

Lame ducks might fly: genome editing, global consensus and geo-ethics

Peter Mills^a

^a Nuffield Council on Bioethics (UK)

Genome editing offers a way of making precisely targeted modifications to DNA in living cells, harnessing the cells' inbuilt repair mechanisms to repair a deliberate, double-stranded DNA break in a way that may either disable or introduce a functional DNA sequence. It has become a commonplace of biological research that the CRISPR-Cas9 genome editing system and its analogues, which emerged after 2012, are radically cheaper, quicker, more efficient, and easier to use than previous techniques [1].

Genome editing, however, is not pixie dust, sprinkled onto an organism to transform it with a wish, though, from a reading of journal editorials over the last few years, one might be forgiven for thinking that it is. It is a biological technique – or, rather, a suite of biological techniques – implicated in a number of hitherto theoretical but emerging biotechnologies and biomedical technologies [2]. The realisation of these technologies will depend upon the convergence of many factors including distinct forms of knowledge and technical skill: on the identification and characterisation of genome targets, on mechanisms that can deliver the editing machinery effectively into the target cells, on conditions that cause the modified cells to function in the organism in the way intended, and, if they do, on the absence of collateral, pleiotropic effects, etc. It will also depend on conditions of political and financial support, governance and public acceptance.

The range of prospective genome-editing technologies is impressive. Extrapolating from current research, last year's Nuffield Council on Bioethics report, *Genome editing: an ethical review*, highlighted applications in drug development, cell-based therapies, public health, ecosystem engineering, agriculture, security, culture and leisure [1]. All of these applications raise distinctive moral challenges. A second stage of the Council's work, now in progress, takes up these challenges from the other end, so to speak: rather than beginning with the technique and asking how it may be put into practice, it starts with challenges facing human societies and asks what the contribution of genome editing might be to these.¹

1 This dual approach is designed to avoid two types of potential reflective limitation previously identified in Nuffield Council on Bioethics (2012), *op. cit.*: first, of hypothecating societal challenges to technological solutions and, second, of hypothecating technologies to particular challenges or applications.

The first issue to which the Council has turned its attention is that of genome editing in human reproduction.² The reasons for giving priority to this area, which is already subject to comprehensive and effective legislation in the UK, are not that reproductive applications of genome editing are necessarily the most proximate. They are, rather, that the moral questions those applications raise are among the most difficult to address and it were better to make an early start, current legislation notwithstanding. This is not, in any case, an issue for the UK alone.

When the prospect of using genome editing techniques in human embryos was raised many responses adverted to the 'international consensus' against human germline modification. (The call to respect this consensus resurfaced recently in reaction to the publication of the latest major contribution to the debate, the US National Academies of Sciences and of Medicine report, *Human Genome Editing: Science, Ethics, and Governance*) [3–5]. This consensus, however, may very well be (as we say in English) a *canard*.

When one seeks evidence of the international consensus against human germline modification the instruments most often cited are those of the United Nations and the Council of Europe, which address such practices explicitly, grounding their provisions in internationally recognised human rights.³ Of these, one (the UNESCO Universal Declaration on the Human Genome and Human Rights), while having identified that practices like 'germline interventions' *could* be contrary to human dignity, has so far not, despite a recent re-examination, decided the issue.⁴ The Council of Europe's

2 The Council prioritised two areas for immediate further consideration: human reproduction and livestock production. The livestock work will begin in 2018.

3 The Council of Europe Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine ('Oviedo Convention') and the UNESCO Universal Declaration on the Human Genome and Human Rights.

4 Art. 11 mandates that practices contrary to human dignity (it mentions human reproductive cloning explicitly) should not be permitted and Art. 24 mandates the International Bioethics Committee to make recommendations "regarding the identification of practices that could be contrary to human dignity, such as germ-line interventions". The 2015 *Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights* (available at: <http://unesdoc.unesco.org/images/0023/002332/233258E.pdf>) calls on states and governments (inter alia) to agree a moratorium on germline engineering "at least as long as the safety and efficacy of the procedures are not adequately proven as treatments" and to "Renounce the possibility of acting alone in relation to engineering the human

Oviedo Convention, on the other hand, which constitutes binding law in the 29 countries that have signed and ratified it, contains an explicit prohibition against a genome intervention for any purpose other than preventive, diagnostic or therapeutic purposes, and against any intervention that has as its aim “to introduce any modification in the genome of any descendants”.

Though the effect is reasonably clear, the elaboration of what became Article 13 of the Oviedo Convention can, however, be seen as the deferral of two unresolved uncertainties.⁵ The first, which occluded the other for much of the preliminary discussion, concerned the predictability of outcomes given the *current state of scientific knowledge*. This provided the main objection to making some exceptional provision in the Convention for modifications to the germ cell line. Despite there being no clear understanding of what would constitute *sufficient* scientific knowledge, the parties were nevertheless able to concur that there was an absence of such knowledge and that this absence was a sufficient reason for the prohibition. At any rate, it was sufficient for the time being: they also agreed that this situation should be reviewed, initially within five years of the Convention’s entry into force (see Article 32 of the Convention) although the provision has, in fact, stood until the present time.

The second uncertainty, although this did not fall to be addressed given the sufficiency of the first, concerned the moral acceptability of intergenerational genome modification for ‘alleviating severe human suffering’ or ‘to eliminate recognised abnormalities and disease’, and how this might be distinguished from modifications aimed at producing people with particular, desired characteristics.⁶ And *this* the advance of scientific knowledge could not be expected to resolve. This is why, now that it is possible to foresee a situation in which the requisite scientific knowledge might come at last within our grasp, the production of *moral* knowledge has resurfaced as a matter of urgent debate.

The point is this: rather than expressing a categorical moral consensus, the international agreement to prohibit intergenerational genome modification should be seen instead as prudential or merely temporizing; on the other hand, the consensus that *did* exist, regarding the mischief to be avoided, did not entail an agreement to prohibit intergenerational genome modification.⁷

genome and accept to cooperate on establishing a shared, global standard for this purpose”.

5 The elaboration of the two instruments mentioned has been described as the ‘first steps’ in a ‘human rights strategy’ towards the elaboration of an international biomedical law. See Andorno R. Biomedicine and international human rights law: in search of a global consensus. *Bulletin of the WHO*. 2002;80(12):959-63.

6 These phrases are taken from the preparatory document available at: www.coe.int/t/dg3/healthbioethic/texts_and_documents/CDBI-INF%282000%291PrepConv.pdf (accessed 2/8/2017). The drafters did not record what consideration might have been given to so-called ‘negative eugenics’.

7 This mischief is, in the words of the Explanatory Report, “modification of the human genome so as to produce individuals or entire groups endowed with particular characteristics and required qual-

In its statement on genome editing of 2 December 2015, at the same time as affirming the existing provisions of the Oviedo Convention as a starting point (in particular, but not exclusively, Article 13), the Council of Europe Committee on Bioethics (DH-BIO) itself recognised the relevance of Article 28 of that Convention, thereby adding its voice to calls for earnest international debate.⁸ I should like, in closing, to draw attention to two principal dimensions of the anticipated debate, the articulation of which, I believe, will be deeply consequential for the project to ground moral consensus on this issue in human rights.

The first of these dimensions is that of democratic engagement. The challenge here is to (re)constitute an effective public sphere by (re)connecting disengaged epistemologies, moralities and imaginaries. This means exploring deferred uncertainties in their immanence to situated experience; without this engagement, democratic processes risk simply aggregating prejudices. This becomes urgent in measure with the faltering of temporal and structural mechanisms for deferring uncertainty (deferral in lieu of future knowledge and deference to authoritative institutions). It is also, not unconnectedly, a more general political exigency in liberal democracies that have experienced rising tension between populism and the protection of human rights.⁹ This, then, requires bioethics to rediscover its relationship with politics.

The second dimension is what I want to call a “geo-ethics”: the interactions of formal institutions, organisations and polities that recognise the potential for the spatiotemporal diffusion of genome-editing technologies across political geographies and legal jurisdictions: the fact that, for example, developments in one field of application are not inconsequential for others; that, for example, practice in a foreign jurisdiction – or even outside law – cannot be ignored at home. Consequently, there is a need to move discussion beyond rarefied decisions about reproductive choice and confront the prospect of reified technologies in play among different social and cultural realities.

ities”. It is the mischief also addressed in Article 3 of the EU Charter of Fundamental Rights and that lies behind the UNESCO Declaration, albeit that the latter is framed in terms of the integrity of ‘the human genome’ rather than the integrity of inheritance (both of which notions are, in their own ways, problematic).

8 For the DH-BIO statement see: www.coe.int/en/web/bioethics/-/gene-editing (accessed 2/8/2017). Article 28 of the Convention, entitled “Public debate”, contains an injunction to promote specifically *public* discussion. The author was a UK member of the Council of Europe Bioethics Committee in December 2015, when the statement was agreed.

9 As Mildred Solomon and Bruce Jennings have recently written (Bioethics and Rising Populism: How Should Our Field Respond? *Hastings Center Report*. 2017;47, no. 2:11-6), bioethics cannot be disengaged from the threat of ‘authoritarian populism’, although this problem may be more acute for bioethics in the US, which has become more disciplinary and institutionalised, than in (for example) the UK, which has managed to remain interdisciplinary and productive of engagements between science, industry and society.

Correspondence

Dr Peter Mills
Assistant Director
Nuffield Council on Bioethics (UK)
28 Bedford Square
UK-London WC1B 3JS
E-mail: pmills[at]nuffieldbioethics.org

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