntingtin gene does not require socio-environmental factors to occur. It is also not to say that genetic interventions necessarily have a weaker, short-lasting and easily reversible impact on future generations than social interventions. This may or may not be the case depending on the level of gene-environmental interactions involved, e.g. intelligence and personality interventions within the normal range. This would be more evident if one takes the aforementioned interactionist perspective for instance. It is also important to note that when one states that genetic interventions have a stronger, longer lasting and less reversible impact, this is referring to the changes to DNA and not necessarily to the phenotypic effects of those changes. On this last point, see Yeung, Karen (2018) Genome editing and human reproduction: social and ethical issues. Nuffield Council on Bioethics: pp71-72.

Vorhaus (2006) previously argued that some of the well-known objections to human genetic modification of human beings rely heavily on genetic determinist assumptions "despite conclusive evidence to the contrary".[60] Contra Habermas (to return to the example above) we have never been the sole undivided author of our lives, but we just continue to write new pages. The ethical concerns that are speculated to arise from the use of genetic enhancements should therefore be considered as concerns from some potential applications or forms of genetic enhancements, and not of genetic enhancements per se. Whether social or genetic, some degree of co-authorship is to be expected and thereby normatively acceptable – this would still hold excessive authorship from parents or others to be still a bad thing. Similar responses can be put toward mastery objections, cheating, and so on. As Resnik and Vorhaus notes:

> a genetically modified person may be a passive subject in the development of certain traits, such as eye color or skin color, he or she must take an active role in the development of most traits in which authenticity might be any concern, such as intelligence, athletic ability, social skills, or musical ability.[61]

What should be added to Resnik and Vorhaus' comment here is another fundamental source of development – namely the social-environmental role – that would have an impact upon a continuum within which the individual can be regarded as passive subject (e.g. early socialisation) to active agent. Some balance between treating the individual as passible subject and active agent is unavoidable and morally required in raising children and, sometimes, whether due to excessive parenting or cultural control, the stage of passive subject can be too pervasive. Nevertheless, that there are bad applications of social interventions, does not count against social intervention per se. This point is similar to Agar's 'Nurture Principle' (holding that genetic interventions are as permissible as the environmental interventions, where the goal is the same).[62] However, rather than simply a thought experiment or intuitive assumption, it is something that is the subject of a longstanding analysis and conceptualisation by the social sciences, and therefore should be supported as such. The expertise that Kass's physician lacks does indeed need to be developed in order for

[60] Resnik, D & Vorhaus D (2006) 'Genetic modification and genetic determinism' Philosophy, Ethics, and Humanities in Medicine 1:9
[61] ibid
[62] Agar, Nicholas, (2004) *Liberal Eugenics: In Defence of Human Enhancement* (Oxford: Blackwell).

adequate normative guidance and a suggestion here would be to incorporate the insight from social scientists to this end. While Resnik and Vorhaus correctly diagnosed the problem where the normative reactions to genetic modification was based on false genetic determinist assumptions, their constructive suggestion was open and without specification. In short, the promising role of sociological insight was insufficiently mapped out.

REFRAMING THE ENHANCEMENT DISCUSSION WITH SOCIOLOGICAL INSIGHT

As in the case of the pre-CRISPR normative literature, sociological insight continues to be insufficiently included. This can be seen in the three reports noted above. In the case of the 2017 EASAC report, there is no sociological input, bar an expressed 'hope' for future social consensus and a mention of needed engagement with the social sciences, but only for public engagement strategies.[63] In the 2016 Nuffield report, there is scant mention of socially constructed view of normality (in the context of defining disability), and nothing significant on enhancement itself.[64] Throughout, there is no mention of social structures 'co-creating' the phenotype (i.e. that which ultimately matters – the resulting person). Similarly, in the 2017 NASEM report, there is a brief mention of socially constructed view of normality with regard to the insight from disability perspectives.[65] While there is some mention of non-genetic enhancements examples (e.g. coffee), these are few and minor and there is no discussion of the notion of social structures 'co-creating' the person.[66] It should be noted that there is a brief objection against Sandel's mastery point with regard to the speculative nature of such fears and the parameters already allowed to parents, but without any significant development and without sociological input.[67] As Wilkinson (2010) had previously argued against Sandel, while it may be speculated that such attitudes exist in prospective parents, the concern that they would spill over into their attitudes when they are actual parents is a

[63] European Academies Science Advisory Council (2017) *Genome editing: scientific opportunities, public interests and policy options in the European Union*. EASAC Policy Report 31. German National Academy of Sciences Leopoldina. Ch.5.
[64] Greenfield, Andy et al. (2016) *Genome editing: an ethical review*. Nuffield Council on Bioethics.
[65] Charo, R. Alta, Hynes, Richard O. et al. (2017) *Human Genome Editing: Science, Ethics, And Governance. Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations.* A Report of National Academy of Sciences and National Academy of Medicine. Washington, DC: The National Academies Press.
[66] ibid
[67] ibid

mere possibility largely based on conjecture without empirical evidence.[68] More fundamentally, as Corrigan (2009) notes, the concerns of Habermas (and others), while widely debated, rely on a view that presupposes "a biological essence to human identity, and as such they contravene many contemporary concepts based on the 'social construction' of the body".[69] In such reports, it is problematic that such conjectures and presuppositions are not further challenged (in the strongest terms) with regard to levels of empirical evidence (or lack thereof) and alongside a more central inclusion of the social constructionist framing of the body. It is not just a case of some papers or commentaries from some authors propounding such conjectures, but reports that profess to highlight the state-of-the-art in terms of the relevant normative literature.

In a more recent Report from the Nuffield Council (2018), there is a genuine change of tone in the fundamental assumptions underlying the dominant normative arguments (including making space for a change to the aforementioned enhancement myth).[70] The report questions why genomic interventions are considered exceptional when compared to other parental interventions such as education and inculcating the moral conscience, highlighting the belief of changes 'indelibly inscribed into a future person's biology' even where the actual effects are of lesser magnitude.[71] Recalling Habermas's aforementioned concerns, the report notes it as "bordering on genetic determinism [and] exceptionalist in the sense that it treats genetic factors as radically more important than other constraints that parents might apply".[72] So far, as evidenced here and elsewhere in the 2018 Nuffield Report, this change in direction is more the exception in the overall normative state-of-the-art, but it is a promising step that such reframing is in progress. Of course, none of this is not to argue that genetic essentialism should be replaced by the pure social constructionism, but rather that they cannot be separated with one side ignored or downplayed. Overall, this argument posits that

[68] Wilkinson, Stephen. 2010. *Choosing Tomorrow's Children: The Ethics of Selective Reproduction*. Oxford: Clarendon Press, pp.136-137
[69] Corrigan, Oonagh, (2009) 'Genetics and Social Theory' in Turner, Bryan S. (eds) *The New Blackwell Companion to Social Theory*. (Blackwell Publishing Ltd): p.350
[70] Yeung, Karen (2018) *Genome editing and human reproduction: social and ethical issues*. Nuffield Council on Bioethics.
[71] ibid. pp.71-72
[72] ibid. p.68; As noted by one of the referees, the common portrayal of Habermas and Sandel as outlined in this paper and as criticised by Corrigan, Yeung and others, is not necessarily the only portrayal. For the purposes of this paper, I will keep to the common portrayal.

the lacuna of such a basic 'genetic-social environmental co-creation' premise likely continues to imbalance the discussions on enhancement and the subsequent ethical conclusions.

Given the well-established and fundamental nature of this genetic-environmental co-creation, it begs the question why this scientific frame is replaced with an effective genetic essentialist frame when one moves to the normative context, and why it is so resilient. In addition to normative responses most likely not being appropriate nor proportionate (ultimately, 'not fit for purpose'), there is the issue of a lack of responsibility where this approach risks exploiting "the public's worst fears and perpetuates misunderstandings concerning basic human biology and genetics".[73] This could (and likely does) give rise to a vicious circle where normative objections to misperceptions of genetic science contributes to the basis for further normative objections and further public concerns. In fairness to the normative literature, Corrigan reports how this is a much wider cultural phenomenon where the gene has become a powerful icon.[74] She also highlights how exaggerated claims by scientists themselves as well as the media play significant roles.[75] This is not to say that the social sciences have not been giving longstanding attention to the biological and genetic sciences and potential developments in genetic modification. Sociologists have, for instance, been concerned that genetics could serve to legitimate existing unjust social arrangements or that the genetics of behaviour is a eugenicist project in disguise.[76] Nevertheless, as Freese (2008) notes, the accumulating evidence from genetics suggests many individual-level outcomes of sociological interest are genetically influenced to a substantial, but not determinist, degree.[77] Freese and Shostak (2009) note that while social science and genetic science have fairly little engagement with each other, there are emerging developments that

[73] Resnik, D & Vorhaus D (2006) 'Genetic modification and genetic determinism' *Philosophy, Ethics, and Humanities in Medicine* 1:9
[74] Corrigan, Oonagh, (2009) 'Genetics and Social Theory' in Turner, Bryan S. (eds) *The New Blackwell Companion to Social Theory*. (Blackwell Publishing Ltd): p.350
[75] Corrigan, Oonagh, (2009) 'Genetics and Social Theory' in Turner, Bryan S. (eds) *The New Blackwell Companion to Social Theory*. (Blackwell Publishing Ltd): p.350
[76] Bearman, P (2008) 'Introduction: Exploring Genetics and Social Structure' in Bearman, P (ed) Exploring Genetics and Social Structure special issue, *American Journal of Sociology*, Vol. 114, Supplement 2008.
[77] Freese, J (2008) 'Genetics and the Social Science Explanation of Individual Outcomes' in Bearman, P (ed) Exploring Genetics and Social Structure special issue, *American Journal of Sociology*, Vol. 114, Supplement 2008.

can create a larger space for genetic and social scientists to incorporate each other's insights without a sense of capitulation to the other.[78]

It is also not to say that ethicists or moral or legal philosophers developing the normative literature should be replaced by sociologists or social scientists. However, in positing what should, or should not, be requires one to know better what *is*, of which effects of social structures are central. A greater dialogue is required between normative theorists and social scientists, as well as genetic scientists, in order to first identify the empirical basis to many assumptions that then inform the subsequent normative reflections and discussions. It is at this point that the proper work of speculation can begin.[79]

CONCLUSION

In dealing with future technologies and future societies, anticipatory bioethics and speculation is needed and can fruitfully lead to an identification of the ELS issues that may arise and what subsequent responses might be required. But this speculation can be better framed (and some potential scenarios, futures and technical consequences already dismissed as idle fantasy) by being better underpinned with more robust empirical assumptions than is done in many cases. The notion of 'responsible speculation' is relevant here due to the fast-evolving scientific developments and the pressing issue of developing adequate ELSI responses. As was particularly evident in the context of 'incidental enhancements', this speculation must be done with a greater sense of responsibility for how it may drive current discussions, attitudes and policy approaches with regard to emerging gene editing scenarios

[78] Freese, Jeremy & Shostak, Sara (2009) 'Genetics and Social Inquiry' *Annual Review of Sociology*, Vol. 35:107-128 (August 2009).

[79] While this paper had the more modest, yet worthwhile, goal of highlighting the persistence of this genetic essentialist framing in CRISPR-Cas9 discussions, there are some indications of an emerging alternative (sociologically-informed) framework taking formation. Some examples of this promising work can be seen in Owens (2013) 'Towards a New Sociology of Genetics and Human Identity'; Hauskeller, Sturdy, and Tutton (2013) Genetics and the Sociology of Identity; Tamir (2016) 'Postnatal Human Genetic Enhancement – A Consideration of Children's Right to Be Genetically Enhanced', Frontiers in Sociology; Laura Yenisa Cabrera (2017) 'Reframing Human enhancement: A Population Health Perspective', Frontiers in sociology. Also see: Garrison, Nanibaa' A., Brothers, Kyle B., Goldenberg, Aaron J. & Lynch, John A. (2019) 'Genomic Contextualism: Shifting the Rhetoric of Genetic Exceptionalism', *The American Journal of Bioethics*, 19:1, 51-63,

with real world medical and societal consequences. Resnik & Vorhaus had noted that the day was coming when such genetic discussions move outside the world of academia and into the world of public policy and political decision-making.[80] At this point, they continued, there will be a "need for well-reasoned scientific policy [that] cannot be built on logical or biological errors and misunderstandings".[81] Given the rapid post-CRISPR advances in progress, this day appears to have come. To this end, there is an urgent need for an alternative 'default' framing giving greater role for sociological input (i.e. the pervasive effects of social structures) into the normative debates on genome editing, as particularly notable in the enhancement myth, for more balanced and productive discussions, attitudes and policy approaches.

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[80] Resnik, D & Vorhaus D (2006) 'Genetic modification and genetic determinism' *Philosophy*, *Ethics*, *and Humanities in Medicine* 1:9

[81] Resnik, D & Vorhaus D (2006) 'Genetic modification and genetic determinism' *Philosophy*, *Ethics*, *and Humanities in* Medicine 1:9