Received: 15 December 2021 | Accepted: 10 June 2022

DOI: 10.1111/jwip.12237

ORIGINAL ARTICLE

THE JOURNAL OF WORLD INTELLECTUAL PROPERTY WILEY

Patent power in biomedical innovation: Technology governance in biomodifying technologies

Edison Bicudo[1] | Michael Morrison[2] | Phoebe Li[3] | Alex Faulkner[4] | Andrew Webster[5†] | Miranda Mourby[2] | Jane Kaye[2]

[1]Department of Science, Technology, Engineering, and Public Policy, University College London, London, UK

[2]Centre for Health, Law and Emerging Technologies (HeLEX), Faculty of Law, University of Oxford, Oxford, UK

[3]School of Law, Politics and Sociology, University of Sussex, Brighton, UK

[4]School of Global Studies, University of Sussex, Brighton, UK

[5]Science and Technology Studies Unit (SATSU), Department of Sociology, University of York, York, UK

Correspondence
Edison Bicudo, Department of Science, Technology, Engineering, and Public Policy, University College London, Shropshire House (4th Floor), 11-20 Capper St, London WC1E 6JA, UK.
Email: e.bicudo@ucl.ac.uk

Funding information
Leverhulme Trust; Economic and Social Research Council

Abstract

Biomedical innovation is often rewarded by exclusive proprietary rights such as patents. In the case of gene editing, induced pluripotent stem cells, and three-dimensional (3D) bioprinting (here described as biomodifying technologies), the limitations of the patent system come into stark relief, generating both technical and political doubts. Generally, political and technological limitations are supposed to be solved with so-called good governance, based on some principles. We focus on three of such governance principles (participation, accountability, and transparency) to show how they have been weakened, instead of strengthened, by the current patent system. We demonstrate that although patent applications are submitted by both public and private players, the latter have imposed a growing dominance in gene editing, induced pluripotent stem cells, and 3D bioprinting, disseminating their aggressive and exclusive strategies. As a consequence, a logic of experimentality tends to prevail where the three fundamental governance principles fail to be enacted.

†In memoriam.

KEYWORDS
3D bioprinting, experimentality, gene editing, iPSCs, patents, technology governance

1 | INTRODUCTION

1.1 | Governance and experimentality

Is it sufficient that therapies be effective and safe, as attested in clinical trials, or is it also important that they be originally developed and owned via inclusive and transparent schemes? Differently said, are the institutions and companies responsible for the development and intellectual appropriation of therapies exclusively subjected to technical and scientific standards or should they also comply with democratic mandates to be transparent, inclusive, and accountable? To explore these questions, this paper focuses on the patent system as it has evolved in three areas: gene editing, induced pluripotent stem cells, and 3D bioprinting.

This analysis will be guided by the concept of experimentality, as proposed by Petryna.[1] Pharma and biomedical companies, in order to argue for the viability of their products, may conduct some studies whose design is controversial (because minimal superiority over alternative products has to be shown) and whose outcomes have limited publication (due to market secrets). Experimentality emerges when the logic of market secrecy leaves the realm of industries and laboratories. At such moment, the targets of experiments are not only products but also institutions, populations, and social relations.

In other words, experimentality is the logic disseminated by global schemes of biomedical innovation where a few market players subject populations and countries to an innovation process in which corporate rationales tend to prevail. For example, the formation of a global clinical trials industry has turned national regulatory frameworks into useful cogs in the commercial, globalised clinical trials system while turning national populations into potential research subjects.[2]

Parallel to such logic of experimentality, there is a rationale frequently described by means of the concept of governance. Biomedical innovation, because of its growing complexities, requires inputs from a variety of institutions and companies.[3] It is frequently difficult to strike a good balance in this social interplay, as some players have greater capacity to impose their agendas on their collaborators. With its political legitimacy, the nation state is expected to intervene and foster the balanced relations associated with governance.

In his review of the literature on governance, Reich[4] verified that accountability and transparency are the principles discussed the most frequently. 'Mechanisms of good governance can include transparent, democratic institutions as well as efficient and effective public services'.[5] D'Orville provides us with an even more detailed picture:

> There are three features of governance. First, it has been defined as the rules of a political system established to solve conflicts between actors and adopt decision—this provides the legality. Secondly, governance also describes the proper functioning of institutions and their acceptance by the public—in other words the legitimacy. Thirdly, governance invokes the efficacy of government and the achievement of consensus by democratic means, thus defining a participatory dimension.[6]

However, governance is practised not only by the government; it is rather a social arrangement formed by the state, companies, research institutions, citizens, and so on.[7] In a widespread approach, also adopted in this paper, governance can be defined as a balanced framework where all relevant stakeholders contribute towards maintaining accountability and transparency in technology development. This definition is in line with the

participatory governance approach[8] and, more broadly, with the tenets of the so-called deliberative democracy perspective.[9] It deviates, then, from another approach where governance is equated with management, leading to ideas such as 'private governance', which is said to occur 'when certain phenomena, such as the use of new biotechnologies, are regulated by private agents'.[10] From the social perspective adopted here, private management is certainly part of the governance landscape but is too narrow to fully characterise governance.

In the development of biomedical technologies, which may be funded by government agencies and whose clinical effects may reach large populations, it seems particularly important to promote transparency and accountability, thus reducing the weight of experimentality. For the control of these technologies can result in public health tragedies if realised in abusive ways. Examples of such abuses have been identified in the conduct of clinical trials in lax regulatory environments[11]; in the murky relations between pharma companies and regulatory agencies[12]; in the restrictive composition of research ethics committees[13]; in confidential agreements leading to the diffusion of magnetic resonance scanners of controversial safety[14]; among other issues.

It is hoped that once good governance is in place, then knowledge, skills, industrial knowhow, and technologies can circulate so as to safeguard the public interest. This assumption, which puts the concept of participation at the core of the governance debate,[15] has been strengthened by analysts asking for more participatory schemes to enhance democracy.[16]

Governance could then constitute a realm of transparent and publicised measures, in opposition to the convoluted and restrictive schemes disseminated by the principle of experimentality. However, in spite of the efforts made by the nation state, some barriers to governance can emerge as a result of advanced globalisation. One example was seen in 2020 when national governments, called upon to deal with the urgent needs brought about by the COVID-19 pandemic, realised that a proper response depended on access to technologies strongly subjected to intellectual property rights and the rules of the market. The need for quickly developing a vaccine showed that market rationales are frequently at odds with the public interest.[17] Suddenly, it seemed impossible to conceal what Maskus[18] described as the tension between 'private rights and public problems'.

To understand the interplay between experimentality and governance, this paper focuses on the emergent landscape of patent protection of innovations in gene editing, induced pluripotent stem cells, and 3D bioprinting. It will be seen that even though patent applications are submitted by both public and private players, the logic of experimentality tends to prevail, shape the patent landscape, and defy governance principles.

To understand patent issues, it is, therefore, necessary to consider not only the patent law itself but other parallel aspects. In this way, whenever we talk about the 'patent system' in this paper, we also bear in mind factors such as the shape of biomedical markets, competition law, and the structure of intellectual property in each technology.[19]

This paper is organised in four parts. After presenting the features of what we call biomodifying technologies, our research methods are outlined. We move on to analyse the patent landscape of our three case technologies in light of the governance principle of participation. Subsequently, we analyse some strategies of patent protection by considering the governance principles of transparency and accountability. The closing section brings some considerations related to governance as well as some policy recommendations.

1.2 | Biomodifying technologies

The analysis of gene editing, induced pluripotent stem cells, and 3D bioprinting can shed some light on the roles of good governance and experimentality as they are reflected in the patent regime. Such analysis is particularly important for pharmaceutical and biotechnology innovation, where patents have played a key role. As these three technologies imply the modification of basic life structures (cells, tissues, and genetic codes), we characterise them as *biomodifying technologies*. Due to their relative novelty, and also because they have been the object of constant investigation and patent submissions, they constitute a suitable empirical topic for the discussion proposed here.

Gene editing can be considered an upgrade on older genetic modification techniques, in terms of speed and accuracy. It consists of the alteration of DNA using molecular tools such as CRISPR/cas9, TALENS, and Zinc fingers. Each of these tools contains a programmable 'targeting' domain (such as the 'CRISPR' part of CRISPR/cas9) that can be designed to attach itself to a particular sequence of genetic material in a living cell. Once the target sequence is bound, a 'molecular scissors' part of the tool (e.g. the 'cas9' enzyme) can cut out a particular piece of the DNA, replace it, or change its content.

Induced pluripotent stem cells technology takes mature cells of the adult body, usually of an accessible type such as skin cells (fibroblasts) or hair follicle cells (keratinocytes), and 'reprograms' them to an immature state, so that, like the cells of an early embryo, they can be directed to become any type of cell in the body. They have the same genetic material as the original donor and can be used for both modelling human disease and as a source of new material to replace diseased or damaged tissues in the human body.

In bioprinting, by means of software-controlled devices (bioprinters) that deposit successive layers of substrates containing cells (bioinks), it is possible to generate organoids or tissues that might potentially be used in clinical applications.[20] Although scientists can now bioprint only simple structures like skin or cornea, it is expected that sophisticated structures, and even functional organs, will be bioprinted in the future.[21]

In these three domains, it is possible to take advantage of the human body's plasticity to generate therapies, which characterises the field of regenerative medicine.[22]

The question that arises is: considering the ways in which biomodifying technologies have been developed and appropriated, have principles of good governance been safeguarded? To what extent are such principles compromised by the presence of experimentality?

2 | RESEARCH METHODS

This paper derives from two collaborative research projects: *Biomodifying technologies: organisational and regulatory implications for the translation & valuation of health research*;[23] and *Biomodifying technologies: governing converging research in the life sciences*.[24] The studies were carried in a collaboration between researchers based in the University of Oxford, the University of Sussex, and the University of York.

Three main research methods have been mobilised. First, an extensive literature review has been conducted, so as to identify the main topics being debated not only in scientific domains but also in social science analyses.

Second, by using two platforms (Google Patents and The Lens), we conducted a patent analysis for the three technologies focused on in our projects. As these technologies were developed in different moments, it was necessary to 'normalise' the analysis in terms of historical focus. The year 2006 was taken as the starting point of our analysis. This is when the technique for engineering iPSCs became available.[25] The first phases of gene editing and bioprinting can be traced back to the 1990s and even before. However, these two techniques only acquired modern forms in the 21st century with the use of bioinks and the foundation of specialised companies for bioprinting, and the discovery of techniques such as TALENS and CRISPR for gene editing. In this way, it seemed appropriate to take 2006 as a starting point rather than using time warping algorithms that process data in 'aggressive' ways.

The patent search, conducted in April 2020, is summarised in Table 1.

With Boolean operators, we tried to exclude as many patents related to vegetals and animals as possible, thus focusing on human health. For gene editing, it was seen that a search based on the generic expression ('gene editing') tends to overestimate the number of patents, going beyond the limits of gene editing. It was then decided to use keywords related to the main gene editing techniques. For data processing and data visualisation, the R programming environment[26] was used (more specifically, the following libraries: stringr, dplyr, readr, ggplot2, and reshape2).

TABLE 1 Search strategy used: patents from 2006 to 2019

Technology	Keywords used	Patent applications found	Granted patents found	Total
Gene editing	crispr, cas9, cpf1, meganuclease + (gene or genome or edit), talen + (gene or genome), 'zinc finger', and zfn+ (gene or genome)	7879	1837	9716
iPSCs	'human induced pluripotent', and ips + cell	5472	2864	8336
3D bioprinting	bioprint, bioink, biomanufacturing, bioprinter, bioassembly, bioadditive, bioplotting	1013	288	1301

Third, we have conducted in-depth qualitative interviews with various stakeholders involved in the academic study, commercial exploration, and regulation of the three technologies. For the first research project, from 2017 to 2019, 53 interviews were carried out after obtaining ethics approval from the Central University Research Ethics Committee of the University of Oxford. For the second project, with approval from the same ethics committee, 43 interviews were conducted, from 2018 to 2020, in three countries (the United Kingdom, Italy, and Brazil).

In the following section, the analysis of our findings emphasises the governance principle of participation.

3 | PATENT LICENSING AND THE PRINCIPLE OF PARTICIPATION

As already explained, governance depends, to a large degree, on the nation state's capacity to oversee the innovation system and steer its evolution in socially acceptable ways. In more theoretical terms: 'The constitutional structure of the political system is preserved only if government officials hold out against corporate bargaining partners and maintain the asymetrical position that results from their obligation to represent the whole of an absent citizenry [...]'.[27]

However, the advancement of globalisation and harmonised rules of free trade often weakens the efficacy of regulations, widening the space for corporate experimentality. 'People [...] lack resources to address voids in national regulation and international policy, voids that enable the uncharted expansion of experimentality [...]'.[28] In recent decades, corporations have even had the power to bring national governments to court under international investment agreements.[29] The evolution of the patent landscape reflects these trends.

In the three technologies focused on here, there has been a steady expansion in the number of patents filed, as shown in the following chart.

The expansion has been particularly impressive for gene editing, especially after 2012 when Crispr, a gene editing technique that would gain rapid diffusion, was invented, as we described elsewhere.[30] As seen in Chart 1, bioprinting has had relatively modest performance. Indeed, the generation of patentable bioprinting products and techniques has been slower due to two main factors. First, scientists cannot yet bioprint vascular systems, a limitation that restricts the size of bioprinted tissues.[31] Second, techniques allowing the bioprinting of more complex tissues, particularly laser-based bioprinting, are still expensive and therefore less widespread.[32] However, when one considers the pace at which patents have been filed, bioprinting does not occupy the lowest position, as seen in the following chart (Chart 2).

Considering the 1301 bioprinting-related patents we found, around 17% were filed in 2018, and almost 25% in 2019. For gene editing the proportions were around 22% in 2018, and almost 30% in 2019. From this more telling point of view, iPSCs are the technology with the lowest expansion. This is arguably signalling greater anticipated difficulty in commercialising applications of iPSC technology beyond its current use as a tool in preclinical drug screening.

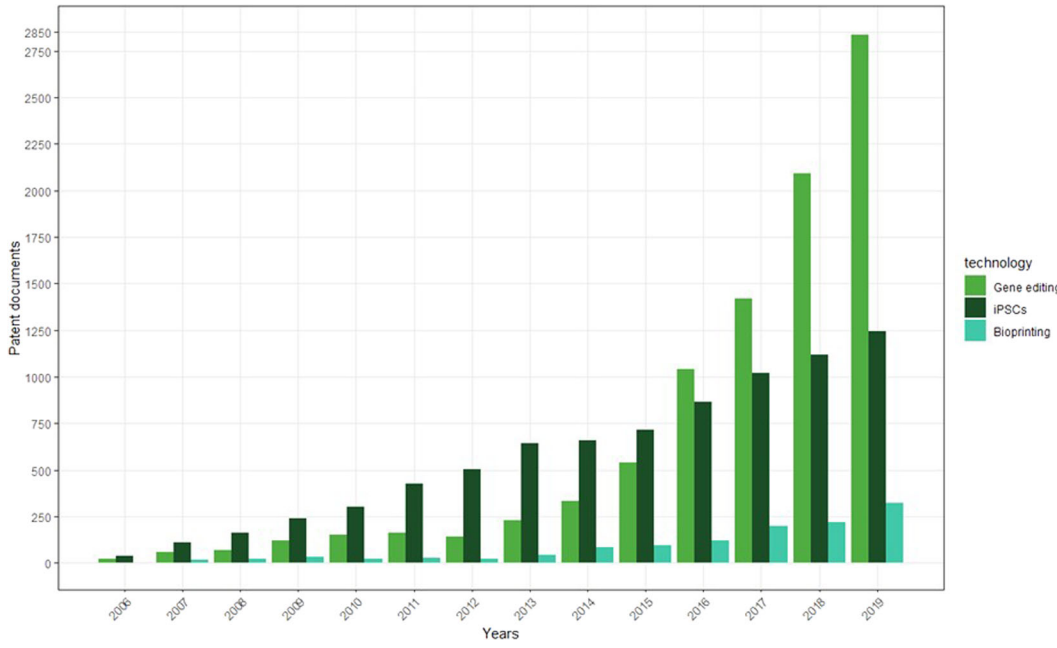


CHART 1 Patent documents published: gene editing, iPSCs, and 3D bioprinting (2006–2019). [Color figure can be viewed at wileyonlinelibrary.com]

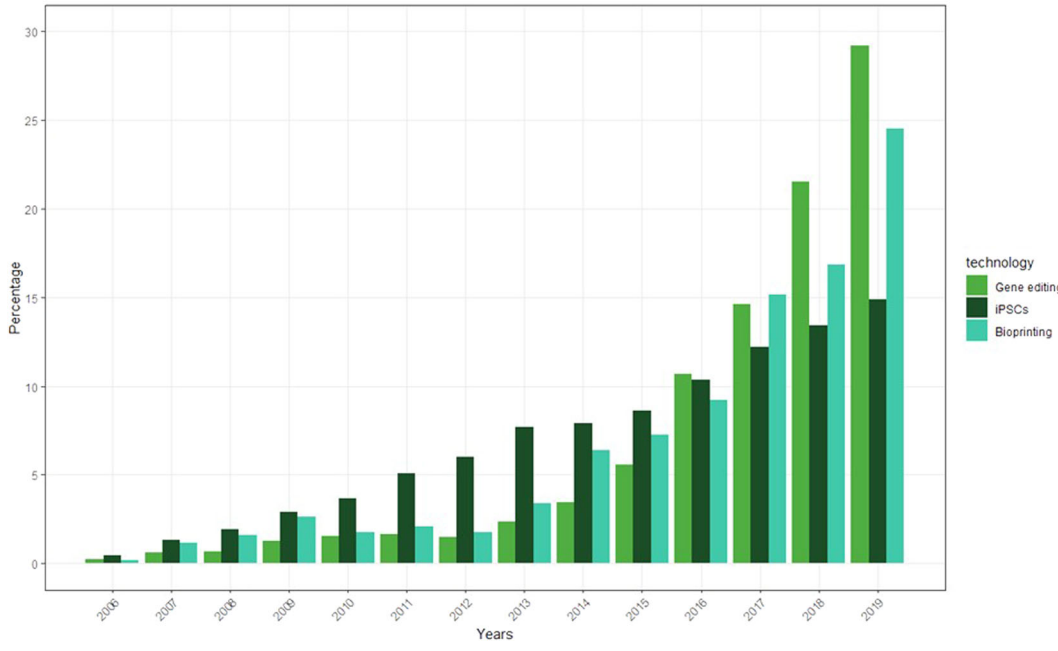


CHART 2 Proportion of patents filed: gene editing, iPSCs, and 3D bioprinting (2006–2019). [Color figure can be viewed at wileyonlinelibrary.com]

The multiplication of patent applications is accompanied by an increase in the number of stakeholders filing patents. Interestingly, all three domains are marked by a concentration in terms of patent holders. Let us consider the ten main patent applicants/holders in each technology, as summarised in Table 2.

The first 10 players hold a substantial proportion of the overall patent portfolio, especially for gene editing (with almost one quarter of patents filed by the main players) and bioprinting (22.2%). Furthermore, private companies have dominated the patent landscape, as seen in the following chart.

In the three domains, companies hold over 50% of the patents, a proportion that reaches around 65% for bioprinting.

In 2007, in their analysis of the stem cell patent landscape, Bergman and Graff[33] concluded that public institutions were as important as private companies. Therefore, the dominance of companies illustrated in Chart 3 is very recent. For example, 33.4% of the iPSCs patents held by companies were filed in the 4 years from 2016 through 2019. The reduction in the relative patent power of universities might be explained by decreasing government investments in academic research. It is certainly explained by two phenomena.

On the one hand, innovations made in universities are frequently taken over by nonacademic players who end up securing the patent. For example, Martinez[34] showed that in most European countries, over 50% of academic inventions have been patented by companies. Furthermore, many companies in possession of promising innovations prefer to create spin-out companies to patent and explore them, a strategy that has been frequent, for instance, in the United Kingdom.[35]

On the other hand, the shifts in the commercial exploration of biomodifying technologies have to be considered. Until the beginning of the 21st century, those technologies were mainly explored by small biotech firms with innovative capacity but modest financial resources.[36] Nowadays, as can be noted in Table 1, biomodifying technologies have been explored by companies that have grown robust and powerful such as Sangamo Therapeutics and Celgene, and even large pharma corporations such as Sanofi Aventis and Merck. The trend has been consolidated by recent mergers and acquisitions, as attested by information on companies submitting patents in the three domains studied here. For example, in 2015 Japanese Astellas Pharma acquired Ocata Therapeutics, an American company developing stem cell therapies.[37] In 2019 Swedish biopharmaceutical company Sobi acquired EmaCo, a Swiss company producing a promising orphan drug candidate.[38]

The two trends described above (the growing patent dominance enjoyed by companies, and the increasing financial and market power of innovative companies) have decisive political implications. Because patent power

TABLE 2 The 10 main patent applicants/holders: gene editing, iPSCs, and 3D bioprinting (2006–2019)

Technology	Players and their location	Percentage of patents
Gene editing	Sangamo Therapeutics (USA), Broad Institute (USA), University of California (USA), Harvard College (USA), Cellectis (France), Massachusetts General Hospital (USA), Editas Medicine (USA), Sanofi Aventis (France), Sigma Aldrich (USA), Temple University (USA)	23.5
iPSCs	Kyoto University (Japan), Janssen Biotech (USA), Wisconsin Alumni Research Foundation (USA), Fujifilm Cellular Dynamics (Japan), University of California (USA), Memorial Sloan Kettering Cancer Center (USA), Merck Patent GMBH (Germany), Viacyte (USA), Riken (Japan), Stanford University (USA)	15.9
3D bioprinting	Organovo (USA), Revotek (China), Modern Meadow (USA), General Electric (USA), Pohang University Industry-University Cooperation Foundation (South Korea), Genzyme (USA), Celgene (USA), Cellink (Sweden), Aspect Biosystems (Canada), National Institute of Health and Medical Research – Inserm (France)	22.2

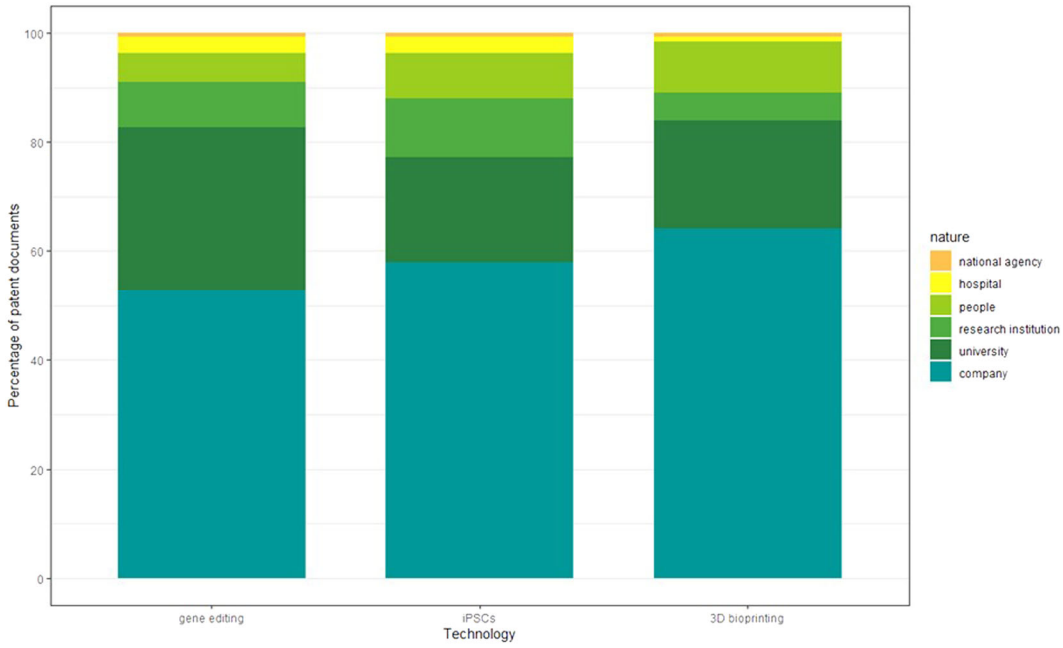


CHART 3 Proportion of patents filed by each kind of player: gene editing, iPSCs, and 3D bioprinting (2006–2019). [Color figure can be viewed at wileyonlinelibrary.com]

tends to be gained by few players (as seen in Table 1), the evolution of biomodifying technologies depends on decisions taken by this small group, in two ways.

First, as patent holders have exclusive rights to control the use of a certain technology, they become gatekeepers for that experimental area. An example was given by one of our interviewees, a patent specialist (IP3): 'I remember Glaxo […] They had some patents that dominated one particular configuration of one part of the cephalosporin molecule […]. If you wanted to make something with that configuration, you needed to deal with them'. For sure, such deal would involve the payment of royalties for the use of Glaxo's patented technology. Some companies may dominate resources of increasing strategic worth, with examples of companies that gained legal control over genes whose genetic sequencing they pioneered.[39]

Second, as we showed elsewhere,[40] patent holders have the power to select other players which will be included in, or excluded from, the development of particular biomedical areas. This can be done by imposing huge prices for the use of patents, thus excluding companies with little funding.[41] It is also frequently done by means of patent licensing, an agreement between the patent owner (the licensor) and an interested player (the licensee), allowing the latter to access the technology, explore it, improve it, and glean the patent's financial benefits. A license can be granted to several licensees at the same time but biomedical and pharma companies prefer exclusive licences, those in which only one company is allowed to explore the patent. As claimed by a patent specialist (IP1): '[…] companies operating in that area just take it as a given that exclusivity is kind of what is demanded'.

Even when universities are involved, exclusive licences are mandated by companies. A patent specialist (IP2) explained: '[…] often universities […] are willing to grant nonexclusive licences. Unfortunately, […] most of the large companies coming to them want exclusive licences. So, it's easier [for universities] to do a deal where you give an exclusive licence'. Many companies now dominating biomodifying technologies managed to initially get on their feet by acquiring exclusive licences on breakthroughs made in academic laboratories. For example, in 2014 Editas Medicine, one of the companies in Table 1, signed exclusive licensing agreements with two academic pioneers of the Crispr gene editing technology: the Broad Institute of MIT, and Harvard University.[42] And Organovo, the leader

in bioprinting patents, '[…] was founded with the support of patented technologies from the University of Missouri (USA) […]'.[43] These examples serve to temper the exalted discourses about the heroic inventiveness of companies, reminding us that biomedical experimentation is increasingly dependent on joint efforts by public and private players.[44] The most resourceful universities, by means of their technology transfer offices, consider these strategic relations at early stages of research projects, with an eye to what can generate revenue through licensing.[45]

The practice of patent licensing has been almost completely subjected to private agreements. As explained by a policymaker interviewed (IP1):

> Actually, that's really more about company behaviour and the issues for policy makers often arise only when there's actually what people perceive as improper behaviour […] by certain companies […] It's quite […] difficult […] for policy makers to actually come down on because essentially at the end of the day it's about two private companies coming to an agreement with each other, or university and a company coming to an agreement with each other.

Critiques have been raised on the legitimacy of exclusive licensing, particularly where research and development have been supported by public funding. To be sure, some principles for dissemination and benefit-sharing have been laid out. In the United States, guidelines for patent licensing have been published.[46] In addition, the OECD[47] has published recommendations on the issue, advising that 'Licensing practices should encourage the rapid dissemination of information concerning genetic inventions'. However, there has not been sufficient time for such guidelines and recommendations to either generate considerable results or be incorporated into constraining legislations. Thus patent licensing remains poorly regulated. Most licensing agreements are deemed as trade secret and never published.[48]

Thus the principle of participation, which lies at the core of governance,[49] is seriously undermined by a system where it is up to companies, by means of unpublished agreements, to decide who will participate in the development of technologies. Eventually, the system tends to favour exclusion, instead of participation, and the logic of experimentally is diffused. 'Regulated state withdrawals make it possible, favouring economic interests over empowered systems of regulatory oversight—even if only for a certain time period'.[50] If the principle of participation is in jeopardy, it is worth asking how the patent system impacts on the principles of transparency and accountability.

4 | THE BORDERS OF PATENTABILITY AND THE PRINCIPLE OF TRANSPARENCY

In order for a technique to be patented, the scientific and technical characteristics of the innovation, compared against previous/current techniques (prior art/state of the art), are assessed. Different patent offices may adopt different approaches in this process. In the United States a decisive aspect of patent evaluations is 'nonobviousnes' while the European Patent Office works with the concept of 'inventive step'.[51] Notably, the European Patent Office adopts a 'problem and solution' approach to assessing inventive steps, requiring technical features and technical problems to be established.

For a socially relevant process (such as a patent application process) to be transparent, some fundamental requirements in disclosure should be satisfied. Particularly, the following criteria should apply: (1) The players responsible for conducting the process should acknowledge the limits of certainty involved in their patent claims, and (2) these players should make public how the process is being conducted, and such publication must be understandable and meaningful for as many interested players as possible. In the domain of patents for biomodifying technologies, both criteria fail to hold.

Criterion 1 (uncertainties made clear) fails to apply, not because uncertainties are lacking. On the contrary, Sherkow[52] is right to claim: 'Patent law does not always neatly align itself with the realities of biological research'. This is because precisely targetted applications, with objective evidence supporting patent claims, can seldom be sumitted to patent offices.

> Given biology's complexity, the outcome of any given experiment is increasingly uncertain. Experimental trial and error—more than design in the 'dry' engineering fields—is critical to research in biology. This complicates courts' and patent offices' obviousness analyses, because even standard combinations of elements in the field routinely yield unpredictable results".[53]

Moreover, patent applications are submitted before the conduct of clinical trials, when researchers have good ideas and reasons to believe such ideas but little evidence showing that therapies will be clinically effective.

Obviously, patent applicants do not disclose their uncertainties about their patent claims. A very widespread strategy used by patent attorneys is to write very broad initial claims. As the technology evolves and clinical data are collected, claims are generally narrowed down when the patent application is supplemented. According to a patent attorney:

> At the start you've got a lot of flexibility. At the first filing stage [...] we might have quite broad claims [...] We might deliberately draft them too broad but the art is to have... even if you've got something broad, that you've got something narrow underneath, that covers the product or what they're going to do and will stand up. That's the art.

The metaphor of art was also mobilised by a policymaker to explain that initial patent applications are usually ambitious:

> In this art, in the biological art, in the organic chemical art, in the pharmaceutical art, you would often have in a single application a claim to the products, a claim to a method for making the product or the process, and quite often then a claim to its use and therapy.

Again, we approach the hidden political upshots of the patent system. In theory, legal provisions disentangle what can be patented from what is excluded. However, the practices of the patent system often defy such delineations. For example, computer software cannot be patented in the European Union but patents would apply when the inventor shows that the software package has a 'technical effect', a vaguely defined concept.[54] As a consequence, some software packages, such as the ones used in computer-assisted diagnosis, have been patented in the Union. This may bring about opportunities for bioprinting companies whose software packages, in association with bioprinting devices, may in the future be considered as generators of an innovative 'technical effect'. Indeed, as we showed elsewhere,[55] bioprinting researchers have used software (mainly proprietary software) for computer modelling, that is the virtual design of the biological structures to be bioprinted. If patent attorneys try and manage to convince patent offices that such modelling tasks provide cells and tissues with a technical effect, that would open up new avenues for the patenting of modelling software for bioprinting, as well as enlarge the scope of experimentality in this domain. This could challenge the spontaneous innovation and collaboration that have been promoted by independent software developers, for example, in the domain of neuroimaging.[56]

In this way, the patent system, tinkered with by experienced patent attorneys, pushes the boundaries of patentability, as explained by an attorney: '[...] a lot of the development in the patent world has been pushing at those margins, where you're on the boundary. There are some things you can push into the patentable side, as it were, and that's developed with the case law'. To be sure, such expansion of the frontiers of the patent system has

important social consequences, which may remain hidden until the outbreak of the next public health crisis or epidemic.

The second criterion of transparency (widespread and clear publication) also fails to hold. There are several ways in which innovations remain removed from the public's eyes. For example, a report by the Hinxton Group concludes that some iPSC cell lines have been produced but the achievement is frequently not published. 'This has created a situation in which even a diligent stem cell researcher or entity that wishes to respect IPR [intellectual property rights] will face considerable uncertainty and enormous costs if they try to survey the IPR landscape'.[57] Due to this and similar practices, claims have been made for clearer systems where information on innovative biomedical technologies and granted patents would be disseminated more largely.[58]

Every patent document must be published but publication takes some years to materialise. Having recourse to our data set, we calculated the difference between each patent's priority year (when the patent is initially filed) and year of publication. For gene editing, the average difference is 2.72, that is, gene-editing patents take, on average, 2.72 years to be published. For iPSCs, the average difference is 3.67; for bioprinting, 2.55.

However, not all patent documents obtain the same level of recognition, as some of them are consulted and cited more frequently than others. We then divided the patent documents in four groups, from those which have rarely been cited by other patent documents to those with high levels of citation. The outcome is seen in Chart 4.

Chart 4 shows that for all three technologies, patent documents cited very frequently (100 or more citations in other patent documents) have publication delays bigger than that of the documents with very low citation levels (from 0 to 9). Therefore, the more frequently patents have been consulted and mentioned, the longer they have taken to be initially published. This pattern is not manifested for bioprinting, arguably because of the relatively low total number of patents (1301), yielding four small groups whose average result is distorted by extreme cases. The pattern becomes visible for gene editing, and is evident for iPSCs. Indeed, the 21 iPSC patents that have received 100 citations or more took, on average, 7.33 years to be originally published. These publication 'waiting times' are considerable, as in biomodifying technologies, even a 1-year delay in the sharing of information may jeopardize human health and lives, as seen in the struggle of African scientists to access patented technologies for Covid-19 vaccines.[59]

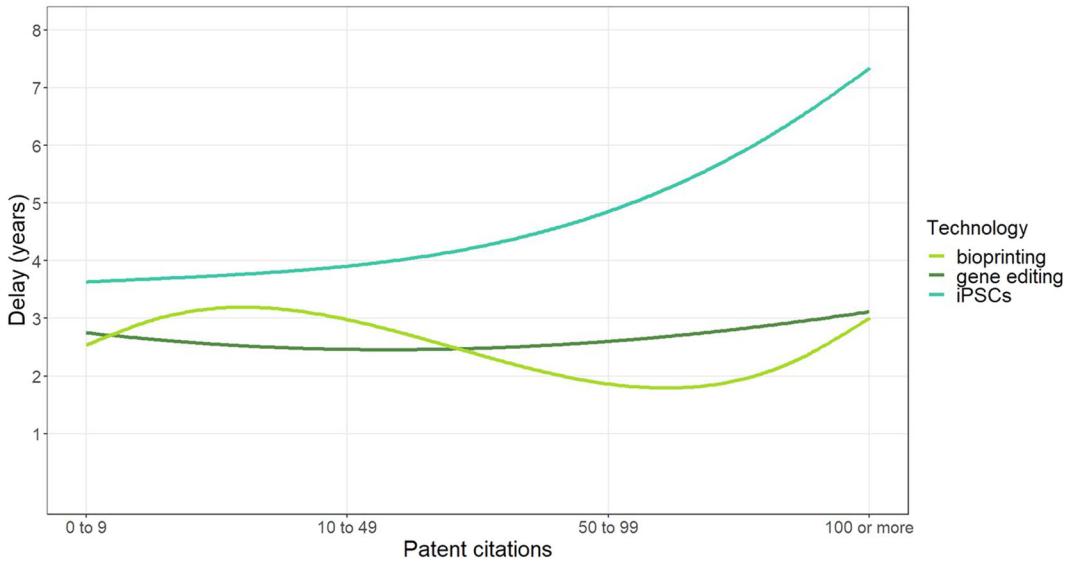


CHART 4 Patents documents according to citation levels and publication delays. [Color figure can be viewed at wileyonlinelibrary.com]

Patent laws have disclosure requirements according to which patents can only be granted if the inventor accepts to clearly disclose the nature of the invention and how replication can be achieved.[60] However, these requirements can be abated by the possibility of delaying patent publication when a substantial amendment to the original filing is realised. As a result, disclosure requirements become another argument and instrument to be used in the framework of experimentality whereas from the viewpoint of governance, the relevant practice (i.e., the one that promotes transparency) is patent publication.

Even when publication finally happens, it is made in a legal language that few people understand.[61] Given the uncertainties associated with developing biomodifying technologies, the usual approach is to focus on technicalities, expecting that patent attorneys, who master the language of patent claims, proposals, and litigations, will engineer innovation into applications. As explained by a patent attorney (IP4): '[…] you try to frame things in terms of problems, technical problems and solutions to those problems, or a particular technical problem when you're drafting something, as an attorney'.

Gradually, the dialogues involved in patent applications have gained a technical tone which most citizens would find obscure, even though everybody might eventually need products made expensive by patent protection. As patent granting has been institutionally separated from health technology assessment, every supposedly well-conducted patent assessment tends to disregard points that may be crucial for most citizens, such as technology impact and technology access. So far the most central offices, such as the European office, have been reluctant to make public issues or social considerations part of their assessments, thus restricting themselves to the conduct of techno-scientific assessments.

Therefore, the principle of transparency is shattered because, often, the coverage of patent applications is not clear for the applicants themselves. In the course of their experiments, they learn what can be taken in or out of the boundaries of property rights. The viability of this strategy is enhanced by the features of the patent system where applications can remain unpublished for considerable lengths of time. In the course of this process, applicants and patent offices engage in a conversation in which various aspects of social life (such as technology governance and social impacts) are completely absent.

This reveals another face of experimentality: 'It creates its own measures of success that, at times, have fallen short of broader public health goals'.[62] Moreover, a system is slowly constituted where the most powerful players manage to shun accountability, as argued below.

5 | HIDDEN PUBLIC HEALTH STRATEGIES AND THE PRINCIPLE OF ACCOUNTABILITY

According to the principle of accountability, actors should be made responsible for the strategies they adopt and the decisions they make, as long as those strategies and decisions have social implications. It may seem that patent applicants and offices are dealing with technical matters with little social effect. However, a more detailed analysis reveals that patent strategies have amounted to hidden public policies to which multiple players contribute but for which nobody is made accountable. 'Decentralized and diffused in character, this experimentality does not lend itself easily to prevailing tools of accountability'.[63] This is manifested in at least three ways.

First, patent strategies can block a certain technological field, shaping opportunities for market exploration and investment. One of these strategies is the division of industrial know-how into a combination of patents and confidentiality agreements. Another strategy is so-called patent thicket, whereby a certain company (or partner companies) files a series of patents targeting different subdomains of the same technology, preventing competitors from getting hold of areas of the technological territory.[64] The conditions of a patent thicket have been verified in the field of stem cell research.[65] Another example comes from the field of engineered meganucleases where most of the existing patents are owned by two companies: Cellectis (which appears in Table 1) and Precision Biosciences; in 2014 they decided to cross-license their patents after a patent litigation settlement.[66]

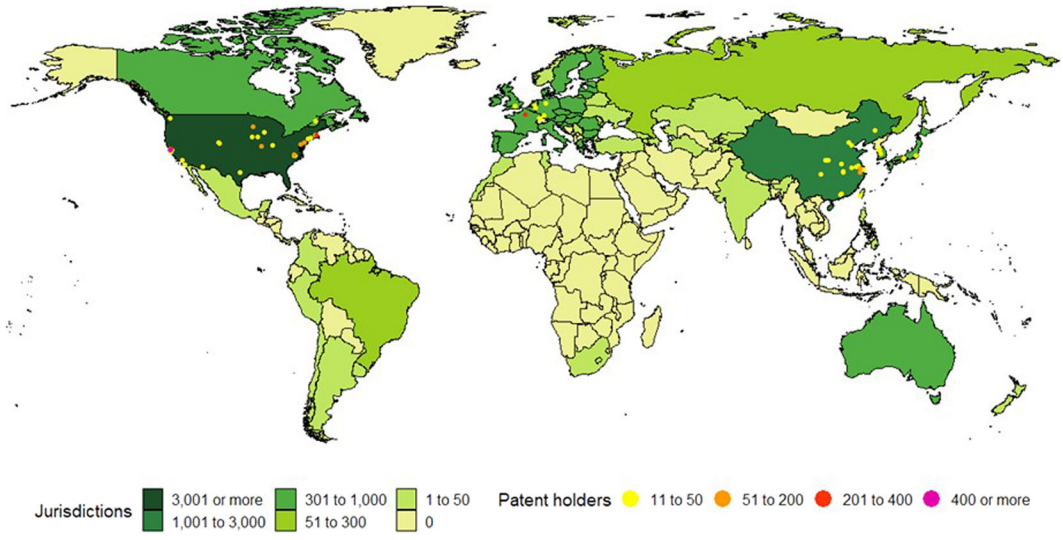
Consequently, technologies may end up being completely controlled by some key players, reproducing the trajectory of information technologies. For, as a patent specialist (IP2) recalled: 'If you want to get into the mobile phone business now, forget it'. Eventually, the possibility to develop or use certain technologies, including biomodifying technologies, becomes dependent on global patent strategies.

Second, the high prices paid by those engaging in the patent system creates restrictive geographic strategies. Indeed, only very large corporations are economically able to file and maintain patents in various countries. A patent attorney (PAT02) disclosed the advice given to patent applicants: '[…] if people haven't got a lot of money, at the end of the day the essential thing is we will say "Keep the US, let everything else go." […] What we would normally recommend is Europe, US, and China'. The outcome of this approach is illustrated on Map 1, which shows the jurisdiction of patents, as well as the location of patent holders, for the field of gene editing.

As companies are generally not willing to take their key products to countries where the underlying technology is not protected, world patent strategies become associated with the uneven distribution of cutting-edge therapies. For example, CAR-T cell products, a gene-edited therapy first approved in 2017 to fight rare and resistant cancers, are now available only in the United States, China, Europe, Canada, Japan, Australia, New Zealand, Israel, and Singapore.[67] Most of these regions also appear, on Map 1, as those with the most intense patent activity for gene editing. To be sure, the coincidence does not mean that the patent system is the only reason why the vast majority of countries have failed to access CAR-T cell and other gene-edited products. However, the costs associated with filing and maintaining patents are among the reasons leading to this global health failure.

Finally, the ways in which biomodifying therapies have been developed, as well as the associated development costs (including investments into securing and maintaining patents), result in products of skyrocketing prices.[68] For example, if gene therapies were developed to treat 1% of the American population, the costs would be equivalent to the yearly amount spent on all healthcare in the country.[69] If a proliferation of gene therapies has 'the potential to push the US healthcare system to the breaking point',[70] their impact on other, less robust national systems would obviously be even more drastic.

In a sense, patents can be considered as a delayed funding system whereby society, by purchasing the patented technology, reimburses the inventor for the initial research and development costs. In biomedicine, the sacrifice



MAP 1 Gene editing: Jurisdictions and patent holders: 2006–2019. [Color figure can be viewed at wileyonlinelibrary.com]

made by society can be very high, as the prices of some therapies are mostly well above the product's marginal cost, excluding some consumers willing to pay prices which are not so high but would still secure profits for the producer.[71] In this way, the patent system underpins economic strategies that may impose heavy burdens on health systems or on the shoulders of citizens not supported by health reimbursement schemes.

Therefore, patent holders have used the patent system to indirectly design policies having impacts on: technology governance and access to markets; the global distribution of therapies; and the costs to be faced by health systems and patients. However, nobody is made accountable for these strategies and decisions because they are not seen as actual policies, but as issues of intellectual property. When the need is felt, by either the nation state or citizens, for having quick access to some therapies made vital, all doors may be closed but it may be impossible to identify the players responsible for such closure in the convoluted landscape of patents, licences, and commercial agreements.

As claimed in a United Nations document: 'Accountability is a key theme running through and underpinning many aspects of governance [...]'.[72] However, when patent issues hide governance issues, a situation emerges where key decisions depend on a techno-scientific dialogue between attorneys and patent offices. Thus the patent system remains impervious to social concerns that have led, for example, to the concept of Responsible Research and Innovation, which the European Union has tried to promote.[73]

If such policy impacts can be verified, then it would be reasonable to expect that the assessments made by patent offices could transcend technical concepts such as 'nonobviousness', 'inventive step', and 'technical effect'. More comprehensive assessments can indeed be envisaged by means of some changes, some of which are sketched in the concluding section.

6 | TOWARD MORE PARTICIPATIVE, ACCOUNTABLE, AND TRANSPARENT PATENT ASSESSMENTS

In this paper we have examined the current governance of biomedical innovation, focusing on three biomodifying technologies (gene editing, iPSCs, and 3D bioprinting). More specifically, we have analysed how subfields of these technologies have been appropriated through patent protection. It was seen that technology development and appropriation are supposed to be guided by governance principles which, nevertheless, have not always been effectively incorporated in the existing patent system. Frequently, what prevails is the logic of experimentality whereby social and political issues are overshadowed by a market rationale. Although academic researchers might, in theory, put in practice alternative rationales, current state and university policies on funding, performance evaluation, and technology transfer, especially in terms of licensing, tend to usher academic research into market logics.

The governance principle of participation has been marginalised in a system where the patent power of some companies has increased, consolidating mechanisms of exclusion. As seen in Section 3, small groups of companies have secured the largest proportion of patents, with weak participation of government institutions that can be involved in national health policies. The principle of accountability is threatened because the complexification of the commercial and intellectual property landscape makes it increasingly difficult to identify the actors responsible for the potential impacts of therapies of increasing prices on public health systems. In Section 5, it was seen that key decisions have been taken in the framework of secret private contracts and agreements. Eventually, it gets very hard to identify the players responsible for the current configuration of the pharmaceutical and biomedical domain. Finally, the principle of transparency is threatened by the delayed publication of patents, as well the secretive stance of companies that frequently withdraw information on their most innovative achievements, as part of trade secrecy. This point was also made in Section 4, which drew attention to the technical dialogue between patent attorneys and patent offices, without consideration for the social implications.

To be sure, the current patent system has some characteristics that make room for social considerations. For example, by means of an opposition mechanism called 'observations by third parties', the European Patent Office, unlike its American counterpart, considers some arguments voiced by citizens on why a certain patent should not be granted.[74] However, such arguments must have the scientific or legal basis recognised as legitimate in patent applications. Thus the European Patent Office has taken social considerations into account in a limited manner whereas the US Patent and Trademark Office has shunned them altogether, arguing that this would involve an unacceptably subjective reasoning harmful to commercial activity.[75]

Patent laws generally contain experimental exemptions where the technology, albeit protected from commercial exploration, continues to be available, free of cost, for academic research. This exemption has been important, for example, for academic groups conducting studies on iPSCs. However, as explained above, patent publication is always delayed in the granting process, making universities (which might be facing shrinking research budgets) work on technologies that are no longer highly innovative.

When governance schemes are weakened, strategies for strengthening them may be sought. On those occasions, '[…] one calls into question the foundations of governance itself, that is, the concepts, practices and institutions by which societal development is governed, and […] one envisions alternatives and reinvents and shapes those foundations'.[76] For improving the governance of biomedical technologies, suggestions have been made, such as the creation of more efficient systems for patent publication,[77] the establishment of an intellectual property clearinghouse mechanism[78] or the clarification of the contexts in which the targeted technology has been developed.[79] Considering the three governance principles highlighted here (participation, accountability, and transparency), the following draft measures are proposed to enforce them in the patent system.

First, patent licensing can be the object of more specific regulations. For example, ways to increase the publication of licensing agreements signed by companies can be sought, with the establishment of a minimal amount of information to be disclosed. In so doing, it would be possible to keep track of the commercial pathways taken by particular technologies. The value of so-called ethical licensing, where the licensor prevents the licensee from exploring socially harmful potentialities of the technology, has been pointed out.[80] Regulations could also be created so ethical practices do not depend exclusively on companies' good will, with the promotion of 'some combination of public and private efforts'.[81] These measures would promote transparency, making it possible for interested observants to keep track of how technologies are evolving, as well as identify signs of patent holders violating competition laws.

Second, the fees practised by patent offices could be re-examined. To a large degree, they have been a deterrent for smaller companies and researchers based in marginal economic countries. A new system could be envisaged where reduced fees would apply for some groups of companies and countries. In addition, more collaboration between patent offices can be encouraged, aiming at streamlining the procedures of less strategic offices, so they can become more attractive to innovative players. These measures would foster participation at both the national and international levels.

Third, along with the concepts of 'innovative step', 'nonobviousness' or 'technical effect', patent offices could embrace the concept of social impact. In recent years, academic researchers have become accustomed with such concept, as academics looking for research funding are now urged to show the social relevance of the studies they wish to conduct. By the same token, researchers and companies planning to patent a certain technology could be asked to submit arguments and evidence to demonstrate the social impact that their patent will generate, including access and benefit-sharing aspects. This documentation would be made largely available (thus heightening transparency and accountability) and would show why and how obtaining a patent would enable the applicants to bring about social benefits, disseminate the technology geographically, hire professionals to speed up its development, target diseases of public relevance, or any other socially beneficial effect. This requisite would be based on the recognition that patents block imitative activities, which can sometimes have positive economic and social effects.[82] It might be considered that patent holders are promoting social impact by manufacturing products based on the patented technology. However, in cutting-edge therapies, manufacture has been highly centralised,

with few manufacturing units producing for the world,[83] which implies a concentration of expertise and skills. Moreover, as seen in the previous section, some cutting-edge therapies have failed to reach the vast majority of countries.

Finally, as the views of the lay public and patient organisations have been taken into account in the conduct of health technology assessment,[84] the adoption of clinical strategies,[85] the design of clinical research,[86] the development of clinical guidelines,[87] and the evaluation of clinical research protocols,[88] mechanisms for promoting the participation of lay members in the assessments of patent offices could also be sought. In this way, patent applicants would be encouraged to speak a nontechnical language and pay more attention to the social impacts of their innovations. For sure, such measure would be politically controversial, for one of the cornerstones of experimentality has been the creation of regulatory niches (such as the patent system) where technical considerations block the emergence of social concerns. Therefore, many companies would probably react to what would be seen as a 'lay invasion' of a technical realm. However, the measure would be important not only for promoting the principle of participation but also for doing so in assertive ways. Something very similar is proposed by Parthasarathy,[89] within the aim of '[...] ensuring that technologies reflect societal needs and priorities and are also rooted in the realities on the ground'.

We are aware that social concerns, when translated into institutional mandates like those proposed above, may lead to mere ceremonial procedures whereby companies tick boxes to show their corporate social responsibilities. For some analysts, this has been the case, for example, for the assessments made by research ethics committees.[90] However, institutional changes may be helpful by at least triggering social debate where debate is either nonexistent or, as in the case of patents, restricted to a few elite stakeholders. It can be said that governance mirrors the evolving nature of the nation state, which 'does not represent a finished structure but a delicate and sensitive—above all fallible and revisable—enterprise, whose purpose is to realise the system of rights *anew* in changing circumstances'.[91]

The measures sketched above could evidence the need for the 'supportive collaborative-based discursive relationships among public and private sectors' referred to by Fischer.[92] They could help make the patent system undergo the move described by Nowotny,[93] whereby scientific and technical activities transcend the scope of limited expertise to become grounded on socially robust knowledge. It has been claimed that the patent system fails to stimulate innovation and development in biomedicine and pharmaceuticals,[94] and creates a bias towards short-term gains.[95] Such discussion is out of the scope of this paper but the proposed measures would contribute toward more transparency and accountability even if economic and scientific outcomes are poor.

Currently, the patenting of biomodifying technologies is strongly shaped by the logic of experimentality, which creates weaknesses and gaps that may only be noticed in the future, in contexts of pressing health needs. 'Ultimately, this experimentality underwrites a research agenda that does not necessarily provide the most valid and relevant medical outcomes, and it introduces added risks'.[96] Among these risks, we identify not only the biological risks to which future patients may be subjected but also the risks imposed on weakened health systems, as well the political risks faced by nation states overwhelmed by corporations' economic and scientific power. Indeed, the issues dealt with here are particularly relevant for nation states, considering that most patent offices have a national mandate.

When states decide to enforce austerity measures, finding a balanced governance strategy becomes even more complex.[97] Then, political wisdom may be replaced with political desperation. London and Kimmelman[98] warned that sometimes, the eagerness with which some countries welcome international clinical research '[...] might represent the desperation of host communities more than their zeal for advancing the research agenda [...]'. Equally, the willingness to receive patent applications might be reflecting countries' desperation about their scientific relevance or patent offices' anxiety to attract fees paid by innovative players. If the principles of governance are not shielded and put into practice, then the patent system is likely to turn into a generator of such political fragilities, which tend to be worsened by the primacy and globalisation of experimentality.

ACKNOWLEDGEMENTS

We are grateful to Dr. Andrew Bartlett who helped in the elaboration of the patent search for gene editing and iPSCs. This study is supported by the Leverhulme Trust under grant number 68387. The agency did not have any involvement in the conceptualisation and design of this publication. Professor Andrew Webster (SATSU, University of York), who had pivotal intellectual input into the entire research project, sadly passed away before this paper was finished. He will be deeply missed by all his colleagues.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Edison Bicudo http://orcid.org/0000-0002-8198-3357

ENDNOTES

[1] Adriana Petryna, *When Experiments Travel: Clinical Trials and the Global Search for Human Subjects* (Princeton University Press 2009).

[2] Adriana Petryna, 'Globalizing Human Subjects Research' in Adriana Petryna, Andrew Lakoff, and Arthur Kleinman (eds), *Global Pharmaceuticals: Ethics, Markets, Practices* (Duke University Press 2006); Petryna (n 1).

[3] Nick Fox, Katie Ward, and Alan O'Rourke, 'A Sociology of Technology Governance for the Information Age: The Case of Pharmaceuticals, Consumer Advertising and the Internet' (2006) 40 Sociology 315-334.

[4] Michael R. Reich, 'The Core Roles of Transparency and Accountability in the Governance of Global Health Public-private Partnerships' (2018) 4 HSR 239-48.

[5] United Nations Development Programme, *Governance for Sustainable Development: Integrating Governance in the Post-2015 Development Framework* (Discussion Paper, 2014) 4.

[6] Hans d'Orville, 'The Impact of Political, Economic and Social Transitions on Order and Governance, their Vulnerabilities and Predictabilities' in Lijun Yang and Wei Shan (eds), *New Humanism and Global governance* (World Scientific 2019) 34.

[7] Benjamin Cashore, 'Legitimacy and the Privatization of Environmental Governance' (2002) 15 Governance 503-529; Fox et al. (n 3); J. N. Rosenau and D. Johnson, 'Information Technologies and Turbulence in World Politics' in J. E. Allison (ed), *Technology, Development and Democracy* (State University of New York Press 2002).

[8] Frank Fischer, 'Participatory Governance: From Theory to Practice' in David Levi-Faur (ed), *The Oxford Handbook of Governance* (Oxford University Press 2012); Vasudha Chhotray and Gerry Stoker, *Governance Theory and Practice* (Palgrave Macmillan 2009).

[9] Jürgen Habermas, *Between Facts and Norms: Contributions to a Discourse Theory of Law and Democracy* (Studies in Contemporary German Social thought, MIT Press 1996); John S. Dryzek, *Deliberative Democracy and Beyond: Liberals, Critics, Contestations* (Oxford University Press 2000); Seyla Benhabib, *Democracy and Difference* (Princeton University Press 1996).

[10] Nienke de Graeff and others, 'Fair Governance of Biotechnology: Patents, Private Governance, and Procedural Justice' (2018) 18 AJB 57-59.

[11] Petryna (n 2); Sonia Shah, *The Body Hunters: Testing? New Drugs on The World's Poorest Patients* (New Press 2006).

[12] John Abraham, 'Sociology of Pharmaceuticals Development and Regulation: A Realistic Empirical Research Programme' in Simon J. Williams, Jonathan Gabe and Peter Davis (eds), *Pharmaceuticals and Society: Critical Discourses and Debates* (Wiley-Blackwell 2009).

[13] Lisa Eckenwiler, 'Moral Reasoning and the Review Of Research Involving Human Subjects' (2001) 11 KIEJ 37-69.

[14] Anja G. van der Kolk and others, 'Clinical Applications of 7T MRI in the Brain' (2013) 82 EJR 708-748; Ewald Moser, 'Ultrahigh-Field-magnetic Resonance: Why and When?' (2010) 2 WJR 37-40.

[15] Andy Stirling, 'Participation, Precaution and Reflexive Governance for Sustainable Development' in W. Neil Adger (ed), *Governing Sustainability* (Cambridge University Press 2009).

[16] Ethan J. Leib, *Deliberative Democracy in America: A Proposal for a Popular Branch of Government* (Pennsylvania State University Press 2004); James Bohman, *Public Deliberation: Pluralism, Complexity and Democracy* (MIT Press 1996); Luigi Pellizzzoni, 'Uncertainty and Participatory Democracy' (2003) 12 EV 195-224.

[17] Mariana Mazzucato and Els Torreele, 'How to Develop a Covid-19 Vaccine for All' Social Europe <https://www.socialeurope.eu/how-to-develop-a-covid-19-vaccine-for-all> accessed 15 July 2020.

[18] Keith E. Maskus, *Private Rights and Public Problems: The Global Economics of Intellectual Property in the 21st Century* (Columbia University Press 2010).

[19] We are grateful to an external reviewer who pointed out this aspect of the patent system.

[20] Samad Ahadian and Ali Khademhosseini, 'A Perspective on 3D Bioprinting in Tissue Regeneration' (2018) 1 BDM 157-160; Guifang Gao and others, 'Organ Bioprinting: Are We There Yet?' (2018) 7 AHCM 1-8; Xyanyi Ma and others, '3D Bioprinting of Functional Tissue Models for Personalized Drug Screening and in Vitro Disease Modeling' (2018) 132 ADDR 235-251; Christian Mandrycky and others, '3D Bioprinting for Engineering Complex Tissues' (2016) 34 BA 422-434.

[21] Leonardo Azael Garcia-Garcia and Marisela Rodriguez-Salvador, 'Uncovering 3D Bioprinting Research Trends: A Keyword Network Mapping Analysis' (2018) 4 IJB 1-8; Seung-Schik Yoo, '3D-Printed Biological Organs: Medical Potential and Patenting Opportunity' (2015) 25 EOTP 507-511.

[22] John Gardner, Andrew Webster and Jacqueline Barry, 'Anticipating the Clinical Adoption of Regenerative Medicine: Building Institutional Readiness in the UK' (2018) 13 RM 29-39.

[23] <https://www.law.ox.ac.uk/research-and-subject-groups/biomodifying-technologies> accessed July 2022.

[24] <https://www.law.ox.ac.uk/biogov> accessed July 2022.

[25] Kazutoshi Takahashi and Shinya Yamanaka, 'Induction of Pluripotent Stem Cells From Mouse Embryonic And Adult Fibroblast Cultures By Defined Factors' (2006) 126 Cell 663-676.

[26] R Core Team, 'R: A Language and Environment for Statistical Computing' <https://www.R-project.org/> accessed July 2022.

[27] Habermas (n 9).

[28] Petryna (n 1) 44.

[29] Rochelle Dreyfuss and Susy Frankel, 'Reconceptualizing ISDS: When is IP an Investment and How Much Can States Regulate It?' (2018) 21 VJETL 377-415; Ruth L. Okediji, 'Is Intellectual Property "Investment"? Eli Lilly v. Canada and the International Intellectual Property System' (2014) 35 PL: LSR 1121-1138.

[30] Paul Martin and others, 'Genome Editing: The Dynamics of Continuity, Convergence, and Change in the Engineering of Life' (2020) 39 NGS 219-242.

[31] Vladimir Mironov and others, 'Organ Printing: Promises and Challenges' (2008) 3 RM 93-103.

[32] Deepak Choudhury, Shivesh Anand and May Win Naing, 'The Arrival of Commercial Bioprinters: Towards 3D Bioprinting Revolution!' (2018) 4 IJB 1-20.

[33] Karl Bergman and Gregory D. Graff, 'The Global Stem Cell Patent Landscape: Implications for Efficient Technology Transfer and Commercial Development' (2007) 25 NB 419-424.

[34] Catalina Martinez, 'From Academic Inventing to University Patenting' WIPO Workshop on PCT Fee Reductions for Universities <https://www.wipo.int/edocs/mdocs/pct/en/wipo_pct_uni_ge_18/wipo_pct_uni_ge_18_martinez.pdf> accessed April 2022.

[35] Intellectual Property Offfice, 'IP Filing Habits of UK Higher Education Institutions' <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/887908/ip-filings-habits-of-uk-higher-education-institutions.pdf> accessed April 2022.

[36] Michael M. Hopkins and others, 'The Myth of the Biotech Revolution: An Assessment of Technological, Clinical and Organisational Change' (2007) 36 RP 566-589.

[37] <https://www.prnewswire.com/news-releases/astellas-to-acquire-ocata-therapeutics-300175438.html> accessed July 2022.

[38] <https://www.swissbiotech.org/listing/novimmune-to-rebrand-as-light-chain-bioscience-after-divesting-emaco-to-swedish-biopharmaceutical-sobi/> accessed July 2022.

[39] Heidi L. Williams, 'Intellectual Property Rights and Innovation: Evidence from the Human Genome' <https://www.nber.org/system/files/working_papers/w16213/w16213.pdf>; Bhaven Sampat and Heidi L. Williams, 'How do Patents Affect Follow-on Innovation? Evidence from the Human Genome' (2019) 109 AER 203-236.

[40] Phoebe Li, 'Intellectual Property for Humanity: A Manifesto' in Daniel J. Gervais (ed), *The Future of Intellectual Property* (ATRIP Intellectual Property series, Edward Elgar 2021).

[41] James Bessen and Michael J. Meurer, *Patent Failure: How Judges, Bureaucrats, and Lawyers Put Innovators at Risk* (Princeton University Press 2008); Gregorio Giménez, 'The Impact of the Patent System on the Social Welfare: A Critical View' (2018) 14 IC 253-269.

[42] <https://ir.editasmedicine.com/news-releases/news-release-details/editas-medicine-licenses-genome-editing-technology-broad>

[43] Marisela Rodríguez-Salvador, Rosa María Rio-Belver and Gaizka Garechana-Anacabe, 'Scientometric and Patentometric Analyses to Determine the Knowledge Landscape in Innovative Technologies: The Case of 3D Bioprinting' (2017) 12 PLoS One 1-22, 12.

[44] Frederick M. Abbott, 'Public-Private Partnerships as Models for New Drug Development: The Future as Now' in M. Chon, P. Roffe and A. Abdel-Latif (eds), *The Cambridge Handbook of Public-private Partnerships, Intellectual Property Governance, and Sustainable Development* (Cambridge University Press 2018).

[45] Fiona Alice Miller, Carrie B. Sanders and Pascale Lehoux, 'Imagining Value, Imagining Users: Academic Technology Transfer for Health Innovation' (2009) 68 SSM 1481-1488.

[46] U.S. Department of Justice and Federal Trade Commission, *Antitrust Guidelines for the Licensing of Intellectual property* (2017).

[47] OECD, *Recommendation of the Council on the licensing of genetic inventions* (OECD Legal Instruments 2020).

[48] Bergman and Graff (n 29).

[49] Stirling (n 15).

[50] Petryna (n 1) 30.

[51] Jacob S. Sherkow, 'Inventive Steps: The CRISPR Patent Dispute and Scientific Progress' (2017) 18 EMBO Reports 1047-1051; Paul England and Scott Parker, 'Obviousness in the New European Order' (2012) 7 JIPLP 805-515.

[52] Sherkow (n 42) 1047.

[53] Ibid 1048.

[54] Yahong Li, 'The Current Dilemma and Future of Software Patenting' (2019) 50 IRIPCL 823-859.

[55] Edison Bicudo, Alex Faulkner and Phoebe Li, 'Software, Risks, and Liabilities: Ongoing and Emergent Issues in 3D Bioprinting' (2020) JRR 1-16.

[56] Edison Bicudo, *Neuroimaging, Software, and Communication: The Social Code of Computer Code* (Palgrave McMillan 2019).

[57] The Hinxton Group, *Statement on Policies and Practices Governing Data and Materials Sharing and Intellectual Property in Stem Cell Science* (2011).

[58] Debra J. H. Mathews and others, 'Access to Stem Cells and Data: Persons, Property Rights, and Scientific Progress' (2011) 331 Science 725-727.

[59] <https://www.bbc.co.uk/news/health-60258088#:%7E:text=But%20because%20Moderna%20said%20it,more%20quickly%20than%20many%20expected> accessed July 2022.

[60] WIPO, *WIPO Technical Study on Patent Disclosure Requirements Related to Genetic Resources and Traditional Knowledge* (2004). See also the WTO TRIPS Agreement, Article 29.1.

[61] Colleen Chien, *Contextualizing Patent Disclosure* (Legal Studies Research Papers Series 2017).

[62] Petryna (n 1) 46.

[63] Ibid 30.

[64] Bergman and Graff (n 29); Mathews and others (n 48).

[65] Bergman and Graff (n 29).

[66] <https://www.cellectis.com/en/press/precision-biosciences-and-cellectis-sa-announce-cross-license-and-settlement-agreement-for-gene-editing-technology> accessed July 2022.

[67] <https://www.susupport.com/which-countries-car-t-cell-therapy-available/> accessed July 2022.

[68] Nafees N. Malik, 'Reimbursement and Adoption of Advanced Therapies: The 5-C Framework' (2014) 9 RM 573-578; Shobita Parthasarathy, 'Innovation as a Force for Equity' (2022) 18 IST 30-36.

[69] Grace Marsden and others, *Gene Therapy: Understanding the Science, Assessing the Evidence, and Paying for Value* (2017).

[70] Ibid 30.

[71] Giménez (n 33).

[72] United Nations Development Programme (n 5) 4.

[73] <https://ec.europa.eu/programmes/horizon2020/en/h2020-section/responsible-research-innovation> accessed July 2022.

[74] Sherkow (n 42).

[75] Parthasarathy (n 55).

[76] Jan-Peter Voss and Rene Kemp, 'Sustainability and Reflexive Governance: Introduction' in Jan-Peter Voss and Rene Kemp (eds), *Sustainability and Reflexive Governance: Introduction* (Edward Elgar 2006) 4.

[77] Mathews and others (n 48).

[78] Bergman and Graff (n 29).

[79] Chien (n 50).

[80] Christi J. Guerrini and others, 'The Rise of the Ethical License' (2017) 35 NB 22-24.

[81] Ibid 24.

[82] Giménez (n 33).

[83] Richard P. Harrison, Qasim A. Rafiq, and Nicholas Medcalf, 'Automating Decentralized Manufacturing of Cell and Gene Therapy Products' (2016) 2 CGTI 489-497.

[84] Karen Facey and others, 'Patients' Perspectives in Health Technology Assessment: A Route to Robust Evidence and Fair Deliberation' (2010) 26 IJTAHC 334-340; Devidas Menon and Tania Stafinski, 'Role of Patient and Public Participation in Health Technology Assessment and Coverage Decisions' (2011) 11 ERPOR 75-89.

[85] Hazel Thornton, 'Alliance between Medical Profession and Consumers Already Exists in Breast Cancer' (1998) 316 BMJ 148.

[86] Sandy Oliver and Phyll Buchanan, *Examples of Lay Involvement in Research & Development* (EPI Centre 1997); J. Francisca Caron-Flinterman, Jacqueline E. W. Broerse, and Joske F. G. Bunders, 'The Experiential Knowledge of Patients: A New Resource for Biomedical Research?' (2005) 60 SSM 2575-2584.

[87] Anthony J. Culyer, 'Involving Stakeholders in Healthcare Decisions: The Experience of the National Institute for Health and Clinical Excellence (NICE) in England and Wales' (2005) 8 HQ 56-60.

[88] Eckenwiler (n 13).

[89] Parthasarathy (n 55) 34.

[90] Charles L. Bosk and Joel Frader, 'Institutional Ethics Committees: Sociological Oxymoron, Empirical Black Box' in Raymond G. De Vries and Janardan Subedi (eds), *Bioethics and Society: Constructing the Ethical Enterprise* (Prentice Hall 1998); L. B. Edelman, 'Legal Ambiguity and Symbolic Structures: Organizational Mediation of Civil Rights Law' (1992) 97 American Journal of Sociology 1531-1576.

[91] Habermas (n 9) 384.

[92] Fischer (n 8).

[93] Helga Nowotny, 'Democratising Expertise and Socially Robust Knowledge' (2003) 30 SPP 151-156.

[94] Yi Qian, 'Do National Patent Laws Stimulate Domestic Innovation in a Global Patenting Environment? A Cross-country Analysis of Pharmaceutical Patent Protection, 1978-2002' (2007) 89 RES 436-453.

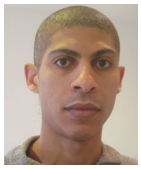
[95] Eric Budish, 'Do Firms Underinvest in Long-term Research? Evidence From Cancer Clinical Trials' (2015) 105 AER 2044-2085.

[96] Petryna (n 1) 194.

[97] Carlos Solar and Martin Smith, 'Austerity and Governance: Coordinating Policing and Mental Health Policy in the UK' (2020) Early access Policy Studies 1-18.

[98] Alex John London and Jonathan Kimmelman, 'Justice in Translation: From Bench to Bedside in the Developing World' (2008) 372 Lancet 82-85, 83.

AUTHOR BIOGRAPHIES



Dr. Edison Bicudo is a sociologist and geographer. For over 20 years, he has studied the social and geographical implications of biomedical technologies. In 2012 he completed his PhD in International Politics at King's College London. In 2019 he published *Neuroimaging, software, and communication* (Palgrave).

Michael Morrison has an MA (by Research and Thesis) and PhD from the interdisciplinary Institute for Science and Society (ISS) at the University of Nottingham. He also holds a BSc in Biology from the University of St. Andrews (2000). Michael has recently acted as Principal Investigator on the ESRC-funded project Biomodifying technologies and experimental space (2017–2020) and is now working on the 'sister' prohect BioGov: Governing biomodification in the life sciences.

Dr. Phoebe Li is a Senior Lecturer in Law at Sussex University in the UK. Her research interests revolve around intellectual property, regulation of science and technology, development, and international trade. Her work aims to map the global commons in science and culture with a view to redressing polarisation and inequality under globalisation. She is particularly interested in exploring the convergence and divergence of risk regulation and IP in relation to emerging technologies.

Professor Alex Faulkner is a sociologist specialising in biomedicine and biomedical technology, and previously worked in the UK's national Health Technology Assessment programme. His research encompasses the governance of medical technology innovation especially in UK and EU regulatory contexts, issues of cancer detection and screening, and adoption of technologies into healthcare systems.

Prof. Andrew Webster was Professor in the Sociology of Science and Technology at York since 1999. He was also the Director of the Science and Technology Studies Unit at York which he established originally at Anglia Ruskin University in 1988. He was Head of the Department of Sociology at York between 2004 and 2009 and then Dean of Social Sciences and a member of the University's Senior Management Group until 2013. He directed national research programmes for the ESRC and MRC in the fields of emerging health technologies and stem cells and held major grants from UK research councils and the European Commission.

Miranda Mourby is a Researcher in Law within the Centre for Health, Law, and Emerging Technologies ('HeLEX'). Her work mostly focuses on privacy, confidentiality and data protection in health and life sciences research. Her current work centres on the BioGOV project: mapping the laws, standards and policies which collectively regulate new 'biomodifying' technologies such as gene editing. She joined HeLEX in 2017, working as part of the Administrative Data Research Network. Prior to this she practised as a barrister, providing advice and representation to the NHS on a range of patient-related issues.

Prof. Jane Kaye is the Director of the Centre for Law, Health and Emerging Technologies (HeLEX) in the Faculty of Law at the University of Oxford and also leads a research team with Associate Professor Mark Taylor, at the Centre for Health, Law and Emerging Technologies at Melbourne Law School, University of Melbourne, Australia. Her teams consist of lawyers and sociologists who use mixed-method empirical approaches combined with legal analysis to explore the relationships between law, governance, and best practice in the area of health.

How to cite this article: Bicudo, E., Morrison, M., Li, P., Faulkner, A., Webster, A., Mourby, M., & Kaye, J. (2022). Patent power in biomedical innovation: technology governance in biomodifying technologies. *The Journal of World Intellectual Property*, 25, 473–494. https://doi.org/10.1111/jwip.12237