Openness, the UK Stem Cell Bank and the delivery of cell therapies: conceptual foundations for facilitation

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INTRODUCTION

This paper is based on my doctoral research on openness and the role of the UK Stem Cell Bank (UKSCB, or Bank) in the delivery of stem cell-based therapies for use in regenerative medicine. Stem cell science and technology hit the news in 1998, when scientists discovered how to isolate human embryonic stem cells (hESCs) from early human blastocysts, giving them access to cells characterised by 'pluripotency', the capacity to generate any tissue type in the human body. Fourteen years on, the first two hESC-based therapies - for treatment of spinal cord injury and macular degeneration – are now undergoing clinical trials. Significant hurdles have, however, yet to be overcome, posing the question as to how policymakers are to approach governance of the use of human stem cell lines to facilitate the goals of regenerative medicine in the face of complexity, uncertainty and controversy. The Bank was established as a vehicle for ethical oversight of hESCs derived from donated embryos, and secondarily makes ethically sourced and quality-controlled cells widely available to qualified researchers. It is highly regarded for its expertise in biological standards and control, and provides international guidance for good practice in the banking and use of stem cell lines. What is at issue is the role of the Bank in the commercialisation and delivery of cell-based products, in conjunction with research.

In this paper I formulate preliminary questions as an analytical framework for policymakers interested in the development of facilitative strategies aimed at the delivery of public goods. I start from the premise that the policy goal is not merely the advancement of knowledge, but the delivery of cell-based therapeutic products for clinical use or 'improvements in public health',[2] a daunting proposition given that such 'a public good is not a single good, but an *effect* with complex antecedents made up of a set of complementary goods (private and public) and different types of social actors'.[3] My second premise is that the means to the end is modern 'scientific technology', through which science and technology, in synergy with one another, are capable of outcomes that neither is able to produce on its own. I consider that 'scientific technology' requires facilitation as a whole system rather than as a set of isolated components, necessitating an integrated conceptual framework that encompasses public and private sector involvement, scientific and technical research, commercial development and industrial production. My framework is based on an integrative concept of 'innovation' that occurs throughout the enterprise, and a reconceptualisation of 'openness' that envisions enhancement of accessibility and 'communicability' of resources across all user domains and property regimes. I

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[2] UK Stem Cell Bank, Research Use Licence, annexed to the Code of Practice for the Use of Human Stem Cell Lines, s. 2.17.

[3] Drahos P, 'The Regulation of Public Goods' 7:2 *Journal of International Economic Law* (2004) 321.

outline the technology in its UK context, and the salient features of the Bank before setting out my analytical framework.

THE PROMISE OF CELLS

Stem Cell Technology

Stem cells, which reside within many adult tissues, have unique properties: they are unspecialised as to tissue type, they have the capacity to proliferate in this state for long periods, and they are able to generate specialised cells and tissues through a process of differentiation. Embryonic derivation, enabling scientists to isolate and manipulate pluripotent cells, creates the potential for cultivation of most cell types in the human body and treatment of a wide range of diseases and conditions including Alzheimer's, Duchenne's muscular dystrophy, stroke, heart disease, diabetes, and arthritis. With the capacity of hESCs to replicate indefinitely, and reliable methods for directing cell differentiation, there is potential for scalable manufacturing of therapies for repair or replacement of tissues impaired by damage or disease.[4]

The fact that the embryo does not survive the disaggregation of the blastocyst is a source of irresolvable social debate, despite the fact that embryos used in UK research are donated with informed consent, are surplus to the needs of the donor in relation to the fertility treatment for which they were created, and would otherwise have been permitted to perish. The induction of embryo-like pluripotency in adult or 'somatic' cells does not entirely address the ethical problem for, although they instil greater social confidence than their embryonic counterparts, induced pluripotent stem (iPS) cells are capable of generating germ cells and thus embryos as a further source of stem cells.

Pluripotent stem cells are capable of significant contribution in three main areas of work: cell differentiation, the testing of new drugs, and the creation of cell-based therapies. Research into the role of molecular and genetic signals that regulate cell division and specialisation facilitates greater understanding of human development and the invention of techniques for direction of the process. Ability to cultivate differentiated cell populations will expand the number of tissue types available for use in toxicity screening of new drugs. Thirdly, stem cells can provide basic materials for use in therapies that may alleviate the demand for donation of transplantable organs and tissues and expand the arena of treatable conditions. To achieve these ends, scientists must be able to manipulate cells to ensure that they differentiate into the desired cell type, survive transplantation without rejection, integrate into surrounding tissue, and function appropriately without harming the recipient.

Regenerative Medicine

Research is closely aligned with the practice of regenerative medicine (RM), which emphasises the use of whole human cells, as distinct from small chemicals, larger biological molecules or medical devices. The therapeutic use of cells began over 50 years ago with transplantation of bone marrow and haematopoietic (blood) stem cells,

[4] For a useful stem cell science primer, see US National Institutes of Health and US Department of Health and Human Services, 'Stem Cell Basics' in *Stem Cell Information*, available at http://stemcells.nih.gov/info/basics/, accessed 8 August 2012.

but its scope has expanded dramatically with advances in 'classic tissue engineering' of skin, bone and cartilage[5] and tools for cultivation of hESCs. The objective of RM is the replacement, regeneration[6] and possibly repair[7] of human cells, tissues and organs by provision of cells - particularly cells that can stimulate wider regeneration - to restore or establish normal function.[8] Pluripotent cells can be used as 'pure' therapies, but RM generally delivers cells in conjunction with other technologies, including stem and progenitor cell therapy, tissue engineering, materials science and genetics. It may also use non-cellular materials such as soluble molecules and gene therapy as vehicles for transference of therapeutic material to patients.[9] It is the combination of technical approaches, often stimulating and supporting the self-healing capacity of the body, that takes it beyond traditional transplantation and replacement therapies.[10]

The first two therapies incorporating embryonic stem cells for human application are now in Phase I clinical trials. Geron trials started in 2010, in relation to a hESC-based treatment containing oligodendrocyte (nerve) progenitor cells (OPC), have indicated no serious adverse events in four patients with complete thoracic spinal cord injuries.[11] Advanced Cell Technology Inc (ACT) initiated trials in 2011 to establish the safety and tolerability of transplantation of hESC-derived retinal pigment epithelial (RPE) cells in two patients with macular degeneration - the leading cause of blindness in the developed world;[12] in January 2012, cells had reportedly attached and continued to persist without hyperproliferation or abnormal growth.

Cell Therapy Industry

Stem cell technology and RM have not developed in a commercial vacuum, but in conjunction with the cell therapy or 'CT-RM' industry that began in the 1990s with the establishment of firms developing blood therapies, diabetes treatments and first generation tissue engineering. After initial disappointment,[13] there was a shift in 2002-2006[14] toward second generation stem cell-based RM, new disease targets and a new focus on translation, resulting in growth in sales, numbers of patients treated,

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[5] Martin P, R Hawksley and A Turner, *The Commercial Development of Cell Therapy – Lessons for the Future, Survey of the Cell Therapy Industry and the Main Products in Use and Development, Part 1: Summary of findings*, EPSRC Grand Challenge, remedi, Institute for Science and Society, University of Nottingham (2009), 8.

[6] Daar AS and HL Greenwood, in 'A proposed definition of regenerative medicine', 1 *Journal of Tissue Engineering and Regenerative Medicine* (2007) 179, 181, define RM on the basis of points of consensus identified by comparison of a number of definitions.

[7] Mason C and P Dunnill, in 'A brief definition of regenerative medicine', 3:1 *Regenerative Medicine* (2008) 1, 4, exclude 'repair', as it is classically considered to involve synthesis of scar tissue instead of regeneration of normal tissue and restoration of normal structure and function, whereas Daar and Greenwood consider that cell regeneration may be the vehicle for repair.

[8] *Ibid.*

[9] Daar AS and HL Greenwood, *supra* note 6, 181.

[10] *Ibid.*

[11] Presentation of Geron to the Pre-Conference Symposia of the joint 2011 American Congress of Rehabilitation Medicine and American Society of Neuro-Rehabilitation Annual Meeting.

[12] Schwartz SD, J-P Hubschman, G Heilwell, V Franco-Cardenas, CK Pan, RM Ostrick, E Mickunas, R Gay, I Klimanskaya, R Lanza, 'Embryonic stem cell trials for macular degeneration: a preliminary report', *Lancet,* (January 2012), 713.

[13] Lysaght MJ and AL Hazlehurst, 'Tissue engineering the end of the beginning' 10:1/2 *Tissue Engineering* (2004) 309.

[14] Martin P, R Hawksley and A Turner, *supra* note 5, 9.

products in development and staff employed.[15] The industry is now capable of producing a wide variety of cell-based applications[16] including permanent cell-replacement therapies, immuno-modulation cell therapies, transient cell therapies that disrupt the natural progression of diseases, 'organoids' and 'primordia'. Despite advances, however the industry is still encountering challenges to commercial viability and corporate investment.[17] The difficulty in establishing an evidence base for clinical utility, lack of clinical uptake and poor sales creates a significant risk of market failure for most stem cell-based therapies. Effective therapeutic production requires closer collaboration with clinical end-users, funding for clinical studies, more regulatory certainty, clearer reimbursement policies and reduction of costs through development of 'enabling' technologies.[18]

GOVERNANCE

Legislative Regimes

The highly complex[19] UK regulatory system governing stem cell research and manufacture is based on three main legislative regimes, each administered by a statutory authority, which together implement the European Directives in relation to tissues and cells[20] and medicinal products for human use.[21] The Human Fertilisation and Embryology Authority (HFEA) governs the use of reproductive tissue in fertility treatment and embryo research; the Human Tissue Authority (HTA) regulates quality and safety in the handling of 'other' human tissue, including cell lines intended for human application;[22] and the Medicines and Healthcare products Regulatory Agency (MHRA) governs pre-market authorisation of medicines and healthcare products. Although a restructuring of the tri-partite system is presently on the political agenda, the new policy is likely to collapse the functionaries themselves (including the HFEA in its present form) without dispensing with the functions of these bodies, so that the regulatory landscape will not necessarily be significantly altered.

At the intersection of these regimes are human stem cell products for clinical use. All activities related to research involving human embryos including the derivation of human embryonic stem cell lines, are licensed and monitored by the HFEA. Embryos donated or created for stem cell research remain under the remit of the HFEA until the point at which the blastocyst is disaggregated and stem cells harvested. Thereafter, the process of cell line purification and tissue differentiation is governed by the HTA. Once 'master banks' of cells are established and have a reasonable expectation of

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[15] *Ibid*, 10.
[16] Mason C and E Manzotti, 'Regen: the industry responsible for cell-based therapies' 4:6 *Regenerative Medicine* (2009) 783.
[17] *Ibid.*
[18] *Ibid.*
[19] As illustrated by the *Interim UK Regulatory Route Map for Stem Cell Research & Manufacture* published on the MRC website in March of 2009; available at http://www.mhra.gov.uk/Howweregulate/Medicines/Medicinesregulatorynews/CON041337, accessed 13 August 2012.
[20] Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.
[21] Directive 2001/83/EC of the European Parliament and of the Council of the 6 November 2001 on the Community code relating to medicinal products for human use.
[22] The Human Tissue (Quality and Safety for Human Application) Regulations 2007 No 1523.

clinical utility, they may be classified by the MHRA either as an Investigational Medicinal Product (IMP or 'medicinal product'),[23] which requires compliance with MHRA pre-market criteria for manufacture, clinical trials and approval, or an Advanced Therapy Medicinal Product (ATMP)[24] which is subject to a centralised procedure for marketing authorisation conducted by the European Medicines Agency (EMA).[25] The ATMP classification is a recent development that accommodates innovative therapies, including cells that have been substantially manipulated by a manufacturing process, that typically fall somewhere between UK medicinal products and devices. Absence of the requisite degree of manipulation implies that applications such as cell or tissue grafts are not 'products' and remain within the scope of the *Human Tissue (Quality and Safety for Human Application) Regulations* 2007.

Stem Cell Steering Committee

The Steering Committee for the Stem Cell Bank and for the Use of Stem Cell Lines (Steering Committee) is appointed by the UK Medical Research Council (MRC) to ensure governance of the use of all human stem cell lines in the UK, including but not limited to the activities of the UKSCB. Its primary objective is provision of ethical oversight of the use of human embryonic stem cell lines, to ensure the promotion of public confidence in the conduct of embryo research. Through its continually evolving Code of Practice for the Use of Human Stem Cell Lines (Code),[26] the Steering Committee provides best practice guidance for those working with human stem cell lines, establishes mechanisms for specific oversight of hESC research, and defines requirements for the activities of the UKSCB.[27] The Code applies specifically to research involving established hESCs, because they result in the destruction of human embryos,[28] while pluripotent lines of other derivation, though also subject to ethical considerations, fall outside the Code.[29] The Code nevertheless refers to non-embryonic stem cell lines because the UKSCB will curate and distribute cell lines from all sources.[30]

The oversight regime of the Steering Committee is implemented through the Code, the custodianship of the Bank, and the terms of the MTAs, which require depositors and users to obtain its approval at each step in the process of banking, transfer and use of cell lines. Such controls, although not designed to impose commercial constraints, do have implications for commercial aspects of deposit and ongoing use.

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[23] EU Directive 2001/83/EC, Article 1, as amended.

[24] See http://www.ema.europa.eu/ema/index.jsp?curl=/pages/home/Home_Page.jsp&jsenabled=true, accessed 22 February 2012. See definition of ATMP in Article 2 of EC Regulation No 1394/2007 of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004.

[25] The EMEA was established by Regulation (EC) 726/2004 of the European Parliament and of the Council of 31 March 2004. The European authorisation procedure involves a single scientific evaluation of quality, safety and efficacy that will be conducted by a specialised Committee for Advanced Therapies, reporting to the Agency's Committee for Medicinal Products for Human Use.

[26] HL Select Committee on Stem Cell Research, Report, 2002, para 6.1.

[27] UKSCB Code of Practice for the Use of Human Stem Cell Lines s. 1.

[28] *Ibid*, s. 2.3.

[29] *Ibid.*

[30] *Ibid*, s. 1.

UKSCB

The Bank was established on the recommendation of a 2002 House of Lords Select Committee on Stem Cell Research, to fill a legislative gap in regard to the handling of embryonic stem cell lines. At that time the statutory authority of the HFEA over embryo research did not extend to the stem cell lines themselves, and the law governing human tissue was fragmented and limited in scope. Even when the *Human Tissue Act* came into effect in 2004, consolidating existing legislation and establishing the Human Tissue Authority (HTA), it did not apply to human stem cell lines, as they are 'created outside the human body',[31] but only to material taken 'from a human body'.[32] Cells cultivated *in vitro* were not addressed until the remit of the HTA was amended by the *Human Tissue (Quality and Safety for Human Application) Regulations* 2007 to include activities ('procurement, testing, processing, distribution, import or export') related to tissue and cells intended for human application'.[33]

The banking condition, applied by the UK Human Fertilisation and Embryology Authority (HFEA) to every UK embryo research licence, initially mandated that the Bank take custody of the whole of any stem cell line derived thereunder, a requirement that was modified over time to enable cell developers to retain some portion of each hESC line, while depositing in the Bank a sample from which stocks can be cultivated for access by other researchers. The role of the UKSCB as custodian of hESCs enables the Steering Committee to vet potential users of cells held by the Bank, and impose on them, at the point of access, both ethical standards and legal obligations regarding use. The objective of requiring the sharing of stem cell lines was not to create common property in the banked cell lines, but to minimise the number of embryos used in research, itself a somewhat misleading notion, given the IVF practices from which the donated embryos originate.

The day to day operations of the Bank, managed by the National Institute for Biological Standards and Control (NIBSC), pertain largely to quality control. Its aims are to: work with scientific, clinical, commercial and regulatory communities to ensure the quality of human stem cell lines used in research and clinical therapy; to develop and disseminate best practice in the culture, testing, characterisation and preservation of stem cell lines; to bank or curate all hESCs in the UK; to establish, test and release well-characterised seed stocks of ethically-sourced stem cell lines within a stringent quality framework; to promote basic research through the provision of 'laboratory grade' cell banks; to promote clinical therapy through the provision of 'EUTCD grade' cell banks produced under EU good manufacturing practice (GMP) conditions; and to provide products and services to aid translational research in regenerative medicine.[34]

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[31] Human Tissue Act 2004, s. 54(7).

[32] *Ibid.*

[33] Human Tissue (Quality and Safety for Human Application) Regulations 2007, s. 7(3).

[34] Hunt C, *Voluntary Regulation of Embryonic Stem Cell Research: The Role of the UK Stem Cell Bank in the UK Governance Structure*, unpublished paper presented at Conference of the AHRC-SCRIPT Centre for Research in Intellectual Property and Technology Law, University of Edinburgh, School of Law, June 2012.

Materials Transfer Agreements

The MTAs[35] impose contractual obligations that shape the organisation of the Bank. The Steering Committee defines two main banking routes: one for laboratory or research grade stem cell lines, and one for clinical grade hESC lines that meet the requirements of the EU Tissues and Cells Directives (EUCTD), as implemented by the HTA, for human application.

Laboratory grade cell lines

The laboratory grade route, which applies to cells derived in the UK or overseas, requires a standard Materials Deposit Agreement (MDA) between depositor and Bank and, upon dissemination, a standard Research Use Licence (RUL) between depositor, Bank and potential user. The RUL restricts the user to research uses of the banked material, but - in the event of an unanticipated opportunity for commercial use - the user may, with the approval of the Steering Committee enter into a private Commercial Use Licence (CUL) with the depositor. The RUL constitutes the grant from depositor to user of a non-exclusive royalty-free licence to use the banked material[36] in 'laboratory-based, non-commercial *in vitro* preclinical' research pre-approved by the Steering Committee.[37] It does not define 'commercial' or 'non-commercial' use, but the user agrees that it provides no right or licence to sell or make other commercial use of the banked materials or any derivative materials or products made from them.[38] The depositor retains intellectual property rights in the banked material;[39] the user owns any intellectual property arising from use of the cells obtained from the Bank, but agrees to grant a non-exclusive royalty-free licence (without right to sublicence) back to the depositor and NIBSC to use any intellectual property or results or discoveries or inventions or derivative materials, whether patentable or not.[40] The user also agrees to obtain the prior permission of the depositor regarding any publication reporting on the research, such permission not to be unreasonably withheld or delayed.[41]

EUTCD grade cell lines

The EUTCD grade route applies to hESCs derived within the UK, and is more complex, as it entails a UKSCB due diligence process that is not currently spelled out in the Code of Practice. Upon application to deposit, along with a standard Materials Deposit and Distribution Agreement (EUCTA-MDDA) between it and the Bank, the depositor must supply a Quality Agreement (QuA) assuring that the cell line meets EUTCD requirements as implemented by the HTA, as well as a Due Diligence Initial Assessment Form (DDIAF) upon which the UKSCB carries out a panel review of EUTCD compliance prior to recommendation of acceptance of the cell line as EUTCD grade. Upon dissemination of the cell line the potential user will enter into a standard Material Access Agreement (EUTCD-MAA) with the Bank as well as a

[35] Current versions of the standard MTAs are available on the UKSCB website: http://www.ukstemcellbank.org.uk/ accessed on 27 August 2012.
[36] UKSCB, Research Use Licence s. 2.5.
[37] *Ibid*, s. 1.1(o).
[38] *Ibid*, s. 2.10.
[39] *Ibid,* s. 3.2.
[40] *Ibid,* s. 3.3.
[41] *Ibid*, s. 4.4.

separate private Materials Use Licence (MUL) or CUL with the depositor, for research, clinical or commercial use, depending on the type of use anticipated for the cell line.

The EUTCD-MAA specifies that clinical grade cells obtained from the Bank are to be used strictly for a project or 'programme of work' approved by the Steering Committee, with express prohibition of attempts to identify the donor (of the embryonic source) of the hESC cells,[42] and of reproductive cloning.[43] If the banked material is intended to be used in a clinical trial or work leading to a therapy, the user must ensure its traceability, and instigate procedures for potential notification to NIBSC of any serious adverse event or any reaction during clinical application that may be linked to the quality or safety of tissues or cells. The EUTCD-MAA prohibits the transfer of banked materials to third parties without Steering Committee approval, and grants no right or licence to make clinical or commercial use of the banked materials. Any such licence, to be negotiated directly between depositor and user, should define intellectual property rights, is to be annexed to the EUTCD-MAA. The Bank disclaims any liability for the merchantability or fitness of the banked material for any particular purpose of the user, declines to warrant that it is free from contaminants, and cautions the user to satisfy itself that it is not hazardous or infectious.

Property rights

Under these arrangements, personal and intellectual property in the cell 'line' in the custody of the Bank ostensibly remains with the depositor, although the HFEA mandate prevents the withdrawal of hESCs once deposited. Property in banked material and any progeny arguably passes to the user, which can be used to cultivate a master stock of undifferentiated cells to ensure a perpetual supply. The MTAs do not address personal property rights in the tangible materials, but focus on allocation of intellectual property created by the user during the course of research involving the banked material and its derivatives.

So, although the Bank accepts custody of cells on something like terms of bailment, no common ownership is established in the group of depositors and users such as would constitute a 'common pool resource' or 'controlled commons' for governance of resources held in common.[44] Presently the creation of cell lines is largely publicly funded but private cell developers may find it difficult to deposit a part of each cell line, which constitutes a significant financial investment, regardless of the foreseeability of its commercial or clinical potential. Deposition of any portion of a particular line (defined by its genome) for access by others denies the depositor 'exclusive' control of the line, which is problematic for cell developers and investors concerned about reputational damage due to unreliable practices or results arising from the work of other researchers. These developers would prefer something other than a 'one-size fits all' system in the Bank, to permit them to retain and control certain specified lines, and deposit others. There is now provision for a limited (two

[42] UKSCB Materials Access Agreement for Human Embryonic EUTCD Stem Cell Lines (EUTCD-MAA) s. 2.6.
[43] *Ibid*, s. 2.3.
[44] Ostrom E, *Governing the Commons: The Evolution of Institutions for Collective Action*, Cambridge University Press, (1990), Cambridge, xi.

year) embargo on the release of a cell line from the Bank, giving the depositor a small window of exclusive control.

SCIENTIFIC TECHNOLOGY

Integration

Given this set of circumstances and the relationship between science, technology and industry, what is an appropriate policy approach to facilitation of delivery of stem cell therapies? So far, ethical and legal issues related to the use of cells of embryonic origin have been much debated, and the promotion of research has been strongly advocated, but the discourse around industrial and commercial aspects of development and production of therapies is more limited.

My proposition is that the facilitation discourse is inhibited by the use of traditional conceptual frameworks that emphasise distinctions between science and technology, and more recently 'research and development', and fail to consider scientific technology as a whole system. Certain key concepts used to frame the dialogue are unclear or caricatured in a particular way that predisposes us to entrenched and fragmented approaches, and prevent the integrative thinking necessary for promotion of the enterprise in ways that harness the full potential of both science and technology. The distinction between public and private, for example, is deeply inscribed in the conventional narratives of science and technology. In the open science model, openness is associated with the production of knowledge through *publication* and *commonality of property*, reinforced by social norms and moral imperatives that communicate that 'sharing is good'. The enterprise of technology in a free market environment, by contrast, is characterised by utilitarian objectives aligned with *exclusivity* of property and the *private* pursuit of profit and wealth creation, and tarred with negative connotations of 'exploitation'. The traditional dichotomy between 'public' and 'private', and conceptions of 'property', 'innovation', 'exploitation' and 'human enterprise' reinforce a dichotomised rather than integrated view of science and technology. Conceived in this way, there is a dilemma as to how to facilitate both open science and closed technology, which flourish in potentially conflicting conditions. Since the market is self-sustaining and science is a public good, facilitation is typically concerned with the protection of science rather than the promotion of the enterprise of scientific technology as a whole.

These separate narratives of science and technology have persisted despite changes that have eroded the boundaries between them. Science and technology have always had potential to inform one another, through the technological use of scientific knowledge, and the inspiration of new avenues of scientific enquiry that arise from technical advances. In fields of study (including medicine) that fall within 'Pasteur's quadrant'[45] however, the interconnections between them have become markedly increased and strengthened as a result of closer institutional arrangements and rapid and sophisticated technical advances. The nature of the amalgamation of science and technology is debatable: some suggest that it is a complete fusion or merger; my view is that it is an intense synergy - dependent upon the distinctive orientations and

[45] Stokes DE, *Pasteur's Quadrant: Basic Science and Technological Innovation* (1997) Brookings Institution Press, Washington DC, 19.

objectives of science and technology for unique contributions of knowledge and practical utility.

In addition to technical advances, research funding increasingly comes from private as well as public sources and activities in the conduct of science and technology are less compartmentalised: academic scientists develop technical tools to facilitate their enquiries, and firms employ in-house scientists to advance their technical interests. Patent law has also seen a reduction in the gap between invention and discovery, permitting patentability of discoveries associated with a patentable technique or method of isolation. Universities and public institutes encourage early patenting of academic work, implying that scientists now compete for patents and economic results as well as scientific priority.

This evolution toward a deeper synthesis of science and technology poses a threat to the tradition of open science that is not felt by technology. Scientists are concerned about the subordination of 'pure' science to the utilitarian goals of both private enterprise and policymakers who favour practical benefits and economic growth, fearing the ultimate impoverishment of science as a result of non-disclosure of research findings. There is also a less well-articulated suggestion that not only will the scientific ethic of sharing be lost, but it will be replaced by a corrupted ethic of capitalism that will taint social policies that enable private production of otherwise welcome public goods. Technology on the other hand anticipates few adverse effects from its closer association with science. Increased embeddedness of science, which has always augmented and strengthened technology, renders science a more integral and elemental component of the technology, thus creating new and potentially stronger platforms for innovation and production.

What is clear is that support for the pursuit of the benefits promised by scientific technology is not going to go away. Public and private entities continue to pursue utilitarian goals, embedding use-inspired science in technological and economic agendas, thus challenging the scope or meaning of 'pure' science in the modern context. 'Pure' science and 'technical' science are not however mutually exclusive options: they can co-exist, and there are strong arguments in favour of support for avenues of pure curiosity-inspired research driven by a solely scientific agenda, the results of which are widely communicated, thus promoting the greatest possible knowledge base for the pursuit of scientific and technical innovation in future generations.[46] Allocation of resources to this end is however an issue for both public and private sectors: the dedication of public funds to 'blue skies' research without visible return is politically difficult, as it poses an opportunity cost to the pursuit of more immediately foreseeable social benefits; similarly, the private sector is, for economic reasons, unlikely to be willing or able to sustain long term investment in research that has no immediate bearing on its practical objectives.

As a result, 'scientific technology' is becoming the predominant *modus operandi* and the battle to protect science as an 'open enterprise'[47] is being fought largely within it rather than on separate terrain. Attempts to defend science in a potentially threatening situation reaffirm and promote the features that have traditionally defined and

[46] *Ibid*, 99-102.
[47] The Royal Society UK, *Science as an Open Enterprise*, Science Policy Centre Report (June 2012).

distinguished it from technology. Initiatives designed to facilitate sharing of knowledge and resources in support of research essentially try to recapture the intellectual norms of open science in the absence of its original institutional and social organisation; they may for example invoke 'hybrid' mechanisms that involve a commons or semi-commons that is grounded in a legal property regime, limited by proprietary interests, or linked to a downstream commercial market. Such attempts to reinstate or bolster scientific norms are unable to fully recreate the culture of the 'Republic of Science'[48] that was held together by social incentives, rewards and values in a non-market environment; instead they instate pockets of disclosure within an enterprise that is essentially technological in its orientation toward utility and the production of private goods within a market economy. These pools of openness, if effectively designed, may be accommodated to serve specific purposes, but do not embrace the notion of science as an integral part of a technical system of production in a market environment driven by a capitalist ethic. To what extent does facilitation of scientific technology depend upon the public domain or a commons approach to accessibility of resources? How do efforts to use such means of facilitation affect the productivity of scientific technology? Does the long term sustainability of innovation and exploitation in modern scientific technology depend upon them?

My thesis is that scientific technology is a dynamic complex of scientific and technical innovation and commercial exploitation, facilitated by networks of private commercial transactions that enable accessibility of resources and dissemination of outcomes appropriate to its objectives. If science is focused and directed in this context toward a select group rather than an expansive domain of users, it is in order to harness the extraordinary propensity of capitalism for self-generated change[49] and to generate public goods that could not be produced by pure science alone, or by technology in the absence of science.

Innovation

My conceptualisation of 'scientific technology' is based on a notion of innovation that is integral to science and technology. I understand innovation to be a cognitive event - a new idea - which in traditional narratives of science gives rise to a body of original knowledge and in technology results in the development of novel products. The industrial literature refers to innovation as the new product or method that embodies utility, or the whole process of technical development and realisation of the product, rather than the mental process behind its invention or modification. Scientific innovation is traditionally construed as discovery because its methods identify natural 'facts' not previously observed, without having to demonstrate any utility for such understanding. These seemingly different concepts of innovation share a common foundation in scientific and technical research,[50] which facilitates interaction with intellectual elements or resources including data, information and existing knowledge. The elements can be conceived of as pieces of a jigsaw puzzle, or 'pixels' of illumination of a digital image that can be rearranged or reconfigured in relation to

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[48] Polanyi M, 'The Republic of Science: its political and economic theory', Chap 17, in Mirowski P and E-M Sent (eds), *Science: Bought and Sold*, (2002) Chicago and London, U of Chicago Press, 465.

[49] Heilbroner R, *Twenty-first Century Capitalism*, (1992) Canadian Broadcasting Corporation, CBC Massey Lectures Series, House of Anansi Press Limited, Ontario, 25.

[50] For a categorisation of types of research, see Cooksey D, *A review of UK health research funding*, HMS Treasury, 2006.

one another until a new image is recognisable. Material resources are tools of research, a further source of pieces of intellectual illumination. Although research is active and diligent work, and in the case of science employs well-defined methods, innovation is never entirely predictable: even with many compatible pieces and collaborative minds to interact with them, the identification of novel and meaningful outcomes cannot be taken for granted. Innovation necessarily involves uncertainty, which is a relevant consideration for public policymakers and funders as well as industrial strategists.

Innovation as the result of a creative cognitive process accords not only with the traditional model of science, but also with models of dynamic industrial innovation based on complex interactions between technical advances, firm organisation and the competitive marketplace. In industry, the pursuit of innovation is not limited to a particular 'upstream' phase of basic research, but pervades the whole technological enterprise, and its results vary from radical to incremental developments in products and processes, depending on an array of factors. Research, development and stabilisation of marketable products all involve degrees of innovation. My treatment of innovation does not correspond to 'invention', which in patent law is the tangible expression of the novel idea in a form that meets specified criteria for patentability. What or who constitutes the elements, the actors and the appropriate means of enabling accessibility and engagement with the elements of innovation depends upon the nature of the enquiry, and is a primary question in any approach to facilitation.

Exploitation

Scientific technology is distinguished from the tradition of open science by its capacity for exploitation, which is inextricably bound up with innovation and transforms cognitive innovation into tangible expressions or products. Various models of industrial technology attempt to explain how the synthesis of innovation and exploitation generates economic goods: it requires the reconciliation of conditions of uncertainty that are conducive to rapid innovation with those of exclusive control necessary for stabilisation of products and maximisation of productivity.[51] Stabilisation involves the consolidation of technical advances leading to reliability characterised by few 'stochastic events'[52] or 'surprises',[53] which recede as learning develops. The conundrum is that excessive stabilisation can threaten continual innovation by collapsing it into operations and commodification, which makes technology vulnerable to stagnation and to being superseded by competitors who continue to seek innovation despite ongoing uncertainty.

Exploitation serves an essential role in the realisation of benefit or addition of value, contradicting its negative construction as the taking of an unjust or unfair advantage, or a use that derides or depletes resources. Scientists for example 'exploit' existing knowledge in order to develop new ideas, theories and information; regenerative medicine 'exploits' the natural attributes of stem cells to combat debilitating diseases. In the production of economic goods, 'exploitation' consumes less valuable materials to produce more valuable outcomes. The advantage or benefit achieved by technical exploitation is an *economic* gain – whether production is profitable or not for profit.

[51] Utterback JM, *Mastering the Dynamics of Innovation* (1994) Harvard Business School Press, Boston USA, 80.
[52] Scranton P, 'Technology, Science and American Innovation', 2006, 48:3 *Business History*, 26.
[53] *Ibid.*

It is derived from 'utility' - the usefulness or practical value of a thing - which has economic value. In a commercial context, economic gain is measured by consumer demand and financial profit, but may otherwise be assessed by reference to the social or public value of goods and services in relation to the cost of the materials used in their production.

Exploitation in the context of scientific technology is driven by the demands of commercial markets, but like science, the social order of capitalism is supported by social values external to markets, which act as conduits for the energies of the system.[54] The drive for acquisition of capital that begets more capital, rather than the amassing of wealth *per se*, itself signifies a human desire for development and change beyond simply the prestige, power - and inequality - of wealth. An analysis of the market is not within the scope of this paper, but I raise it because at the root of capitalism is a desire for freedom of enterprise that although aimed at production of goods and profits is not very different from the desire for freedom of scientific enquiry and the production of knowledge. Although they operate through different systems and seek different outcomes, each has implications for a society that pursues every kind of self-improvement,[55] and each espouses public values, which are flouted to the detriment of the system.

Networks

Finally, I consider the means of facilitation of scientific technology - innovation and exploitation - for the delivery of science-based technical products. First, if the pursuit of innovation involves accessibility, engagement and interaction with resources, then vehicles for this purpose need not be limited to those that invoke the public domain or commons but can extend to means of promoting 'communicability' of resources across all user domains, economic systems and property regimes. Where release of exclusively held resources into the public domain or commons will inhibit operations and sustainable production, dissemination of technical knowledge and products may be achieved through private transactions, such as non-exclusive licensing of exclusive property rights. Neither openness nor exclusivity is an absolute good. Publication is only as public as the domain of users that it extends to, and as public interest limitations will allow; private commercial transactions, particularly in non-rival goods such as intellectual property (and perpetually replicating stem cells) may be individually exclusive, but permit dissemination of the same resources to multiple users. The comparative effectiveness of public and private modes of openness will depend on individual technologies in all of the circumstances. Private networks of 'modulated openness' that link resources with expertly qualified users, may contribute as much to the advance of a sophisticated technology, and the public good, as does publication of resources to a world of users, the vast majority of whom will neither access nor contribute to them. Facilitation of accessibility and interaction with technical resources can therefore be approached from either side: rooted either in publication, with limitations as to content or domain of users, or in private transactions that partially relinquish exclusively held property rights.

[54] Heilbroner R, *supra* note 49, 25.
[55] Polanyi M, *supra* note 48, 484.

QUESTIONS

I submit the following preliminary questions for use by policymakers or others interested in the facilitation of scientific technologies. The list is a work in progress, as is its specific application to stem cell technology.

Objectives

1. What is the nature of the technology?
2. What is the nature and purpose of the project or enterprise related to the technology? Is it aimed for example at regulation or governance, resource management, or the enhancement of research, innovation or production?
3. What is it intended to achieve? What are the anticipated outcomes, products or deliverables?
4. Who are the actors directing or facilitating it? Is the agenda driven by public policy, funding bodies, scientists, or industry?
5. Who is intended to benefit? To what extent are various 'publics' in society interested in the endeavour?

Resources

1. What are the intellectual 'elements' or resources that must be accessed and manipulated to enable innovation in the field? Knowledge resources, including datasets and information, for example?
2. What is the role of tangible materials in the technology and in the pursuit of innovation?
3. Consider the technical, legal, and economic properties of the elements or resources of innovation:
    a. How they are generated, created, or obtained?
    b. Where are they located?
    c. Who is in control of them?
    d. Are they subject to legal property rights? Intellectual property rights?
    e. What is the economic and/or scientific value of the resources in question?
    f. Do they have any foreseeable commercial potential?
    g. To what uses might they be put?
    h. To what extent are the resources rival economic goods?
    i. To what extent are they excludable economic goods?

Communicability

1. Who are the potential users of the technical resources? Who is capable of and/or interested in accessing and manipulating them?
2. For what purpose might potential users wish to access the resources?
3. Is it necessary to define the domain of users? What policy choices will naturally shape the domain?
4. What domain of users is most relevant, appropriate or useful? Why?
    a. 'Public domain'. What type of limitations might reduce its scope?
    b. Specific group. By what criteria, on what grounds, and by whom should the group be defined?
    c. Individuals. In what circumstances will it be necessary to specify users?
5. How important is the size of the domain of potential users? Is bigger necessarily better?

6. Are the resources available or accessible by potential users, with or without financial cost?
7. Assuming access, is it possible to engage the resources sufficiently to facilitate innovation?
8. What are the technical means of engaging with or manipulating the resources for pursuit of innovation?
9. What legal means, mechanisms or organisational structures might optimise the 'communicability' of resources, making them more available, accessible and engageable by users?
10. Does the means or mechanism invoke the public domain or commons?
    a. To what extent is it possible to share the resources in common?
    b. Is it feasible to apply controls to the free use of the common resource?
    c. What type of controls will permit greatest communicability/accessibility?
11. Does the means or mechanism default to private commercial transactions?
    a. To what extent is exclusivity of control necessary to the goals, methods, and anticipated outcomes?
    b. What type of legal rights will facilitate these ends? What is the nature of the property involved?
    c. At what point and in favour of whom might property be generated (or granted) in the resources?
    d. Is it feasible to impose limitations on such property rights? What are the implications of doing so?
    e. What type and means of restriction might be used to free up exclusively held resources to facilitate widest communicability?
12. What are the incentives or mandates for use of such means or mechanisms?
13. To what extent and in what way might use of the resources by one party affect their use by other parties?
14. What positive or negative impact does engagement of the resources have on commercial exploitation of the technology?

Society

1. What are the social and political circumstances surrounding the emergence or development of the technology?
2. What existing laws, regulatory regimes or institutional structures are relevant to the governance or management of the technology? How might they affect the adoption of new approaches?
3. To what extent is social confidence or controversy a consideration in the development of policy approaches to the technology?
4. Are there public policy reasons for:
    a. preventing access to the elements or resources of innovation?
    b. restricting the domain of users?
    c. monitoring ongoing use of the technology?
    d. imposing conditions on private property rights or regime?
    e. restricting use of common property?
    f. adoption, or refraining from adoption, of new regulatory regimes?
5. Who has the power to provide oversight or otherwise protect public interests in regard to the development and use of the technology?
6. What are the competing interests and how ought they to be prioritised?
7. By what means or mechanisms might protection of public interests be implemented?

CONCLUSIONS

The use of stem cells in regenerative medicine holds immense promise for treatment of serious diseases that will be realised through facilitation of the technology in all of its technical, economic and social circumstances. Based on the integrative feature of innovation, 'scientific technology' may be facilitated by enhancement of 'communicability' of knowledge and material resources through various means across all user domains and property regimes. Whether starting from a commons approach or private networks, mechanisms to enhance exchange and accessibility of resources may be designed to promote not only the opening of research, but product development and commercial exploitation for addition of value and delivery of public goods.

REFERENCES

Cooksey D, *A review of UK health research funding*, (2006) HMS Treasury, UK.

Daar AS and HL Greenwood, in 'A proposed definition of regenerative medicine', 1 *Journal of Tissue Engineering and Regenerative Medicine* (2007) 179.

Drahos P, 'The Regulation of Public Goods' 7:2 *Journal of International Economic Law* (2004) 321.

Heilbroner R, *Twenty-first Century Capitalism*, (1992) Canadian Broadcasting Corporation, CBC Massey Lectures Series, House of Anansi Press Limited, Ontario, 25.

Lysaght MJ and AL Hazlehurst, 'Tissue engineering the end of the beginning' 10:1/2 *Tissue Engineering* (2004) 309.

Martin P, R Hawksley and A Turner, *The Commercial Development of Cell Therapy – Lessons for the Future, Survey of the Cell Therapy Industry and the Main Products in Use and Development, Part 1: Summary of findings*, EPSRC Grand Challenge, remedi, Institute for Science and Society, University of Nottingham (2009) 8.

Mason C and P Dunnill, in 'A brief definition of regenerative medicine', 3:1 *Regenerative Medicine* (2008) 1.

Mason C and E Manzotti, 'Regen: the industry responsible for cell-based therapies' 4:6 *Regenerative Medicine* (2009) 783.

Ostrom E, *Governing the Commons: The Evolution of Institutions for Collective Action*, (1990) Cambridge University Press, Cambridge, xi.

Polanyi M, 'The Republic of Science: its political and economic theory', Chap 17, in Mirowski P and E-M Sent (eds), *Science: Bought and Sold*, (2002), U of Chicago Press, Chicago and London, 465-485.

Royal Society UK, *Science as an Open Enterprise*, Science Policy Centre Report, (June 2012) London.

Schwartz SD, J-P Hubschman, G Heilwell, V Franco-Cardenas, CK Pan, RM Ostrick, E Mickunas, R Gay, I Klimanskaya, R Lanza, 'Embryonic stem cell trials for macular degeneration: a preliminary report', *Lancet* (2012) 713.

Scranton P, 'Technology, Science and American Innovation', 48:3 *Business History*, (2006) 26.

Stokes DE, *Pasteur's Quadrant: Basic Science and Technological Innovation*, (1997) Brookings Institution Press Washington DC, 19.

Utterback JM, *Mastering the Dynamics of Innovation,* (1994) Harvard Business School Press, Boston USA, 80.