Genetic Engineering Regulation

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A comment on the regulatory environment in the field of genetic engineering

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Introduction

The discovery of the structure and function of DNA in the 1950's was a monumental event in the history of humanity. It was naturally followed by the question of our ability to change it. This resulted in a number of experiments, around the early 1970's, in which it was shown that DNA could be collected from different sources and deliberately recombined. It became clear that it was possible to make genetic patterns that were different from those found in nature.

This "recombinant DNA" gave rise to the field of genetic engineering. There were plenty of opportunities to put this technology to practical use and the industry of "biotechnology" formed around this.

It was not long after this, that a human gene, somatostatin, was spliced into the bacteria E. coli.[1]

The era of 'synthetic biology' had arrived. The ambition for the field included not only describing and analysing existing genes in nature, but also constructing new genetic patterns through re-arrangement.[2] In fact, the early ideas of re-arrangement had been superseded by the ideas of *de novo* design and "programming" of genes, and therefore, life itself.

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[1] Itakura, K., Hirose, T., Crea, R., Riggs, A., Heyneker, H., Bolivar, F. and Boyer, H., 1977. Expression in Escherichia coli of a chemically synthesized gene for the hormone somatostatin. *Science*, [online] 198(4321), pp.1056-1063. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/412251> [Accessed 22 April 2020].

[2] *Gene*, 1978. Nobel prizes and restriction enzymes. [online] 4(3), pp.181-182. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/744485> [Accessed 22 April 2020].

It is hard to imagine higher stakes than this. The development of synthetic biology is faced with interest from all spheres of society. A point of influence in the field is the interplay of the ethos of open science and intellectual property law. Another important aspect of the field is the regulation that surrounds it.

Current state of regulation in the field

In 2016, the CRISPR patent dispute in the United States, clearly brought forth the issue of intellectual property in the field. The dispute, which is ongoing currently, between the Broad Institute and University of California, Berkeley, has had major ramifications for the bio-technology industry.[3]

In 2018, reports came out about the gene editing experiments conducted on human babies by researchers in the People's Republic of China. They claimed to have created "the first genetically modified human babies". This sent shockwaves throughout the world, and put the question of regulation of the field at the forefront.

There is a difference of opinions among researchers regarding the adequate level of concern and the capabilities of the technology. OvaScience, a company based in the United States, argues that this technology will allow parents to choose not only "when and how they have children [but also] how healthy those children are going to be". David Sinclair, a geneticist at Harvard University and a co-founder of OvaScience, stated at a presentation that "there is no reason to expect" that the ability to remove defective genes, referring to those in genetic diseases, "won't be possible in coming years."[4]

[3] Cross, R., 2018. Broad Prevails Over Berkeley In CRISPR Patent Dispute. *Chemical & Engineering News*, [online] Available at: <https://cen.acs.org/policy/litigation/Broad-prevails-over-Berkeley-CRISPR/96/web/2018/09> [Accessed 22 April 2020].

[4] Regalado, A., 2020. Engineering the Perfect Baby. *MIT Technology Review*, [online] Available at: <https://www.technologyreview.com/2015/03/05/249167/engineering-the-perfect-baby/> [Accessed 22 April 2020].

It is easy to understand the concerns surrounding the field, especially on the topic of extreme scenarios.[5]

However, some researchers state that the capabilities of the technology, currently, do not extend as far as people are touting it to be. Dr. Stuart Kim, a genetics professor at Stanford University, argues that the notion of making an individual faster or more resilient is "still far enough off, [that it] might as well be the stuff of science fiction".[6] Similarly, Rudolf Janeisch, a biologist at the Massachusetts Institute of Technology, stated that any "attempts to edit human embryos [are] totally premature".

The focus of the technology is, for the most part, on single-gene disorders, whereas traits such as increasing resistance to muscular injury for example, involve multiple genes. In order to make modifications on the level of these traits, it would first need to be understood how these genes interact. However, the difference of opinion among researchers illustrates the uncertainty about the current and near future capabilities.

It is prudent, given the profound consequences, to address the regulatory and ethical issues through a global discussion. Internationally, the countries of the People's Republic of China, the United States, and the United Kingdom are at the forefront of genetic engineering. It is useful to look at the regulations in place in these jurisdictions, since it is likely that other countries will also look to their actions.

People's Republic of China

[5] Brownell, C., 2016. From curing diseases to making designer babies, human gene editing is coming. *Financial Post*, [online] Available at: <https://business.financialpost.com/executive/smart-shift/from-curing-diseases-to-making-designer-babies-human-gene-editing-is-coming > [Accessed 22 April 2020].

[6] Beresini, E., 2016. Could CRISPR Genetically Tailor Athletes? It's a Nice Idea. *Outside*, [online] Available at: <https://www.outsideonline.com/2045666/could-crispr-genetically-tailor-athletes-its-nice-idea> [Accessed 22 April 2020].

In theory, there is an outright legislative ban on gene editing of human embryos in China.[7] However, China's stem cell research is often referred to as "wild" and it being "one of the most unrestrictive regulatory regimes".[8]

The problem is the lack of enforcement of the regulations, and the loopholes in them. The Chinese researchers recently used one such loophole to edit the genes of human babies for the first time in history.[9]

The Guidelines for Ethical Principles in Human Embryonic Stem Cell Research, a 2003 joint issuance from the Ministry of Science and Technology, covers this field of research. The National Health and Family Planning Commission (NHFPC), in charge of guidance and formation of scientific programs related to health and family planning, and the Chinese Food and Drug Administration (CFDA), which regulates genetic testing, are other agencies that could also be involved in such a scenario.

The guidelines dictate a ban on "using human egg plasma and nuclear transfer technology for the purposes of reproduction, and the manipulation of the genes in human gametes, zygotes or embryos for the purposes of reproduction". However, the guidelines permit research using embryonic stem cells from specified sources, such as unwanted embryos from IVF, miscarriages, voluntarily induced abortions, and donated germ cells.

It is important to note that the ban allows clinical applications of gene sequencing to continue if they are approved by the NHFPC and are done according to regulations. The ban actually mostly

[7] Gould, S. and Loria, K., 2015. This map shows where researchers might design the first genetically engineered baby. *Business Insider*, [online] Available at: <https://www.businessinsider.com/what-countries-allow-researchers-to-edit-human-embryos-2015-10?IR=T> [Accessed 22 April 2020].

[8] Juan, S., 2015. Health authority announces step to rein in 'wild' stem cell treatment. *China Daily*, [online] Available at: <http://www.chinadaily.com.cn/china/2015-08/21/content_21662613.htm> [Accessed 22 April 2020].

[9] Fox, M., 2018. Chinese researcher says he is 'proud' of gene-editing twins. *NBC News*, [online] Available at: <https://www.nbcnews.com/health/health-news/chinese-researcher-says-he-proud-gene-editing-twins-n941201> [Accessed 22 April 2020].

consists of guidelines, which are considered “soft laws”. This might also make the use of sanctions, as a control mechanism, ambiguous or unenforceable.[10]

United States

The National Institutes of Health (NIH) in the United States issued a statement, after the news of the Chinese researchers’ experiments on human babies, that it would "not fund any use of gene-editing technologies in human embryos."[11] The NIH states that “it is a line that should not be crossed” and that “there are multiple existing legislative and regulatory prohibitions” to that effect.

The Dickey-Wicker amendment prohibits the Department of Health and Human Services (HHS) from using any appropriated funds for both, "the creation of a human embryo or embryos for research purposes", and "research in which human embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on foetuses in utero" according to the applicable federal law.

There are indications, however, that the United States might remove some of these restrictions. David Magnus, the Director of the Stanford Centre for Biomedical Ethics, and Nicole Martinez, a lecturer and fellow at Stanford University, have criticized the United States regulatory control of gene editing "as a 'wild west' of reproductive technology."[12]

One of the concerns is, that there is no government authority that regulates privately funded projects. Therefore, it is not illegal to implant a genetically modified embryo to begin a pregnancy. Moreover, owing to the separation of powers between the states and the federal

[10] Friedman, L., 2015. Tweaking the genes in human embryos is technically legal in many countries, and a new experiment could open up the floodgates. *Business Insider*, [online] Available at: <https://www.businessinsider.in/science/tweaking-the-genes-in-human-embryos-is-technically-legal-in-many-countries-and-a-new-experiment-could-open-up-the-floodgates/articleshow/47032030.cms> [Accessed 22 April 2020].

[11] National Institutes of Health, 2015. *Statement On NIH Funding Of Research Using Gene-Editing Technologies In Human Embryos*. Director, NIH. Available at: <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos>

[12] Magnus, D. and Martinez, N., 2016. In Embryo Research We Need Laws First, Then Science. *Time*, [online] Available at: <https://time.com/4204059/crispr-regulation/> [Accessed 22 April 2020].

government, states such as California are considering funding research on gene editing of human embryos as per their own laws.

United Kingdom

England was the first country to have a test-tube baby. It was also the first to use pre-implantation genetic diagnostics, and to clone a higher vertebrate. It has been a leader "in human embryonic stem cell derivation and banking."[13] The United Kingdom is always at the forefront of any discussion on reproductive medicine.

The Human Fertilisation and Embryology Act governs the Human Fertilisation & Embryology Authority (HFEA). It is responsible for regulation of all research involving human embryos. The Act imposes an outright ban on the use of modified embryos for pregnancy. It only permits implantation of an embryo if "no nuclear or mitochondrial DNA of any cell of the embryos has been altered and no cell has been added to it other than by division of the embryo's own cells."[14]

There is, however, a point of interest, which is the licensing system. In February 2016, there was a research license granted that allows for the keeping, use, and storage of embryos for a period of three years, with the option of renewal. This was used to genetically edit human embryos. The embryos were donated by a couple, from their surplus after IVF treatments, since the researchers could not have implanted it as per regulations.[15] The license notes that these activities are for the purpose of "developing treatments for serious disease or other serious medical conditions,"

[13] Franklin, Sarah, and Celia Roberts. Born and Made: An Ethnography of Preimplantation Genetic Diagnosis. STU - Student edition ed., Princeton University Press, 2006. JSTOR. Available at: <https://jstor.org/stable/j.ctt4cgd33>. [Accessed 21 April 2020].

[14] *Human Fertilisation and Embryology Act*, 3(5)(4)(b-c). Available at: <https://www.legislation.gov.uk/ukpga/2008/22/section/3 > [Accessed 22 April 2020]

[15] Callaway, E., 2016. UK scientists gain licence to edit genes in human embryos. *Nature News*, [online] Available at: <https://www.nature.com/news/uk-scientists-gain-licence-to-edit-genes-in-human-embryos-1.19270> [Accessed 22 April 2020].

"increasing knowledge about the development of embryos," and "promoting advances in the treatment of infertility."[16]

This license can be seen as the first global endorsement for such research by a national regulatory authority, and as a precedent for the future. The HFEA committee did reiterate that the research project cannot involve placing non- permitted embryos, eggs, or sperm in a woman, or keeping or using embryos after fourteen days from the date of creation or upon the appearance of a primitive streak. It also stressed that no gene editing research can take place without an ethics approval.

Final remarks

The field of genetic engineering affects global concerns such as medicine, law and trade. Moreover, as a matter of financial opportunities or prestige, in the race to make the breakthroughs first, few countries are willing to adopt binding measures. UNESCO's Universal Declaration on Bioethics and Human Rights is an illustration of this.

It is true that early success shows the promise of this field. This makes the advocates of openness concerned to see it develop in a publicly beneficially manner. However, what that looks like remains unclear.

[16] 2015. License Committee Minutes. [online] Human Fertilization & Embryology Authority. Available at: <https://ifqlive.blob.core.windows.net/inspectiondocuments/5768.pdf> [Accessed 22 April 2020].