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# Regulating Induced Pluripotent Stem Cells Ethically in the Bio-Economy:
## A Preliminary Enquiry*

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**Abstract**

Human induced pluripotent stem cells (IPSCs) are an exciting development, and conspicuously avoid some of the pitfalls of embryonic stem cell research - principally there is no need to destroy nascent human life to obtain them because they are reprogrammed

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from somatic cells. This has led some to proclaim that IPSCs are 'ethically clean'. In this paper, I counter this claim by describing some of the issues that do pertain to IPSCs; while they do not have the same ethical baggage as their embryonic counterparts, they do challenge existing legislative regimes and create regulatory puzzles, and, depending on how we choose to approach them, intriguing opportunities and challenges to socio-legal convention. This enquiry begins by considering the context in which these challenges arise - what some have called the 'BioEconomy', before evaluating an ELSI approach to ethics and law, and finally analysing some distinct regulatory issues that IPSCs raise.

**Keywords**

Human induced pluripotent stem cells (IPSCs/iPSCs), BioEconomy, Ethical, Legal and Social Implications (ELSI), embryo research

## 1. Introduction

Human induced pluripotent stem cells (IPSCs) first caught the headlines in 2007.[1] They are thought to have comparable characteristics as embryonic stem cells - that is, able to be cultured indefinitely and coaxed into differentiating into any of the cells that make up the body. Their discovery suggested some appealing clinical applications: deriving IPSCs from a patient's own cells seems in principle to be reasonably straight forward to do; involving a simple biopsy followed by 'inducement' to a pluripotent state. The resulting cell lines would be compatible with the patient's immune system making them ideal for autologous regenerative

1. Takahashi K, et al. 2007. Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors. *Cell* 131: 861-872.

therapies. They would also be a neat way to study human development (avoiding the controversies of embryo research), and could be engineered to model and study diseases - a stem cell line from a patient with a degenerative condition would also prospectively have the relevant faults *in vitro*. This paper is a preliminary enquiry into the issues that IPSCs prospectively raise if they meet this potential. It is a forward looking analysis, considering the future of regenerative medicine within existing ethical and legal frameworks, and a reflection on the challenges created by these new technologies. In many ways, IPSCs do not raise any distinctive ethical issues: they fall into existing markets and the rules and ethics that govern them. However, IPSCs, and the ways that they become interwoven with legal frameworks and social conventions, will magnify anomalies and challenges to existing issues in health tourism, property in human derived materials, and reproductive and regenerative medicine.

My enquiry begins by concisely defining the BioEconomy: the social and legal framework in which IPSCs will be expected to have a leading role. The BioEconomy broadly refers to "economic activities relating to the invention, development, production and use of biological products and processes".[2] Yet, as I will later elucidate, this economy prospectively defines how we think about ourselves, our interpersonal relationships, and about society in general in relation to technologies; as such, it raises some regulatory puzzles, and, depending on how we choose to approach them, intriguing opportunities and challenges to socio-legal convention. There is still a lot to do to identify realistic prospects and to scope the margins for legitimate technologies; hopefully, this is done meticulously to

2. Organisation for Economic Cooperation and Development (OECD). 2009. *The Bioeconomy to 2030: Designing a Policy Agenda*. Paris: OECD International Futures Programme.

avoid repercussions creeping up in unexpected ways. To meet these challenges, societies must consider the ethical legitimacy, as well as the currency of regulatory frameworks.

First, then, I will describe the features of the BioEconomy relevant to IPSCs. Next, I look in detail at some of the regulatory issues important to potential IPSCs markets. To start with, I ask whether IPSCs are at all exceptional in raising ethical and legal issues. Perhaps, the most important aspect of this is the idea that they will bypass the ethical controversies of embryonic, cloning and foetal research, thus impacting on the future governance of stem cell technologies. In the final part, I look in detail at some particular aspects of a potential BioEconomy - complicity in the research agenda; and the emergence of stem cell markets in two areas: health tourism; and trading in human body parts. If there is one take home message, it is that, in these three examples, existing regulatory conventions seem somewhat inadequate to deal with the technological and social implications of these emergent technologies.

### *1.1 'The BioEconomy'*

The BioEconomy describes an epoch in which technologies that use or benefit living systems contribute to a significant share of economic output.[3]

3. "Bio-based economy covers a wide area. This means that knowledge will be required from a number of different sources. These will include natural science research in the areas of agriculture and forestry, as well as fishing, ecology and the environment. Sources of knowledge will also include technological research, primarily within the areas of biotechnology, nanotechnology, general material technology and environmental technology. In addition, social science and humanities research will also be required in areas such as economics, behavioural sciences and spatial planning, as well as information and communication research." (Swedish Research Council Formas, on no date). Strategic Call - A Bio-based

It is characterized by sophisticated gene manipulation techniques and novel ways of harnessing complex cell processes, and their integration with advanced material and mechanical technologies. It involves assimilation of technologies across all sectors: health, trade, industry and public service; and interconnects diverse groups and communities across the globe. It has therefore become a common feature of political rhetoric about future investment policies and the key to progress. The BioEconomy is already well underway, with already a great deal of investment spent on strategic biotechnological initiatives; yet there is much to be said about the extent to which this is having actual impact, the influence of commercial research priorities and political commitments, and, in particular, the commitment to the idea of a new 'bio-economy' as a driver for progress, health and happiness.

It has been identified as the next wave of epochal social change after that brought about by the Informational Era (I do not intend to dwell on whether such epochs have temporal identities) - typified by the ubiquity of computers and the spread and speed of global communications via the internet.[4] In parallel, the Genomic Era (or The Genetic Revolution)

Economy; available at: http://www.formas.se/en/Financing/Calls-For-Proposals/Strategic-call---A-Bio-based-Economy/ Accessed January 2013; also see Enriquez-Cabot, J. 1998. Genomics and the World's Economy. *Science* 281: 925-926.

4. "This characterization of our time is based on the widespread proliferation of emerging information and communication technologies and the capabilities that those technologies provide and will provide humankind to overcome the barriers imposed on communications by time, distance, and location and the limits and constraints inherent in human capacities to process information and make decisions. Advocates of the concept of the Information Age maintain that we have embarked on a journey in which information and communications will become the dominant forces in defining and shaping human actions, interactions, activities, and institutions." Alberts, D. and Papp D. (eds.). 1997. *The Information Age: An Anthology on Its Impact and Consequences*. CCRP Publication Series. p.2.

heralded a fundamental shift in our understanding of biology of health and disease in ways that were never before possible.[5] These epochs are technology-interrelated: the large scale genetic sequencing necessary for genomic studies was made possible by computers to do the work quickly and efficiently and the ability to transmit large amounts of data between laboratories. Conceptually, they are also linked: the creation of genetic information is followed by the transmitting and understanding of data, and its use for useful (and some troublesome) bio-products. Together, they have contributed to significant developments within healthcare systems in terms of the prediction, prevention, and treatment of disease.

There is a requirement to scrutinise how these interrelated developments will impact on existing social and legal structures, and to work out the realistic prospects of unanticipated transgressions. Some consider that the BioEconomy already defines society to a significant extent; the incorporation of these new biotechnologies into society is not only inescapable, but to be welcomed. We needn't look too hard to find the admirers of a fully - and potentially radical - future techno-life.[6] They

5. "If the genomic era can be said to have a precise birth date, it was in the midst of the appearance of the series, on April 14, 2003. That was when the international effort known as the Human Genome Project put a close to the pregenomic era with its announcement that it had achieved the last of the project's original goals, the complete sequencing of the human genome." Guttmacher, A. and Collins, F. 2003. Editorial: Welcome to the Genomic Era. *New England Journal of Medicine* 349: 996-998.

6. See: '73. Nick Bostrom *for accepting no limits on human potential*.' The Foreign Policy Top 100 Global Thinkers; December 2009.
http://www.foreignpolicy.com/articles/2009/11/30/the_fp_top_100_global_thinkers?page=0,30;
Accessed January 2013. But, for a more sceptical view, see: Holm, S. and Takala, T. 2007. "High Hopes and Automatic Escalators: A Critique of Some New Arguments in Bioethics." *Journal of Medical Ethics* 33: 1-4.

claim we ought to hurriedly usher in technologies that liberate us from our human limitations and fallibilities.[7] Although, perhaps a more realistic future is one in which we can look forward to utilising regenerative medicine, nanotechnogies and other novel technologies for the commonplace treatment of disease and dysfunction - offering novel cures and preventions that extend life and offer opportunities. Stem cell science is but one of these developments.

However, others are wary of how such developments will impact on our lives - just as technology has changed how some view privacy,[8] they will transform in other ways how current legal and social conventions appear to us. For example, technology dependent health provision will leave more care out of the reach of many less able to afford it, placing further burdens on social security and the ability to pay for health care, and widening the scope for discrimination, disadvantage and exclusion; the controversies about embryo research, cloning, and chimeras - so far the focus of much of the stem cell debate - may be eclipsed by those concerning our own bio-engineered lives;[9] and on-going debates about organ trading may be transformed by made-to-order *ex vivo* products, thus creating conditions for legitimated markets in human parts.

7. For a critique of this, see: Capps, B., Nielsen, L.W. and Stirrat, G. 2012. A Brief Critique of Two Claims about the Social Value of Biotechnological Enhancements. *Asian Bioethics Review* 4: 259-271.

8. "Developments in both medical informatics and bioinformatics show that the guarantee of absolute privacy and confidentiality is not a promise that medical and scientific researchers can deliver any longer"; Lunshof, J. et al. 2008. From Genetic Privacy to Open Consent. *Nature Reviews Genetics* 9: 406-11.

9. Cf. Sandel, M. 2007. *The Case Against Perfection: Ethics in the Age of Genetic Engineering*. Cambridge, MA: Harvard University Press.

Importantly, this raises concerns about the relationship between ethics and economics - asking significant questions in respect to the marketing of human life and the globalization of health. This will force us to take another look at the commericalisation and consumerism of the human body, and how these phenomena affect our relations with one another.

Asking these questions now is important for us all - and to do so, societies have developed frameworks for bioethical enquiry; the most extensive of which was the ELSI project of the Human Genome Project.

## 2. ELSE and Governance

I will start my enquiry by briefly outlining my approach within the traditional framework of Ethical, Legal and Social Implications (ELSI).[10] ELSI, one will recall, has two meanings.

First, it is the program conceived as part of the Human Genome Project (HGP) in 1988.[11] As a framework, it had the basic goal to "forestall adverse effects" associated with genetic biotechnologies.[12] It would do this in two ways: by encouraging sophisticated debate and funding specific research projects. These initiatives would create a platform to shape social policy.[13] The success of this programme is disputable.[14] The

10. This scope for my enquiry was defined by the Ewha Conference agenda.

11. Although the acronym appears to go back only to 1991; Foreman, J. 1991. Working Out the Genome Project Ethics - In Advance. *Boston Globe* Feb 4, 25.

12. Senate Committee on Commerce and Transportation. Human Genome Initiative. Hearing; Subcommittee on Science, and Space; 1989. pp. 101-528.

scholarly contribution (in perhaps a narrow area) is incontrovertible; but despite some notable developments,[15] there has been less impact on policy, because, among other factors, of the shortcomings of an effective political will to actuate ELSI principles.

Second, ELSE is a field of study - and it is this aspect which directly links to stem cell science. In this conception, the ethical, legal and social issues of technologies become rather broad. ELSI activities under the HGP were generally limited to the development of a specific curriculum, and providing a commentary on issues concerning the use of genetic information, such as in employment;[16] now it covers some quite divergent issues in genetics and genomics,[17] and explores cross-cutting issues, equivalent to, or implicated in respect to other emergent technologies.[18]

The impact of ELSI in the BioEconomy is extensive; the

13. F Collins, F. et. al. 1998. New Goals for the U.S. Human Genome Project: 1998-2003. *Science* 282: 682-689.

14. Wolfe, A. 2000. Federal Policy Making for Biotechnology, Executive Branch, ELSI. In: T. Murray, M. Mehlman (Eds.), *Encyclopaedia of Ethical, Legal and Policy Issues in Biotechnology*, vol. 1. New York: Wiley. pp. 234-240.

15. Americans with Disabilities Act 1990; Pub.L. 101-336, 104 Stat. 327, July 26, 1990, codified at 42 U.S.C. § 12101; Genetic Information Nondiscrimination Act 2008; Pub. L. 110-233, 122 Stat. 881; May 21, 2008

16. Greely, H. 2005-2006. Neuroethics and ELSI: Similarities and Differences. *Minnesota Journal of Law, Science & Technology* 7: 599-637.

17. For example, see the work of the HUGO Ethics Committee (now Committee on Ethics, Law and Society);
at: http://www.hugo-international.org/comm_hugoethicscommittee.php.

18. Thus, ELSI is equivalent to studies in bioethics more generally. The originality of the HGP has been followed by the Hapmap Project to associate genes with disease (http://hapmap.ncbi.nlm.nih.gov/) and perhaps inspired the Human Brain Project (http://www.humanbrainproject.eu).

pervasiveness of biotechnologies touches on almost all aspects of daily living and society, extending to political intrigue, public goods and economic interests. For these reasons, it is necessary to take a far-reaching view of ethics, law and society in the assessment of technologies. How, then, might ELSI direct the regulations of IPS cell technologies? Before answer this, I first will indicate just how broad this enquiry should be.

*2.1 Ethics*

There seems to be two ways to think about ethics in respect to a regulated society (one that is not in a 'state of nature'). Firstly, you can break down law or society into components to find out whether 'law A' is legitimate or not, or that a society that acts in a certain way should be applauded or rebuked. Secondly, you can look to principles of engagement to solve policy problems.

Ethics, in the first respect, is the primarily application of logic structures.

On this account, enquiries are defined by a methodology or a theory that purports to uncover "a non-arbitrary practically reasonable viewpoint".[19] Such an enquiry is distinctive because it purports to uncover right answers that can override non-moral inclinations, mere opinions or prejudice. It thus disavowals an entirely open normative pluralism: it is plausible to define a moral anchoring point - something we all can agree on; a normative principle that is coherent, universal, and coextensive with the 'good life'. Accordingly, not every opinion is going

19. Capps, P. 2009. *Human Dignity and the Foundations of International Law*. Oxford: Hart. p.125.

to be *reasonable*; some viewpoints might simply be *un*reasonable.

Ethics, on this understanding, is defined by what we can logically justify - whether it is the utility of Mill, the duties of Kant, or the virtues of Aristotle; and the reasonableness of our actions, intentions and beliefs are judged *within* that regime of moral reason. Often principles given by different actors will conflict, and unless one willingly backs down, there is nothing but fundamental disagreement to be had. At other times, we can agree on the outcomes without necessarily getting there via the same route. Thus, a strategy for dealing with the many kinds of disputes - disputes that relate to matters of both principle and practice - is required. One of the principle tasks of this approach is ground-clearing; establishing the statements that can animate moral regimes. To do so, one is open to reasonable discourse and finds currency in the empirical and observational treatment of facts; but, in the final analysis, the approach is less likely to be inclusive in respect to socio-political debate. Some attest to this approach as a prosaic means to (at least) confront what is "evil and wicked".[20]

Others, however, allow for the plurality of reasonable doctrines to coexist. Thus, the ethical mandate is to develop procedures to separate these out and then decide on one course of ethical action, largely through consensus and compromise. In this way, societies can confront beliefs and prejudices in a rehearsed and coordinated way; and, at its most sophisticated, it is a method to contest significant ideologies. To impart that these systems can be ethical requires quite erudite argumentation,[21]

20. Harris, J. 2011. The Challenge of Nonconfrontational Ethics. *Cambridge Quarterly of Healthcare Ethics* 20: 204-215. Harris has tended to solve ethical conundrums from a starting point of utilitarian libertarianism.

because, as some have argued, compromise often requires one to give up values which one cannot normally be asked to do.[22] Proceduralism, therefore, often does not resolve these kinds of insuperable issues, but then, it sometimes avoids trying to do so by negotiating the best possible - rather than a definitively 'right' - ethical position.[23]

Now, while I am normally more comfortable with working out systematic application of moral theory, for the purposes of this preliminary enquiry, I am content to confine my approach to the second of those just mentioned - to offer up some points for discussion, and perhaps, if I might be so bold, to point out the blatantly unreasonable.

*2.2 Law*

Perhaps the most important questions *about* law concern its relationship with ethics; its logical structure and purpose in society. One debate famously played out between Patrick Devlin and Herbert Hart in the mid-20th Century, as respectively protagonists of 'public' and 'private' morality and their effect on regulatory constraint.[24] These contentions have been recast on a number of occasions since, and have a semblance of similarity with enduring ideas of legal idealism (Natural law) and legal positivism respectively. The central tenet of legal positivism is the separation thesis: that there is no necessary connection between law and

21. Capps, B. 2007. Authoritative Regulation and the Stem Cell Debate. *Bioethics* 22: 43-55.

22. Finnis, J. 1999. Natural Law and the Ethics of Discourse. *Ratio Juris* 12: 354-373.

23. Michelman, F. 2003. Constitutional Legitimation for Political Acts. *Modern Law Review* 66: 1-15.

24. Devlin, P. 1959. The Enforcement of Morals. *Proceedings of the British Academy* XLV: 129-151; Hart, H. 1963. *Law Liberty and Morality*. Oxford: OUP.

morals, or law as it is and ought to be.[25] The opposite is "[legal idealism, which] insists that morality necessarily impinges on legality".[26] I avow that I am from the latter school - law, in so far as it concerns *subjecting human conduct to the governance of rule*, is part of, and cannot be separated from the moral enterprise.

My reason for mentioning this is that the public/private separation signifies just how broad - and radical - an ELSI enquiry can become; technologies, and by definition, those situated within the BioEconomy, touch upon all aspects of our interpersonal relationships and social and institutional interactions; they have the potential to shape the conditions of common life in non-trivial ways. Working out the right kind of 'regulatory environment', for that reason, should ask fundamental questions about the function of law in respect to relationships between individuals, their status within communities, and relations between these groups. But, most of all, it asks 'what ought to be' over 'what is'; it asks questions not only about how law and societies are structured, but also begs further enquiries about how they should frame technologies regardless of social conformance or political expediency.

*2.3 Society*

Lastly, following the procedural method just mentioned, ethics and law are primarily tools of social advocacy - we govern human conduct by rules because of problems of social order and to create the best possible systems for cooperation and coexistence. Science can disrupt these, so we are

25. Hart, *ibid*.

26. Beyleveld, D. and Brownsword, R. 1994. *Law as a Moral Judgment*. Sheffield: Sheffield Academic. p. 11.

always trying to identify contentious practices or purposes, and to assess them with respect to ethical and legal criteria. A distinction may be useful: on the one hand, bioethics (and related fields) is a discipline that identifies issues in emergent technologies and often proposes solutions when they challenge practices or conventions. On the other hand, ELSI projects explicitly combine ethics, law and social studies, and are about applying norms to policy reform. (It should be clear from my discussion on ethics, above, that I do not see a significant difference between 'bioethics' and 'ELSI' projects; although I need not dwell on this any further.)

In both approaches, laws puts those principles we find most reasonable into practice, and, in so doing, attempts to provide security, consistency, coherence and predictability in achieving and maintaining goals. Sometimes we find that law has fallen behind the science - regulations become disconnected, ineffective, and sometimes irrelevant, because they are anchored too narrowly from the start. Such developments - and the public response - should be predicted.

So, to enable well-planned science, we need to envisage systems of good scientific governance that brings together norms that we expect to govern science, and the appropriate laws to makes sure that the oversight is effective. A recent report by Landeweerd, et. al., tries to capture the idea of a best possible framework for 'governance', writing "ideally [it] should bring together parties with different interests, values and agendas leading to a consistent strategy for developing science and technology and their products".[27] ELSI defines an ambitious project to contribute to wider

27. Landeweerd, L. et al. 2012. EPOCH: *Ethics in Public Policy Making: The Case of Human Enhancement*; WP 2 Governance and Ethics. D 2.6. Report on the Best Possible Models of Governance of Science and Technology.

social order - to enable coordination and cooperation - rather than to leave us to stumble into this emerging BioEconomy. In the next part of this paper I will apply these general ideas of good governance to raise questions about the potential emergence of IPSC-technologies.

## 3. Issues in the BioEconomy

### *3.1 Are IPSCs Ethically Exceptional?*

The stem cell debate has tended to court controversy to the degree that its regulation might be conceived in terms of exceptional.[28] The question as to whether IPSCs should be regulated like other cell-based products was addressed by Lomax and Peckman.[29] They concluded that "To the extent there are unique concerns with stem cell based therapies, we believe they may emerge at the interface between research ethics and clinical translation."[30]

I do not think there is much grounding for stem cell exceptionalism in research either: for a start, the embryo research debates are rooted in the abortion controversies,[31] and cloning fears are well rehearsed.[32] Lomax

27. http://epochproject.com/wp-content/uploads/2011/10/EPOCH_Final_Report_2.1FINAL.pdf, p. 6.
28. I.e. the unusual or extraordinary; cf. Sage, W. 2010. Will Embryonic Stem Cells Change Health Policy? *Journal of Law, Medicine & Ethics* 38: 342-351.
29. Lomax, G. and Peckman, S. 2012. Stem Cell Policy Exceptionalism: Proceed with Caution. *Stem Cell Reviews* 8: 299-304.
30. *Ibid*. p. 300.
31. For example, the Human Fertilisation and Embryology (Research Purposes) Regulations 2001 dealing with embryonic stem cell research was just over one page

and Peckman argue that, in respect to the United States at least, IPSCs raise issues of oversight of research design and approval for clinical trials that are already well covered by regulation; and the diverse interests involved in getting treatments from 'bench to bedside', or the bio-business of cells lines, are not new controversies.[33] The issue of trying to bypass clinical evaluation by offering stem cells as 'experimental' are also not unique;[34] and the phenomenon identified as 'tourism' is common to any activities which are subject to subsidiarity organizing principles or a patchwork of regulatory frameworks.

Perhaps what is extraordinary is the potential scope for stem cell therapies to affect lives blighted by diseases, cellular dysfunction and damage; stem cells might be used to cure complex and difficult-to-reach organs and systems, offering (perhaps misplaced) hope to many. The significance of future stem cell treatments rings something like the 'war on

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long and merely added two further purposes to the Human Fertilisation and Embryology Act 1990 (amended 2008). That said, there was some nimble manoeuvring in the courts to ensure that its definitions still applied to new 'embryonic' artefacts, such as those created through somatic cell nuclear transfer; see R. Brownsword. 2004. Reproductive Opportunities and Regulatory Challenges. *The Modern Law Review*, 67: 304-321. And a new section was required to include 'admixed' - hybrid - embryos.

32. These controversies surfaced in the UK in IVF debates of the 1980s. See, for example, the 'Warnock Report': http://www.hfea.gov.uk/docs/Warnock_Report_of_the_Committee_of_Inquiry_into_Human_Fertilisation_and_Embryology_1984.pdf. A recent edition of the American Journal of Bioethics attempts to renew the 'potentiality question' with respect to IPSCs and the controversies of embryo research; volume 13, 2013.

33. Lomax & Steven, *op. cit*. note 29.

34. Lysaght, T. and Sipp, D. In print, 2013. Dislodging Direct-to-Consumer marketing of Stem Cell-Based Interventions from Medical Tourism. In Parry, B. (ed). *Bodies Across Borders: The Global Circulation of Body Parts*, *Medical Tourists and Professionals*. Aldershot: Ashgate Press.

cancer' in respect to the rhetoric of ambitions, hope and opportunity, justified by the expected impact it might have on all of our lives.[35] Moreover, it is plausibly the case that stem cell science has captured the imaginations of the public at perhaps unprecedented levels, through the successes, promises, and controversies. The GMO-agriculture and farming controversy of the 1990s, however, also showed how an interested public can become motivated and polemic.[36] Thus, these seem to be, at most - if at all - trivial concessions to the exceptional label.

But although I disavow exceptionalism in the ethical issues that IPSCs raise, their possible large-scale use contributes to a number of regulatory issues that have so far resisted resolution: complicity in controversial research; appropriation of human cells and tissues; and downstream uses of pluripotent cell lines. These are not distinct issues in themselves; and would pertain to *any* material of human origin - but, unlike Lomax and Peckman, I think that, in some aspects, existing oversight is not always effective or legitimate, principally because there is no clear interface between research and clinical sciences.[37] An IPSC market, in particular, will magnify the anomalies which persist in transactions involving human derived materials; and, therefore, societies would do well to address these issues before, or if, IPSCs become engrained in reproductive and regenerative medicine. It is these issues that I will tackle in the following in respect to the ethical regulation IPSC research, given that the governance of such artefacts - in research and clinical use - will be shaped within the evolving BioEconomy.

35. Sporn, M. 1996. The War on Cancer. *The Lancet* 347: 1377-1381.

36. See: Gaskell, G. et al. 2000. Biotechnology and the European Public. *Nature Biotechnology* 18: 935-938.

37. Lomax & Steven, *op. cit*. note 29.

In many ways, IPSCs do not raise any distinctive ethical issues: they fall into existing markets and the rules and ethics that govern them. However, IPSCs, and the ways that they become interwoven with legal frameworks and social conventions, will magnify anomalies and challenges to existing issues in health tourism, property in human derived materials, and reproductive and regenerative medicine.

*3.2 Are IPSCs an Ethical Alternative?*

The optimism of IPSC technologies has also encouraged the unrelated claim that there were 'ethically clean'; the President's Council on Bioethics concluded that IPSCs were "ethically unproblematic and acceptable for use in humans".[38] Unlike other therapeutic stem cell approaches, the procedure did not require the generation or destruction of human embryos, nor did it involve 'therapeutic' cloning or necessitate the procurement of human oocytes. Thus, it was averred that embryo, foetal and cell nuclear replacement experiments were no longer necessary.

The claim, however, is premature: it is too early to say that such cells are safe to use in humans, or that such cells are even equivalent to the gold standard of human embryonic stem cells (HESCs). It is scientifically reckless to allow a relatively new science to overtake the years of established research in embryonic stem cells.[39] But, most of all, even if

38. The President's Council on Bioethics. 2005. *White Paper: Alternative Sources of Human Pluripotent Stem Cells*. Washington, D.C: PCB.

39. Kim, K., et al. 2010. Epigenetic Memory in Induced Pluripotent Stem Cells. *Nature* 467: 285-290. Araki, R. et al. 2012. Negligible Immunogenicity of Terminally Differentiated Cells Derived from Induced Pluripotent or Embryonic Stem Cells. *Nature* doi:10.1038/nature11807.

IPSC technologies do supplant the use of embryonic counterparts, they contribute to a collection of ethical issues that will need considering in the BioEconomy. It is these controversies that I will discuss for the remainder of the paper.

*3.3 Complicity in Designing Research Agendas*

The bioethicists Insoo Hyun wrote:

> "The study leader and iPS cell [IPSC] pioneer, Shinya Yamanaka, has told me he was inspired by a nonfederally funded study conducted at Harvard in 2002 in which somatic cells were fused to human embryonic stem cells and subsequently began to develop pluripotent characteristics."[40]

This debt to embryo research raises the issue of complicity: that one can *do* wrong by being associated, tolerating, cooperating in, or benefitting, in a certain way, with others' wrongdoing.[41] The key to complicity is finding out whether a wrong has been committed in the first place. Much of the stem cell debate has been focussed on complicity in embryo research, or, in the case of foetal research, abortions. Without here intending to discuss whether destruction of a human embryo for research or any other purpose is an immoral act, there seems to be at least two possible wrongs: one, complicity in destroying human embryos for

40. Hyun, I. 2009. Clarifying the President's Council's Clarification of the Obama Stem Cell Policy. *Bioethics Forum* 03/30/2009; available at: http://www.thehastingscenter.org/Bioethicsforum/Post.aspx?id=3308#ixzz2EnVqsjry

41. Gardner, J. 2007. Complicity and Causality. *Criminal Law and Philosophy* 1: 127-141.

research purposes; and two, complicity in *encouraging* embryo research (and the wrongs that that entails).

In the first of these, complicity seems more or less proximate to the act; either there is some kind of causal link to the wilful destruction of an embryo, or that one's actions directly promote the supposed wrongdoing.[42] In the second case, complicity is more remote. For example, one might make available funds to support researchers to carry out this work (even by paying taxes). In the future, one might actually be injected with an embryonic derived product. Or, one might speak out in favour of pursing the research. The argument is that any encouragement or benefit from controversial research links one to the wrongdoing; in this case, it endangers embryos by creating a demand for additional stem-cell lines and therefore increasing the chances that a particular embryo might be used as a source of stem cells. As Devolder wrote, "if hESC research is wrong for reasons of complicity, then there is at least a good *prima facie* reason for thinking that iPSC research is wrong for similar reasons"[43] - for a number of reasons, embryonic an IPSC research are intrinsically linked. This second kind of complicity, however, can be taken much further.

Consider designing a research policy: taking part in the process of effecting how strategies will play out. In the BioEconomy, this kind of work will ultimately determine the availability and access to potential treatments. In a recent US case, the Plaintiffs' made a number of claims

42. For example, the provision of direct funds to enable the wrong - if it is a wrong - to occur by paying a researcher to procure ES cells for one's own research. In the second case, the wrong is perpetuated by speaking out in favour of the research.

43. Devolder, K. 2010. Complicity in Stem Cell Research: The Case of Induced Pluripotent Stem Cells. *Human Reproduction* 25: 2175-2180.

against Obama's decision to allow Federal funding for conditional embryonic research.[44] One of their complaints was (quoted from the District Court report) the "balance of hardships", arguing that by allowing HESC funding it increased competition with researchers who work on other sources of stem cells and this would "threaten [the plaintiffs'] very livelihood" - themselves working with adult stem cells.[45] This, they alleged, weighed in favour of an injunction in respect to the Obama Executive Order. The claim was thrown out (along with others considered at the time) on appeal, arguing that the Executive Order would not place a significant additional burden upon their ability to secure funding for their research.[46] And in fact, "the hardship a preliminary injunction would impose upon HESC researchers ⋯ would be certain and substantial."

In the widest sense, therefore, regulators will be designing, in one

44. As a result of Obama's Executive Order revoking Executive Order No. 13, 433. Exec. Order No. 13, 505, 74 Fed. Reg. 10,667 (Mar. 11, 2009), allowing the NIH to "support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law." This promulgated the NIH guidelines which stated that an ESC research project may receive NIH funding as long as it utilizes cells from lines (1) created by in vitro fertilization for reproductive purposes, (2) no longer needed for that purpose, and (3) voluntarily donated by the individuals who owned them - even if that line was derived after 2001. One claim was an alleged violation of a statutory prohibition contained in the Dickey-Wicker Amendment, which "provide[d] that no federal funds shall be used for 'research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero'" under other regulatory and statutory regimes. Sherley v. Sebelius, 704 F. Supp. 2d 63, 70 (D.D.C. 2010) (quoting Pub. L. No. 111-8, § 508(a)(2)).

45. Sherley v. Sebelius, *ibid*. pp. 72-73.

46. The Appeals Court Ruled twice: United States Court of Appeals For the District of Columbia Circuit. Argued December 6, 2010 Decided April 29, 2011; No. 10-5287; United States Court of Appeals For the District of Columbia Circuit. Argued April 23, 2012 Decided August 24, 2012; No. 11-5241.

way or another, the future direction of stem cell science, and therefore being complicit in prospective social-institutional activities. Moreover, within the BioEconomy, they are going to be coordinating these activities with respect to the market dynamics of production and exchange, creating and extinguishing economies in biomaterial, and as such, potentially becoming complicit in subjective wrongdoings by promoting and precluding certain kinds of behaviours. There are the intertwined interests that are affected by bio-economic policies: regulations push research and researchers - whether using HESCs or IPSCs - in certain directions, and even into jurisdictions that encourage their work. These economic factors can have profound effects by shifting the onus of underwriting to other sectors - in the USA this is a shift in Federal to private funding; elsewhere the effect is the brain drain of scientist into more favourable regulatory environments. Thus, regulatory policies directly affect the delivery of technologies in not wholly unforeseen ways, often leading to misaligned investment that damages economies, potentially creates inequitable access, and exports untapped investment and benefits.

*3.4 Stem Cell Markets*

3.4.1 Stem Cell Tourism

My second focus concerns the potential entrance of IPSCs into the market. At the moment, IPSC research is subject to a different regulatory framework to HESC, for the reason that IPSCs do not involve the use of human embryos directly. But, it is plausible that IPSCs, once caught by the markets, will be considered under similar governance structures to autologous adult stem cells already in clinical circulation. This raises the issue of ongoing direct-to-market pathways used by practitioners to

operate without IRB or clinical trials in the provision of experimental stem cell interventions. Thus, IPSCs may become operative without proper scientific and ethical oversight.

In many jurisdictions, embryo research is subject to strict statutory control.[47] This normally revolves around two central principles, which were clearly elucidated for the first time in the 'Warnock' deliberations from the 1980s (in the UK):[48]

1) Embryo research should be limited those less that 14 days old or before the emergence of the primitive streak, whichever is earlier; and

2) Research should normally be 'necessary and desirable', meaning that there are no alternatives to using human embryos, and that the research should be of good quality and health related. This permission might be limited to specific research purposes.

In addition, one may also find:

3) That a license or special permission is required to undertake such research.

4) There are divergent rules on what kinds of embryos can be used: only those supernumerary to IVF treatment; those created

47. See: Capps, B. 2006. Procedural Ethics and the European Stem Cell Debate. *Jahrbuch für Wissenschaft und Ethik* 11: 41-66.

48. *Report of the Committee of Inquiry into Human Fertilisation and Embryology*. 1984. Chaired by Dame Mary Warnock DBE. London: Her Majesty's Stationary Office.

specifically for research; or embryos created by other means, such as somatic cell nuclear transfer.

'Adult' stem cells, however, are often subject to less clear oversight. How to regulate a growing industry in reproductive medicine has therefore become the focal issue in respect to stem cells beyond the embryo question. For some, the framework of consent and IRB approval can do the job. But, this may not be adequate - IPSCs are somewhere between ESCs and reprogrammed adult cells - and, as is evidenced, exactly because there is no 'embryo question' has led some to resist proscriptive governance.

The European Union classifies stem cells as Advanced Therapies - 'innovative, regenerative therapies which combine aspects of medicine, cell biology, science and engineering for the purpose of regenerating, repairing or replacing damaged tissues or cells' - concluding that they normally cannot be regulated as 'conventional' drugs and need adapted requirements, but that they should not be exempt from clinical trials.[49] This framework normally requires drugs or biologics to be awarded a license for marketing after providing evidence of safety and efficacy.

There are others, however, who argue that autologous stem cells are *experimental* interventions and should bypass more formal regulation. Formal clinical trials, they argue, has a chilling effect and discourage exceptional, if somewhat maverick science progress. And prohibitive regulatory design is denying patients access to interventions that offer

49. Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004.

enough promise to be delivered in terms of *medical discretion* on a patient needs basis. Finally, the current system results in unfair access to trials for disqualified patients, such as those with multiple aetiologies; and denies opportunities to patients with rare or untreatable diseases. They reason, therefore, that: the derivation of the autologous cells is proximate to patients; interventions should be a matter of consent; and 'cultured' autologous cells are not manipulated to the extent that they are a new or manufactured drug, and thus should be exempt from clinical trials. Thus, these interventions are construed for compassionate use; and they can be provided to patients as experimental interventions in 'paid-for-trial' type therapies. Such experiments are already taking place using autologious cell biopsies, which are purified and cultured before being injected back into patients. They are often, but not exclusively offered in regulatory havens where oversight is lax or ineffective; they are also delivered to patients in regulated jurisdictions either by exploiting loopholes or by eluding more comprehensive oversight. This means that patients who want to access these interventions can do so by crossing borders and/or paying a fee.

Yet, they are advertised[50] as 'treatments' despite no robust evidence of medical effectiveness or peer review of results. These patients are being asked to pay high prices for these 'exceptions', which are, as a matter of fact, the norm in such stem cell clinics. And there is increasing evidence that regulators are finding such activities to be ethically unsound[51] -

50. Often through websites or patient testimonials.

51. I am working with colleagues on a detailed exploration of the ethics and regulation of autologous stem cells; a manuscript is currently in the pipeline, with Tamra Lysaght (National University of Singapore), Doug Sipp (RIKEN Center for Developmental Biology, Kobe) and Gerard Porter (University of Edinburgh).

perhaps most saliently because of questionable safety and effectiveness.[52] Thus, there is a trend to redefine regulatory boundaries and close loopholes.[53]

To take just one example, consider the idea of 'compassionate use'. The Helsinki Declaration considers such use possible:[54]

> "35. In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available."

The context of the Declaration - a largely aspirational document stemming from the atrocities of World War Two - indicates, however, that research should normally follow the more conventional roots of a clinical trial; and clause 35 indicates an exception to this *when care is also involved*. The exception is not made lightly, and, because it is within the context of

52. Amariglio, N. et al. 2009. Donor-Derived Brain Tumor Following Neural Stem Cell Transplantation in an Ataxia Telangiectasia Patient. *PLoS Med* 6: e1000029; Ledford, H. 2011. "Stem-cell Scientists Grapple with Clinics." *Nature* 474: 550.

53. And at least one group has been prosecuted for doing so: http://www.justice.gov/usao/txs/1News/Releases/2012%20September/120907%20Morales%20and%20Stowe.html.

54. 59th WMA General Assembly, Seoul, Korea, October 2008.

care, there is an added obligation on the physician-researcher when using an experimental intervention:

> "31. The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects."

The use of treatments in this way is permitted in many jurisdictions (the following is from the UK's rules on 'Hospital Exemptions' and 'Specials' [under review]), and are covered by specific rules when they are prepared on a non-routine basis in accordance with a medical prescription for an individual patient, thus allowing a degree of flexibility over formal regulatory requirements. Interventions can be provided through joint deliberations between the doctor and the patient, and as long as the patient consents. This kind of one-off, custom treatment might negate requiring research ethics approval in specific cases; although one might expect some form of peer review, patient follow-up, and outcome analysis.

But, this is not a pathway to avoid the inconvenience of clinical trials, or, as some have argued, a plausible justification to market stem cell interventions as 'treatments' when no evidence of their effectiveness.[55] Providing intervention to vulnerable patients, or children for that matter, even with proxy-consent, is highly suspect. And the 'exceptional' clause still requires a reasonable level of pre-clinical data, and traceability, quality

55. Sipp, D. 2011. The Unregulated Commercialization of Stem Cell Treatments: A Global Perspective. *Frontiers of Medicine* 5: 348-355.

and pharmacovigilance standards as for any other (advanced) medical product. Finally, it requires that IRB approved clinical trials are necessary for the exempt treatment to be standardised for general entry into the market.

Now, while doctors might sometimes reach for the justification that "patients ··· cannot wait",[56] 'compassion' is not an opportunity to expose them to greater than normal risk, to try out unproven, clinically insignificant and risky interventions, or to charge them for this privilege. For example, a registered doctor in the UK saw patients at his London surgery and referred them to his Rotterdam clinic for a stem cell treatment costing $15,800. Notwithstanding the legal status of his 'treatments' in different jurisdictions, the doctor himself 'enthusiastically' believed they worked. The GMC fitness to practice panel thought otherwise, stating that the treatments were based on "anecdotal and aspirational information", and calling his actions "unjustifiable" and "exploitative", and "repeated and serious" breaches of many of the "essential tenets" of good medical practice, concluding:

> " ··· You have exploited vulnerable patients and their families. You have given false hope and made unsubstantiated and exaggerated claims to patients suffering from degenerative and devastating illnesses. Your conduct has unquestionably done lasting harm, if not physically, then mentally and financially, to these patients and also to

56. American Stem Cell Therapy Association/International Cellular Medicine Society. 2009. *ICMS Clinical Guidelines*. Version 1.0; Adopted by Committee on 5/13/09; Available at: http://www.cellmedicinesociety.org/attachments/054_ICMS%20Clinical%20Guidelines.pdf; accessed January 2013.

> their families and supporters. It is, therefore, undeniable that you have abused the position of trust afforded to you. You continue to advocate untested and unproved treatments, using your status as a registered doctor to reinforce your personal beliefs."[57]

Thus, doctors and researchers who are expected to "promote and safeguard the health of patients"[58] can anticipate being reproached for pushing the bounds of what is good clinical practice. If nothing else, without good data and good reasons, this might amount to serious professional misconduct even if it doesn't fall foul of any regulatory requirement. I do expect that these avenues for research to close up substantially, however.

In the BioEconomy, nonetheless, these questions should be more broadly construed: if IPSCs can be used at point of care, there will be calls to shift them into standard medicine, and one might see further pressures on the 'autologous' exceptions outlined here (although IPSCs are not minimally manipulated). This would be potentially disastrous for stem cell science, as such cells will go though substantial manipulation and will therefore require robust safety profiles.

### 3.4.2 Property

While stem cell products, and the clinics that offer them, are coming under

57. Fitness to Practice Panel; 11 January-5 March 2010; 27 March 2010; 10-11 April 2010; 6 - 10 & 27 - 29 September 2010; Regent's Place, 350 Euston Road, London, NW1 3JN; Name of Respondent Doctor: Dr Robert Theodore Henri Kees Trossel.

58. "Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles." Helsinki Declaration, sec. A.2.

evermore close inspection, the issues of cell procurement from patients are receiving far less scrutiny. To appreciate the whole picture, one has to reorientate IPSCs in respect to the cell source - the person and their body, and understand the implications at the point of production or manufacture. This *upstream* perspective considers human parts as features of the BioEconomy - as potential commodities and with rights to ownership, rather than actors in the social patterns that develop downstream in respect to the availability of such products. It is not clear how IPSC cells will fully integrate with bio-markets - whether human tissue or body parts, sources of IPSCs and the derived products,[59] ought to be 'gift based', compensated, or subject to a 'free market' - and this is an important issue, because they are not only a potentially perpetual cache of genomic data pertaining to an individual, but soon scientists may also be able to grow objects that attest to this human origin - a heart or an eye - thus giving a tangible quality to human material *ex vivo*.

We can start this next enquiry by stating some parameters. Property is a legally enforceable or morally authoritative prescription that evinces control of an object. The importance of property should not be understated; it has a complex and longstanding relationship with human moral status, and, among other principles, privacy.

Previously, many kind of human cells (but perhaps not reproductive cells) were considered worthless because they were abundant and often designated waste. The legal framework for property in cells was given famously in *Moore*: barring some exceptions, cells and tissues removed

59. One should already appreciate the complexity here, as a human heart is not normally considered as a product; yet an *ex vivo* grown organ might be considered otherwise having its origins in the industry of a scientist.

from the body are *Res nullius*, no one's thing, or as matter distinct from property.[60] So, once these cells are removed the person they came from cannot claim to be the owner. However, those same cells can be the property of an industrious researcher able to apply 'skill' to preserve, modify or manipulate them; in this new form, the cells are property. Patent rights are similarly constructed: they are only available to the inventor. 'Products of nature,' no matter how exceptional, cannot be the subject of patent protection. Thus, patent protection is not available for human tissue in its unaltered form, and the fact that patent protection has been granted to the inventor of a cell-line (or other genetically engineered substance) has no bearing on what rights the source of the original tissue may possess in that tissue.[61] Clinical researchers, therefore, have often not sought consent to use this kind of material, and, as a matter of routine, taken it, manipulated it, and asserted their property rights.[62]

This rule has been challenged both legally[63] and ethically,[64] because, as typified in a number of cases, it does not find a reasonable balance

60. Moore v. The Regents of the Univ. of California, 51 Cal. 3d 120, 793 P.2d 479, 271 Cal. Rptr. 146 (1990), reh'g denied; No.S006987 (Cal. Supreme Ct. Aug. 30, 1990) (1990 CAL. LEXIS 3975, States library, Cal file).

61. Products of nature can become eligible for patents if they have "markedly different characteristics from any found in nature"; Diamond v. Chakrabarty, 447 US 303, 100 S. Ct. 2204 (1980).

62. Hall, D. 2001. "Reflecting on Redfern: What can we learn from the Alder Hey story?" *Archives of Disease Childhood* 84: 455-456; Underwood, J. 2006. The Impact on Histopathology Practice of New Human Tissue Legislation in the UK. *Histopathology* 49: 221-228.

63. Yearworth and others v. North Bristol NHS Trust, EWCA Civ 37 (2009); QB 1. (2010).

64. Capps, B. In press, 2013. Redefining Property in Human Body Parts: An Ethical Enquiry in the Stem Cell Era. In: Akayabashi, A. (ed), *Towards Bioethics in 2050*; *Message to the Next Generation*. Oxford: Oxford University Press.

between two societal values: protection of individuals' rights and biomedical advancement through investment. One solution has been to assert the property rights that one has over cells and tissues from their body.[65] Now modern biotechnology imbues cells with value; even fat and urine can be reprogrammed for the study of disease or as therapeutic agents.[66] It also means many more ways for human cells and tissues to be exploited in forensics, research and health. We are not talking about waste anymore, but cells that someone has an interest in. So now, we may start to demand to know about who is accessing our cells and for what purposes; and rather than passive approbation, one might expect to find dismay that our cells are included in profitable research, or banked indefinitely, or that the cells form the basis of a multi-million dollar product.

This raises two issues: one, that an individual's *interests* can be perpetuated indefinitely though a cellular-genomic artefact; and two, extending one's life by creating an indefinite source of replacement parts to keep you - your consciousness - going *ad infinitum*.

In the first case, privacy is a major concern (the second case is discussed in the final section). The ability to create and maintain data opens up more ways for one's identity to be delved into. Of course, many kinds of data can be kept indefinitely under the right conditions; but in the case of IPSCs, the genetic instructions can *become* ever-more complex

65. Beyleveld, D. and Brownsword, R. 2000. My Body, My Body Parts, My Property? *Health Care Analysis* 8: 87-99.

66. Wang, L. et al. 2013. Generation of Integration-free Neural Progenitor Cells from Cells in Human Urine. *Nature Methods* 10: 84-89; Harmon, K. 2009. Induced Pluripotent Stem Cells Created from Fat Cells. *Scientific American* Sept. 8th; http://www.scientificamerican.com/article.cfm?id=stem-cells-from-fat-cells.

objects as technologies improve. DNA can be stored for some time, so the consent taken at the time can become remote from its futures uses; and although this might now relate to a deceased person who no longer has rights of privacy, it implicates relatives and descendents who share that DNA and may have interests in what happens to it.[67] Like a record of confidential information, such as that a person is HIV+, it reveals one fact; there is little more that the information itself contains. But, an entire genome cultured in a laboratory for undefined purposes relates back to the issue of control: should that person have control not only over how those instructions are read, *but also how they are translated into actual objects that can be owned?*

We might think that consent can do most of the work here, albeit that, as already discussed, the current legal framework does not necessarily require this in respect to cells and tissues; at the very least, informed consent for the biopsy a future immortal cell line requires more robust protections if we leave legal convention as it is. But, the salacious implication for the BioEconomy is that one's body can contribute to the bio-market without agreeing to it; and I see this as raising the need for two distinct enquiries. Firstly, if privacy is drawn out wide enough, we might see donors better able to control what happens to their cells and tissues. Secondly, this right, which attaches to property, might not be construed as far as a right to profit. To date, regulators have been resistant to commodification of human body parts - so bringing into play the second point; and, as I have already explained, transfer and trade are central to the BioEconomy.

67. Holm, S. 2001. The Privacy of Tutankhamen - Utilising the Genetic Information in Stored Tissue Samples. *Theoretical Medicine and Bioethics* 22: 437-449.

The solution, in part, is to revise current frameworks to require the involvement of patients - a policy that many biobanks have welcomed - in decisions about the use of their cells, because it encourages more fruitful participation by donors and shares the benefits between parties: a plausible component in creating an equitable BioEconomy. The first step to this would be defining proper ownership - it is not clear how *Moore* paradigms will fit; but it seems even more likely that the concealed appropriation of cells is unconscionable now that we can do more with cells. At particular risk will those patients from who cells have been taken from because of their aetiologies: they will be potentially identifiable and particularly vulnerable to such practices. But, involving patients may promote a market that tends to produce public goods;[68] and this is to be welcomed. It is apparent that privacy issues are far less important in mutually beneficial relationships than those in which benefits are siphoned off for private interests.[69] The argument that products of industry eventually find their way into public spheres doesn't tell the whole story about inequitable access, unethical practices, and vastly asymmetrical profiteering.

A model based on benefit sharing, would, I believe, at least go some way in exposing the current mischievous appropriation of cells by some researchers to profit from the undisclosed complicity of patients. This alternative is one in which patients play a part in co-production in the

68. The kinds of commodities that have shared benefits because such goods readily attach to benefits that are experienced by persons as rights-holders, but what makes them distinctive is that they can be parceled out to each. Clean water is a matter of human rights; it is also a public good when clean water is provided to the community.

69. Capps, B. 2012. The Public Interest, Public Goods, and Third Party Access to UK Biobank. *Public Health Ethics* 5: 240-251.

BioEconomy - they consent to the use of cells, they are protected by principles of privacy and confidentiality, and they have a right to the return of unmodified materials when practicable.[70] This does not stop researchers from profiting from their products and asserting patents to receive benefits from their industry; but the design is to allow benefit-sharing with those that contribute to the knowledge banks, and the distribution of emergent benefits as public goods: in this case, knowledge about diseases and potential cellular therapies ought to be equitably returned to the originators of the cells as affordable clinical benefits.[71]

### *3.5 The Body in the Market: Engineering Immortality*

#### 3.5.1 Gametes

My last two examples extend this property issue into extending life. Consider, first, human gametes. Previously, these fell into a separate regulatory category, often requiring a license to conduct research or use for IVF purposes. In the BioEconomy, however, gametes will be more like normal commodities because they will no longer reside in a particular reproductive niche: the cells will come from a laboratory - there will be a cell donor, and a technician to reprogram them. Plausibly, researchers will be able to create embryos from gametes induced from a cell-donor 'parent', and, if one was so inclined, these could be implanted to create children.

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70. And might need well thought out protocols at the point of consent; Cf. UK Biobank. 2012. *UK Biobank Ltd Withdrawal Protocol*. Stockport, UK. Version 1.0.

71. Benefit sharing involves an organisation which is intractable from a wider community, agreeing to provide the community with some benefits; see: HUGO Ethics Committee. 2000. *Statement on Benefit Sharing*. http://www.hugo-international.org/img/benefit_sharing_2000.pdf

While offering a potential infertility option, this could also challenge further our attempts to fix ideas of parental responsibility and familial linage (for example, there will be no age limit to having children - and could include resurrecting the fertility of long dead ancestors from well preserved cells).[72] What is more, this reproductive technology will be in reach of far more people - it will no longer be reserved for the community of fertility clinicians and scientists who perhaps are defined by their shared interest in a safe and successful pregnancy and healthy children.[73] We are, to a large degree, already along the path to the commodification of reproduction - gametes are already traded, as are wombs and parenting roles.

### 3.5.2 Organs Avatars

However, consider another example. Few countries allow human organs to be marketed: while voluntarily donating an organ for no financial benefit is considered by most to be morally virtuous, giving up any further claim to it for recompense is more contentious. IPSCs potentially enable an industry in regenerative medicine by production of *ex vivo* organs, and this will challenge our attitudes to organ markets because they are not going to be subject to the kinds of reasoning that prohibits commerce in

72. Callaway, E. and Nature magazine. 2011. Could Stem Cells Rescue an Endangered Species? *Scientific American* Sept. 5th; http://www.scientificamerican.com/article.cfm?id=could-stem-cells-rescue-endangered-species;
Panula, S. et al. 2010. Human Germ Cell Differentiation from Fetal- and Adult-derived Induced Pluripotent Stem Cells. *Human Molecular Genetics* 20: 752-762.

73. Cyranoski, D. 2008. "Stem Cells: 5 Things to Know Before Jumping on the iPS Bandwagon." *Nature* 452: 406-408; Takahashi, K. and Yamanaka, S. 2006. Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors. *Cell* 126: 663-676.

the human body. Cells and tissues already are subject to commercial transactions (subsequent to the skill-rule being applied), so, it would require contorted reasoning to exclude artificial organs from the same kind of transactions on the basis of organ trafficking.

One might expect, for instance, that sometime in the future these body parts will become a *personal* insurance policy, pre-ordered and paid for, and cultured in vast bioreactor repositories. Will such organs be open to normal commerce? And if so, who will own them? Will it be the customer, in whom a near identical heart still beats? Or the service provider with purely contractual interests in recompense for manufacturing bio-instruments?[74] A market in IPSC-derived parts could negate the kinds of exploitation that are necessitated by organ markets, and could even reduce the incidents of vulnerable people being drawn into such arrangements.

How such organs are grown will likely influence the ethical debate - for instance, whether they are formed in headless, human-like vesicles, raising questions about what we understand by 'person', and whether these complexes can be owned at all.[75] When, in 1997, it was clumsily said that technology used to create headless tadpoles could be applied to human beings, the consternation was predominantly expressed as 'yuckiness' and revulsion to potential human organ farms. A leading

74. Organ derives from the Latin *organum*, meaning 'instrument'.

75. Such bioreactors would have to avoid the possibility of being 'persons' otherwise engage quite proper opposition. The way around this is allegedly already in sight: scientists have created headless frogs by using gene-modification techniques to damage the gene that codes for the development of a head, and then inserted this modified DNA into the nucleus of a frog egg; Morton,O. 1997. First Dolly, Now Headless Tadpoles. *Science* 278: 798.

bioethicist and prominent scientist wrote at the time:

> "Intentionally creating defective human bodies would not be an acceptable use of genetic science. The mass production of bodies without brains would cheapen respect for the human image and form beyond any reasonable limit. And intentionally disabling embryos so that they would grow without heads or brains would surely be an impermissible act of creating and sacrificing potential humans solely for the benefit of others."[76]

Yet, since then a number of countries permit the intentional creation of human embryos for research purposes, and there have been suggestions that parthenotes and embryos engineered to spontaneously die can be alternative tools to move us along this regenerative path. It is at least plausible that human artefacts will become part of the future economy.

One way we might surmount the squeamishness of our headless counterparts might be to consider them as *avatars* - mere biological representations of our bodies. These bodies, devoid of agency, are a biological *embodiment* that lacks a real agent presence (able to interact with others), but is able to biologically mirror our own growth. In controlled environment conditions, the systems might metabolize and mature as its person counterpart will - if you need a new heart at 50, the replacement will be genetically and temporally analogous, thus potentially allowing one's health to be perpetuated as long as the parts are available.

76. Caplan, A. and Venter, C. 1997. Letters: Using One's Head. *Science* 278: 1547-1551.

However, encephalic neonates that lack brain development still hold a significant attachment to the parents - they are still their babies. Similarly, acephalic twins sometimes lack human features and are often supported by a baby to whom they are conjoined. Yet the case of the twins, Mary and Jodie, showed that despite Mary's 'parasitic' state, an agonizing decision had to be made to end her life. Whether human avatars will install this same human connection and compassion, since they would be gestated in bioreactors not humans, remains to be seen. Moreover, the CNS has a tendency for plastic development, allowing encephalic neonates to spontaneously breathe and ostensibly sense their surroundings in some limited ways. So although we are able to harvest from non-human animals regardless of their sensations, it may be necessary to engineer a failsafe to avoid *human* sentience. I doubt that such experiments will be attempted; the risks of ending up with a damaged person are too great to justify the experiments. But perhaps the technology opens up avenues for less controversial design? Would artefacts with no resemblance to the human body install such apprehension? Would the BioEconomy receive faceless and morphologically indistinguishable biological systems to be harvested from?

## Closing: The Right Regulatory Environment and Achieving Governance

In this preliminary enquiry, I have raised a number of issues that are significant for the BioEconomy - IPSCs imbue this economy with many more opportunities to exploit human cells, tissues and organs.

The BioEconomy by definition will be pervasive in shaping our lives; changing possibilities for parenthood, clinical care, and opening up opportunities for better health. It might also challenge our social structures in unexpected and perhaps unpalatable ways - how seminal these changes will play out is unknown. I do think that IPSCs, if they come to fruition, will be powerful tools in this change - and I think that we ought to fully prepared for the kinds of ways that these changes might be executed. In the BioEconomy, human parts become even more significant - especially as we can imbue cells with significant immortal properties - to perpetuate organs or gametes in the same way that we often talk of DNA having vital characteristics. How ought we to regulate technologies within this economy? I have here raised some issues that will become challenging in designing an ethical market outside of current conventions. Principally, societies may have to rethink commodification - the precise terms on which it might be ethical - and how this might be developed within legal and social structures. We already know that a BioEconomy exists: Moore's doctors knew for well that his cancerous cells were potentially valuable and could not have produced them without his unbeknownst participation;[77] and health tourism is variously covered by regional oversight of the procurement of clinical services. We ought to work out if, and how IPSCs may become embedded - and certainly ask questions of current practice: stem cell tourism seems to fall into a cynical exploitation of sometimes desperate patients; property rights are skewed to industry interests; and it is not necessarily unjustifiable (at least in terms of exploitation) to create a regulated market in *ex vivo* organs.

77. Although Golde denied misleading Moore about his intentions, the Court found that it was factious that he was unmotivated - otherwise why would he have taken the cells? (See: Golde, D. 1991. Commercial Development of Human Cell Lines: Property, Ethics and Conflicts of Interest. *New England Journal of Medicine* 324: 1745-1746; *Moore,* op. cit. note 46, p. 133).

There is, of course, a great deal more to be said about the BioEconomy; how market ideals - such as 'real value', for instance - will be transferred to biological artefacts, or how a greater patient involvement will challenge patent monopolies (sharing the benefits?); how access will be determined in terms of equity and justice (and the sometimes incompatible aspects of ethical justice and economic ideals); and how societies can frame the 'right' regulatory environment, which will incorporate economic processes with social ideas of public goods and legal ideas of contract. Yet, as I have indicated today, if we are serious about creating ideal structures of 'good governance',[78] it would be negligent to risk such developments coming to fruition without proper ethical, legal and social evaluation.

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