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DESCENDO A TOCA DO COELHO: TRANSFERÊNCIA DE TECNOLOGIA NO CAMPO DA PESQUISA EM CÉLULAS-TRONCO

DOWN THE RABBIT HOLE: TECHNOLOGY TRANSFER IN THE FIELD OF STEM CELL RESEARCH

Yann Joly; Clara Pham; Deborah Schorno; Bartha Maria Knoppers ***

RESUMO: Este artigo postula que os modelos colaborativos de transferência de tecnologia poderiam ser considerados por sua notável habilidade em manter ou aumentar o ritmo e a qualidade do desenvolvimento científico na pesquisa em célula tronco, ao invés de serem considerados por seu potencial em colocar problemas que empiricamente não existem. À luz destas limitações logísticas do campo científico e do seu presente estágio de desenvolvimento, o modelo aberto parece ser um método colaborativo particularmente adequável de gestão de tecnologia para a pesquisa em célula tronco.
PALAVRAS-CHAVE: células tronco; transferência de tecnologia; modelo aberto.

ABSTRACT: This article posits that collaborative models of technology transfer could be considered for their remarkable ability to maintain or increase the pace and quality of scientific development in stem cell research rather than for their potential to fix problems that do not empirically exist. In light of this scientific field's logistical constraints and its current stage of development, the open model appears to be a particularly suitable collaborative method of technology management for stem cell research.
KEYWORDS: stem cell; technology transfer; open model.

INTRODUCTION

Stem cell research is perceived by both academia and the media as a turning point in modern medicine. Indeed, the results of the research in this area are likely to have profound implications for our society. However, the successful transition of this important research from being of merely scientific interest to having concrete clinical

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utility will depend in large part on whether our current technology transfer methods are sufficiently responsive to the characteristics of this novel discipline. Of particular concern is that the use of both patents and restrictive material transfer agreements could unduly interfere with the transfer of foundational stem cells technologies and cause them to be lost down the proverbial rabbit hole. Although supported by little empirical data thus far, this intuitive feeling is very present within the scientific community and has led many to criticize the current technology transfer process and its unsuitability for this new and potentially groundbreaking field. It is thus necessary that we consider the alternatives.

The therapeutic potential of stem cell research along with the vast sums of money invested in this area justify that we pay special attention to the transfer of stem cell research such that these innovations may be translated into clinically beneficial treatments as quickly and efficiently as possible. With this objective in mind, the following article explores the need for, and the benefits of, open science models, i.e. non-proprietary management modes, as suitable alternatives for the transfer of technology in human stem cell research. To do so, the authors will begin with a brief overview of the promise of stem cell research and continue with an explanation of its relationship to systems of intellectual property protection. Then, the article will discuss the various attributes of open science models and assess their potential in the field of stem cell research. Our findings will be supported by the case studies. It will be seen that open models of technology transfer, although not appropriate substitutes for intellectual property rights in all circumstances, could provide interesting alternatives for, or complements to, standard property schemes at various stages in the technology transfer process.

1. THE SCIENTIFIC POTENTIAL OF STEM CELLS

A) The Scientific Potential of Stem Cells

Stem cells are cells that possess two identifiable properties: they are undifferentiated and renewable. An undifferentiated cell refers to a cell that can transform into a specialized cell type and a renewable cell is a cell that possesses the ability to multiply through cell division.[1] It is also precisely because of these two properties that stem cell research is being touted as an exciting new field of development that could shed new light on all aspects of medicine: [2]

> Stem cells have the remarkable potential to develop into many different cell types in the body. Serving as a sort of repair system for the body, they can theoretically divide without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell.[3]

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[1] Douglas C. Wu, Ashleigh S. Boyd & Kathryn J. Wood, *Embryonic Stem Cell Transplantation: Potential Applicability in Cell Replacement Therapy Regenerative Medicine,* 12 Frontiers in Bioscience, 4525-4535 (2007).

[2] The Steering Committee of the International Stem Cell Initiative, *The International Stem Cell Initiative: Toward Benchmarks for Human Embryonic Stem Cell Research,* 23(7) Nature Biotechnology, 796 (2005).

[3] National Institutes for Health, Stem Cell Basics, http://stemcells.nih.gov/info/basics/ (last visited November 30, 2007).

Stem cells are categorized according to the types of cells that they can engender.[4] Totipotent stem cells can differentiate into any type of cell and can therefore transform into any cell needed for the development of a living being. Totipotent stem cells are produced either by the fusion of a sperm cell and an egg cell or by the first few divisions of the fertilized egg. Pluripotent stem cells also retain the ability to differentiate into a number of specialized cells. What pluripotent stem cells cannot transform into however, are the cells necessary to the development of the placenta which is essential for gestation to occur. This type of stem cell is produced between the fifth and seventh days after the fertilization of the egg. Multipotent stem cells, although capable of further differentiation, are only capable transforming into specific types of tissues. For example, haematopoietic stem cells found in bone marrow and the umbilical cord can only engender white blood cells, red blood cells, and platelets.[5] Finally and in complete opposition to totipotent stem cells, unipotent stem cells can produce only one type of cell.[6]

For research purposes, stem cells must be removed or isolated from their tissue source.[7] To date, there are two methods that allow for the isolation of stem cells. First, multipotent and unipotent stem cells can be retrieved directly from born alive individuals. Indeed, whereas multipotent stem cells can be found, among others, in bone marrow, in the umbilical cord, and in the amniotic fluid, unipotent stem cells can be found in the epidermis. However, due to the relatively limited capacity of both these types of stem cells to differentiate, they are not as sought after as embryonic totipotent and pluripotent stem cells.[8] This leads us to a discussion of the other method of isolation that is concerned with *embryonic* stem cells.

Human embryonic stem cells (hESC) are isolated by the extraction of stem cells from an embryo. The embryos in question are often supernumerary embryos resulting from *in vitro* fertilization (IVF) procedures.[9] However,

[4] Comité consultatif national d'éthique pour les sciences de la vie et de la santé, Avis no. 93 Commercialisation des cellules souches humaines et autres lignées cellulaires 7 (Comité consultatif national d'éthique pour les sciences de la vie et de la santé 2006) (2006); Bernard Edward Tuch, *Stem Cells : A Clinical Update,* 35(9) Australian Family Physician, 719-721 (2006).

[5] Alison Murdoch, *Human Embryonic Stem Cells: An Introduction*, 5 Human Fertility, 203-205 (2002); National Institutes for Health, Highlights of Stem Cell Research, http://stemcells.nih.gov/research/scilit/highlights/DefaultPage.html (last visited November 30, 2007). It should also be noted that recent developments have touted amniotic fluid-derived stem cells as being multipotent stem cells. However, these findings have yet to be widely confirmed by the scientific community.

[6] Comité consultatif national d'éthique pour les sciences de la vie et de la santé, *supra* note 4, at 8. For instance, this is the case of keratinocyte cells that make up the skin. In other words, keratinocyte stem cells can only create other keratinocyte cells.

[7] National Institutes for Health, FAQs, http://stemcells.nih.gov/StemCells/Templates/StemCellContentPage.aspx?NRMODE=Published&NRNODEGUID=%7bA604DCCE-2E5F-4395-8954-FCE1C05BECED%7d&NRORIGINALURL=%2finfo%2ffaqs%2easp&NRCACHEHINT=NoModifyGuest#excited (last visited November 30, 2007).

[8] The President's Council on Bioethics, Monitoring Stem Cell Research 7-11, (The President's Council on Bioethics 2004) (2004).

[9] Russell Korobkin & Stephen Munzer, Stem Cell Research and Law 7-8, (UCLA Center for Society and Genetics, UCLA School of Law 2006) (2006); Alison Murdoch, *Human Embryonic Stem Cells: and Introduction,* 5 Human Fertility, 203-205 (2002).

embryos can also be created by somatic cell nuclear transfer (cloning). Cloning is a process whereby the nucleus of an adult cell is inserted into an enucleated oocyte to produce an embryo with DNA that matches that of the donor cell.[10] In any case, the state of science is such that, although there have been developments as to the possibility of obtaining pluripotent human stem cells using alternate procedures not involving embryos,[11] it does not currently seem possible to isolate hESC without also destroying the embryos in which they are found.[12] Indeed, stem cell technologies are still very much at a developmental stage.[13]

B) Ethical Issues Surrounding hESC Research

For all its promises, there are also some important ethical concerns raised by embryonic stem cell research.[14] Some argue that since the embryo's status is identical, or at a minimum very similar, to that of the living person, and given the fact that hESC research necessarily entails the destruction of these entities, then such research ought not to occur. Thus, some hESC research opponents insist that the destruction of these embryos is equivalent to the destruction of human life because life begins when an egg and a sperm unite.[15] However, a popular counter-argument points out that, in situations where stem cells are extracted from excess IVF embryos, were it not for hESC research, these embryos would ultimately be wasted: as these embryos would no longer be needed for purposes of assisted procreation, there would not be any other use for them other than disposal. In this case, it is argued that hESC research is a better alternative for the use of IVF embryos as compared to disposal.[16] Should the alternate

[10] The President's Council on Bioethics, Human Cloning and Human Dignity: An Ethical Inquiry xxv, (The President's Council on Bioethics 2002) (2002).

[11] For example: Kazutoshi Takahashi, Koji Tanabe, Mari Ohnuki, Megumi Narita, Tomoko Ichisaka, Kiichiro Tomoda & Shinya Yamanaka, *Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors*, 131 Cell, 861-872 (2007); Junying Yu, Maxim A. Vodyanik, Kim Smuga-Otto, Jessica Antosiewicz-Bourget, Jennifer L. Frane, Shulan Tian, Jeff Nie, Gudrun A. Jonsdottir, Victor Ruotti, Ron Stewart, Igor I. Slukvin, James A. Thomson, *Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells*, 318(5858) Science, 1917-1920 (2007); Karen Kaplan, *A Stem Cell 'Milestone'*, Los Angeles Times, November 21, 2007 *available at* http://www.latimes.com/news/nationworld/nation/la-sci-stemcells21nov21,0,2192969.story?coll=la-home-nation ; Gina Kolata, *Scientists Bypass Need for Embryo to Get Stem Cells*, The New York Times, November 21, 2007, *available at* http://www.nytimes.com/2007/11/21/science/21stem.html?_r=1&oref-slogin.

[12] The President's Council on Bioethics, *supra* note 8, at 7-11; Star Lopez, *The Children of Science: People, Property, or Something in Between?,* UCLA School of Law Research Paper No. 06-16, 37 (2006) *available at* http://ssrn.com/abstract=891840.

[13] Douglas C. Wu, Ashleigh S. Boyd & Kathryn J. Wood, *supra* note 1, at 4525-4535; Anita Nador & Tina Loucaides, Stem Cells: Patents and Related Legal Issues (Bereskin & Parr 2002) (2002). Some of the fundamental questions that still need to be answered relate to how to maintain stem cells in their undifferentiated states and how to control differentiation once they have been extracted and isolated.

[14] Rosario M. Isasi & Bartha M. Knoppers, *Mind the Gap: Policy Approaches to Embryonic Stem Cell and Cloning Research in 50 Countries,* 13 European Journal of Health Law, 9-26 (2006).

[15] Committee on the Biological and Biomedical Applications of Stem Cell Research, Stem Cells and the Future of Regenerative Medicine 44, (National Academy Press 2002) (2002); The President's Council on Bioethics, *supra* note 8.

[16] Anne McLaren, *Ethical and Social Considerations of Stem Cell Research*, 414 Nature, 129-131 (2001).

procedures that do not require embryos in order to obtain pluripotent stem cells become viable, then this particular ethical concern would recede.[17]

Other hESC research opponents are more specifically concerned with cloning in order to obtain hESC. In addition to the problem of destroying embryos, cloning raises issues such as the inherent discomfort with the idea of playing God, the physical and psychological safety of the cloned individual, and the "slippery slope" towards using cloning processes to create more humans.[18]

The abundance of literature demonstrates that these topics have been fiercely debated. However, whether one is in favour of or against stem cell research as it currently exists, it would seem that all stakeholders respect the great scientific potential stem cell studies have for human health.[19]

2. INTELLECTUAL PROPERTY RIGHTS AND STEM CELL RESEARCH

Human stem cell research, being a relatively new scientific field, the technologies concerned are often research tools, or building blocks for the development of clinically useful downstream products.[20] Due to the upstream nature of these technologies, the expression "transfer of technology" rather than the term "commercialization" will be used when referring to the transmission of knowledge and inventions in the field of stem cell research.[21] It is true that all scientific endeavours, whether upstream or downstream, could technically be "commercialized" given the fact that research, as a product of creative energies and monetary investments, is likely to add commercial value to the project in question.[22] However, in view of the general public's interest in the therapeutic potential of stem cell therapies, while commercial exploitation of upstream technologies can be an accessory goal, it is the sharing of this knowledge that should be the dominant objective due to the need to further develop this relatively new field of science.

A comprehensive evaluation of the impact of the intellectual property protection system on the field of medical research would, of course, be impossible due to the absence of consensus regarding the criteria that should be used for such an evaluation and also due to the current lack of empirical evidence. The more modest goals of this paper are to consider whether existing data confirms, or conversely, refutes the claim that intellectual property laws interfere with technology transfer in human

[17] Karen Kaplan, *supra* note 11.

[18] Russell Korobkin & Stephen Munzer, *supra* note 9, at 17-19.

[19] Melissa Little, Wayne Hall & Amy Orlandi, *Delivering on the Promise of Human Stem-Cell Research,* 7(10) European Molecular Biology Organization, 1188-1192 (2006).

[20] John P. Walsh, Ashish Arora & Wesley M. Cohen, *Research Tool Patenting and Licensing and Biomedical Innovation, in* Patents in the Knowledge-Based Economy, 285-287 (Wesley M. Cohen & Stephen A. Merrill eds., 2003) (2003); Stem Cell Network, *Business is Good*, 5(1) Stem Cell Network, 20 (2006).

[21] Matthew Herder, Open Sourcing Stem Cells in Canada, 6, (2005) (unpublished manuscript issued from two conferences (Canadian Bioethics Society Annual General Meeting and the Stem Cell Network Annual General Meeting).

[22] Comité consultatif national d'éthique pour les sciences de la vie et de la santé, *supra* note 4, at 5-6.

stem cell research and to assess whether open modes of technology transfer would be helpful and practicable complements or alternatives to the current system.

A) Intellectual Property and Stem Cell Research

Stem cell research tools can be protected via a variety of different legal vehicles like contract law, trade secrecy, a *sui generis* regime, copyright, or, as is most often the case, a patent. Copyright and patents are forms of intellectual property and can be used to protect stem cell products depending on the nature of the technology. Due to the nature of most stem cell technologies, patents are the most common form of protection currently used in this field.

Patent law is commonly justified by utilitarian principles: patent laws provide inventors with financial incentive to innovate, and thereby stimulate the development of industry for the benefit of all. In exchange for the public divulgation of their creations, patents give inventors exclusive rights, for a limited period of time, over the creation, use, and commercialization of their inventions[23] such that they may not only recoup the financial outlays made but also profit from them. By the same token, rather than having the invention shrouded in secrecy in order to protect the inventor's interests, patents allow society to reap the medical and scientific benefits of the openly disclosed innovation.[24] Therefore, the patenting of stem cell technologies is believed to be desirable because it balances the competing interests of the inventor (or more practically speaking, the entity providing financial support to the inventor and her research) and the public.

The development of stem cell technologies involves a significant amount of mental and financial commitment on the inventor's part:[25] among other tasks, she must run laboratories, manage clinical trials, and create stem-cell differentiation protocols.[26] As an illustration of the outlays that are required in the field of stem cell research, it took more than 20 years to successfully isolate the first hESC[27] and researchers are currently speculating that it could take up to 15 additional years before hESC can be used for transplantation purposes.[28] Moreover, the collecting of eggs for stem cell research purposes is extremely expensive. One article, commenting on the costs of doing diabetes related stem cell research, stipulated that :

> To treat, for example, the 17 million diabetes patients in the US will require a minimum of 850 million to 1.7 billion human eggs. Collecting 10 eggs per donor will require a minimum of 85 to 170 million women. The

[23] Yann Joly, *Open Source Approaches in Biotechnology: Utopia Revisited*, 59(2) Maine Law Review, 386-390 (2007).

[24] *Id.*

[25] David B. Resnik, *The Commercialization of Human Stem Cells: Ethical and Policy Issues*, 10(2) Health Care Analysis, 130 (2002); Shamnad Basheer, *Block Me Not: Are Patented Genes 'Essential Facilities'?,* 1 University of Illinois Journal of Law, Technology and Policy, 55 (2005).

[26] Sorapop Kiatpongsan, *Intellectual Property and Patent in Stem Cell Research Era*, 11 Journal of the Medical Association of Thailand, 1984 (2006).

[27] Vicki Brower, *Human ES Cells : Can You Build a Business Around Them?*, 17 Nature Biotechnology, 139-142 (1999).

[28] *Id.*

total cost would be astronomical, at $100,000 to $200,000 for 50 to 100 human eggs per each patient.[29]

Thus, given the therapeutic potential of stem cell research, but also the substantial amount of energy and financial investment required to develop these technologies, it is understandable that an inventor would want to have her inventions patented.

Yet, it is not only privately funded scientists seeking compensation for the time and money invested in their research that are looking to patent. Academics also have an incentive to patent under legislation such as the US *Bayh-Dole Act*, "which strongly [encourages] American universities to patent scientific discoveries made with public funds and partner with industry to commercialize them" in order to maximize medical and economic development.[30] Moreover, contrary to popular belief, academics are not necessarily more inclined to share information in the name of scientific progress; rather this idea must be tempered due to evidence of competitive behaviour, animosity, and greed in academia sometimes leading to increased secrecy and patenting in research.[31] Thus, both the private and public sectors have interests, however different they may be, in patenting stem cells and stem cells by-products.

[29] Robert Moffit, Kelly Hollowell, Phil Coelho & Honorable Dave Weldon, Federal Stem Cell Research: What Taxpayers Should Know (May 24, 2005), http://www.heritage.org/Research/HealthCare/wm749.cfm (last visited June 30, 2007).

[30] Herder, *supra* note 21, at 9; Merrill Goozner, Innovation in Biomedicine: Can Stem Cell Research Lead the Way to Affordability? (2006), http://onthecommons.org/node/837/ (last visited June 30, 2007).

[31] Joly, *supra* note 23

B) An Outlook on Contemporary Knowledge Transfer Practices

The patent system is rooted in contradiction: "the system aims to stimulate innovation by granting exclusive rights to the inventor who will then have the means to restrict the use and the perfecting of his invention by others"[32]. In other words, although the patents were intended to encourage the creation of knowledge for the benefit of the public, inventors can wield their exclusive rights and in practice prevent others from accessing their inventions by demanding high fees in exchange for the use of their inventions. Intellectual property rights, when enforced with too much zeal, can therefore slow the progress of science. Another connected reason for research delays is recent the proliferation of complex and invasive material transfer agreements (MTAs) among academic institutions and industry. MTAs are private contracts that govern the transfer of technologies, whether they are protected by intellectual property rights or not, for purposes of research or commercialization.[33] Interestingly, although these designed to encourage scientific advancement by facilitating collaboration, these agreements may in fact be hindering progress on two levels. First, as MTAs become increasingly more convoluted to accommodate the reality of complex intellectual property rights, the negotiations between parties grow correspondingly more

[32] *Id.*

[33] Victor Rodriguez, *Material Transfer Agreements: Open Science vs. Proprietary Claims*, 23(4) Nature Biotechnology, 489 (2005).

difficult. The negotiating process is in fact so difficult that, in a recent study, scientists reported abandoning the transfer project altogether, to the detriment of science. [34] What is also problematic is that when agreements are ultimately concluded, some MTAs contain such strict confidentiality and ownership provisions in favour of the provider, that even if valuable new information is created through research on the provided materials, it cannot be freely circulated.[35] Thus, similarly to the access to technology concerns that patents engender, MTAs can also prevent the timely advancement of research by restricting the flow of information.

Some fear that this access to technology problem is exacerbated in light of the current patenting tendencies and the nature of stem cell technologies. It is suggested that, up until the 1970s, biomedical research conducted in universities was fuelled for the purpose of scientific progress rather than with a profit oriented corporate objective. [36] But, in the 1970s, major scientific discoveries in the field of genetics as well as political pressures added a decidedly financial flavour to biomedical research. The biomedical industry had previously been limited in its range of saleable products due to the relatively undeveloped state of biomedical knowledge. However, the scientific breakthroughs of recombinant DNA and monoclonal antibodies effectively spurred the prospective for new, marketable drugs and technologies. This pecuniary incentive underlying biomedical, and biotechnological research more generally, strengthened the urge to patent scientific inventions in order to maximize their profitability and thereby create interest from the private sector.[37]

Moreover, in the landmark 1980 case, *Diamond v. Chakrabarty*, the US Supreme Court allowed a patent over a bacterium capable of breaking down crude oil. To support its ruling, the court quoted the 1952 *Patent Act* Committee Reports by affirming that "anything under the sun that is made by man" was patentable.[38] This case effectively vindicated the patentability of life forms including certain biotechnologies in the US. Then, in 1980, political pressures in the US provoked the enactment of the *Bayh-Dole Act* "which strongly encouraged American universities to patent scientific discoveries made with public funds and partner with industry to commercialize them".[39] These American legal developments were eventually adopted by the international scientific community such that the patenting of biotechnological inventions, assuming they meet standard patent criteria, is now perceived as both legally appropriate and desirable.

Taken together, these scientific, social, and legal developments have largely

[34] Alan Dove, *When Science Rides the MTA*, 110(4) The Journal of Clinical Investigation, 425-426 (2002).

[35] Rodriguez, *supra* note 33, at 489.

[36] Arti K. Rai, *Open and Collaborative Research: A New Model for Biomedicine*, *in* Intellectual Property Rights in Frontier Industries 131-140 (Robert W. Hahn ed., AEI-Brookings Press) (2005); Joly, *supra* note 23, at 392. However this altruistic portrait of academics must be nuanced by newly uncovered evidence of scientists actively preventing the open dissemination of their discoveries for a variety of reasons such as competition, animosity, and greed.

[37] Rai, *supra* note 36.

[38] 447 U.S. 303 (1980).

[39] Herder, *supra* note 21, at 9.

contributed to the current predilection for actively patenting biotechnological inventions, including stem cell technologies, instead of placing the knowledge in the public domain.

Access to technology concerns may be further aggravated due to the specific logistical set-up of the field of stem cell research. First, it should be noted that stem cell research, like many other scientific research fields, advances incrementally.[40] Secondly, since stem cell research mainly involves the development of foundational technologies into downstream ones, then relying on upstream inventions is necessary in order to create new knowledge in this research field. These two particular features of stem cell research (cumulativeness and newness) give the patent-related problem of access to technology additional levels of complexity.

The Tragedy of the Anticommons

In the field of biotechnological research, Heller and Eisenberg have argued that the "tragedy of the anticommons" is a possible threat to the advancement of this scientific sector. When upstream products and processes, as essential building blocks for downstream innovation, are patented, would-be inventors of downstream products must go through the potentially lengthy and expensive process of obtaining several different licences in order to progress in their research endeavours.[41] This process of obtaining the consent of several different rights holders may deter downstream inventors altogether thereby preventing the transfer of useful technologies and subsequently inhibiting useful development. However, despite these admonitions, several studies have shown that a situation of anticommons has not materialised in biotechnology as of yet because researchers have made use of "working solutions" such as "taking licences (i.e., successful contracting), inventing around patents, going off-shore, the development and use of public databases and research tools, court challenges and [infringement]" to progress in their research.[42]

More importantly, the field of stem cell research does not seem particularly susceptible to the anticommons threat. As it will soon be discussed, stem cells and stem cell by-products are currently protected by a few, broad patents rather than a number of

[40] Rai, *supra* note 36, at 137; Shamnad Basheer, *supra* note 25; Stem Cell Network, *supra* note 20. We must also consider that: "[over] the past twenty years, fundamental changes have revolutionized the science and technology underlying product and process innovation in drugs and the development of medical therapies and diagnostics. Advances in molecular biology have increased our understanding of the genetic bases and molecular pathways of diseases. Automated sequencing techniques and bioinformatics have greatly increased our ability to transform this understanding into patentable discoveries that can be used as targets for drugs development […] The consequences of these changes is that progress in biomedical research is now more cumulative." (Walsh, Arora & Cohen, *supra* note 20, at 285-289)

[41] Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 Science, 698-7011 (1998); Goozner, *supra* note 30.

[42] Walsh, Arora & Cohen, *supra* note 20, at 331.A study conducted in 2005 also denied the reality of an anticommons in research fields where patenting is common (John P. Walsh, Charlene Cho & Wesley M. Cohen, *Patents, Material Transfers and Access to Research Inputs in Biomedical Research* at http://www.uic.edu/~jwalsh/NASreport.html (last visited June 30, 2007).

overlapping patents.[43] But, notwithstanding the questionable existence of an anticommons in this scientific field, patenting stem cell technologies can still present a two-fold dilemma for the development of stem cell research.

Patenting Key Upstream Inventions

Firstly, progress could be hindered if the use of patented research tools is a precondition for the development of further downstream inventions.[44] If a scientist can choose to use one of a number of different research tools to reach a desired result, then the fact that a limited number of these research tools are patented will not slow her work down; this is because there are other unpatented research tools that she could use without having to lose time or money negotiating licences. It follows that if a particular upstream discovery is a necessary building block for a subsequent innovation, then patenting the former discovery may thwart the timely development of that science. This concern echoes loudly in stem cell research due to the interdependent nature of this particular field.[45]

However, the threat of arrested development must be mitigated in light of recent studies. It has been suggested that stem cell research is not as cumulative as once believed because new methods could potentially be used as different "pathways" for achieving a same result.[46] For example, James Thomson, a researcher at the University of Wisconsin, was the first to isolate hESC in 1998. He was awarded two patents which he then assigned to the Wisconsin Alumni Research Foundation (WARF), the organization that provides financing for scientific research at the University of Wisconsin.[47] It was widely believed that these two patents on stem cell derivation technologies effectively blocked major branches of stem cell research because the use of these two inventions were thought to be necessary for the differentiation processes of hESC.[48] However, methods such as "parthenogenesis, embryo biopsy, cellular fusion, altered nuclear transfer" have recently been touted as alternate, unpatented, processes for deriving hESC[49] such that the WARF patents may not necessarily be needed to further develop hESC technologies.

Moreover, the concern that stem cell research will be delayed due to patented upstream inventions should again be

[43] Walsh, Arora & Cohen, *supra* note 20, at 308

[44] Timothy Caulfield, Robert M. Cook-Deegan, F Scott Kieff & John P. Walsh, *Evidence and Anecdotes: an Analysis of Human Gene Patenting Controversies*, 24 Nature Biotechnology, 1091-1094 (2006); Walsh, Arora & Cohen, *supra* note 20, at 334; Matthew Herder, *Proliferating Patent Problems with Human Embryonic Stem Cell Research?,* 3(1-2) Journal of Bioethical Inquiry, 71 (2006); Basheer, *supra* note 25; Lori Andrews, Jordan Paradise, Timothy Holbrook & Danielle Bochneak, *When Patents Threaten Science,* 314(5804) Science, 1395-1396 (2006).

[45] Rai, *supra* note 36, at 137; Walsh, Arora & Cohen, *supra* note 20, at 289; Basheer, *supra* note 25.

[46] K.S. Taymor, C.T.Scott & H.T. Greely, *The Paths Around Stem Cell Intellectual Property*, 24(4) Nature Biotechnology, 411-413 (2006).

[47] Walsh, Arora & Cohen, *supra* note 20.

[48] John Simpson, The Missing Link in Stem-cell Research: Op-Ed Commentary in the Sacramento Bee (July 2, 2006), http://www.consumerwatchdog.org/co/?postId=6532 (last visited June 30, 2007).

[49] Taymor, Scott & Greely, *supra* note 46.

questioned because the therapeutic capacity of stem cells derives not only from human *embryonic* stem cells, but from stem cells originating from the born alive individual as well.[50] Since positive medical results can be achieved using both types of stem cells, then perhaps the patenting of a limited number of stem cells or stem cell by-products will not create such an acute problem for the advancement of stem cell research. Therefore, it is possible that the field of stem cell research can still progress despite the patenting of a few key inventions.

Patent Scope

Broad patents over stem cell technologies present yet another potential barrier to the advancement of stem cell research: a patent that protects the use of an invention in an overbroad manner could block subsequent inventors from engaging in any number of research activities that are covered by the initial patent. In other words, patent claims that do not accurately describe the exact scope of the invention may grant exclusive rights over a wide area of research thus "blocking off whole areas of research and development".[51]

WARF's patent No. 5,843,780 claimed primate embryonic stem cells, primate embryonic stem cell lines derived from the former original stem cells, and the process used to create them.[52] WARF's patent No. 6,200,806, which claimed the same but for *human* embryonic stem cells, was similarly broad in scope.[53] Both these patents expire in 2015. To put it simply, until 2015, "[this] means that WARF essentially claims ownership rights to all hESC and downstream products, regardless of how they are derived [...] it is likely that any attempts at commercialization of a product based on hES cells without WARF's consent will lead to an infringement lawsuit."[54]

But, there are two important reasons why a researcher would be reticent to obtaining a licence to WARF's patents. Firstly, despite WARF's commitment to grant non-commercial use licences at a low fee,[55] academics will probably not have the incentive to avail themselves of this opportunity because of existing legislation (for example, the *Bayh-Dole Act*) "which strongly [encourages] American universities to patent scientific discoveries made with public funds and [...] to commercialize them".[56] In addition, in light some American caselaw,[57] academic research involving patented stem cell technologies now carries greater risks of patent infringement due to the narrowed scope of the research exception in American law. Thus, scientists who would like to make use of the WARF non-commercial

[50] Walsh, Arora & Cohen, *supra* note 20.

[51] Dianne Nicol, *Cooperative Intellectual Property in Biotechnology*, 4(1) SCRIPT-ed, 137-139 (2007), *available at* http://www.law.ed.ac.uk/ahrc/script-ed/vol4-1/nicol.pdf (last visited June 30, 2007).

[52] Taymor, Scott & Greely, *supra* note 46, at 411.

[53] Munzer &Korobkin, *supra* note 9, at 45-46.

[54] Sander Rabin, *The Gatekeepers of hES Cell Products*, 23 Nature Biotechnology, 817 – 819 (2005).

[55] Jeanne F. Loring & Cathryn Campbell, *Intellectual Property and Human Embryonic Stem Cell Research*, 311(5768) Science, 1716-1717 (2006).

[56] Herder, *supra* note 21, at 9.

[57] *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002); Jennifer Miller, *Sealing the Coffin on the Experimental Use Exception*, 12 Duke Law and Technology Review (2003).

use licence must tread carefully in order to avoid patent infringement. However, as mentioned above, there are legislative pressures to patent the results of strictly academic research. By consequence, academics wanting to patent any of their WARF-related inventions would be obliged to concede these commercial rights to WARF pursuant to the terms of the non-commercial use licence.[58] This chain of restrictions on academic research could ultimately discourage scientists from obtaining non-commercial WARF licences altogether.

Although WARF has announced that as of January 2007, it has granted over 350 academic licences,[59] one would reasonably assume that these figures could be higher but for the strictly non-commercial character of the licence. Therefore, the scope of the WARF patent is likely having the effect of suppressing hESC academic research.[60]

Secondly, it is evident that commercial researchers could also be deterred from any hESC research due not only to the negotiation delays but also to the high costs associated with obtaining licences from WARF.[61] In fact, a commercial licence costs up to 125, 000 USD and then an additional 40, 000 USD per year to retain the licence.[62] For young start-ups focussed on the development of stem cell technologies, these fees may simply be too heavy to bear.[63] The result is that there will be less stem cell-related research initiatives being launched than there potentially could be, were the licensing procedures less complicated and less costly.[64] Indeed, authors have noted that potential company-builders vying for a piece of the stem cell market have been dissuaded due to the difficulty of "[accessing] embryonic stem cells at a reasonable price from the Wisconsin Alumni Research Foundation".[65]

The Wilmut patents are another example of how the scope of a patent may negatively affect the progress of stem cell research. Although these patents claim several cloning processes for the production of non-human stem cells, they may still inhibit the development of hESC research because it has been suggested that "the series of techniques that they describe are one likely means of producing hES cells by [cloning]".[66] Taking into consideration the supposition that the WARF patent protects arguably *all* hESC and their downstream products, and assuming that the Wilmut patents protect one important method for cloning hESC, then there are perhaps very limited ways for producing, differentiating, and reaping the commercial benefits of hESC without using, and by

[58] Jennifer Washburn, *The Legal Lock on Stem Cells: Two Patents that Cover Key Research Areas are Setting Back Science*, Los Angeles Times, April 11, 2006, *available at* http://www.newamerica.net/publications/articles/2006/the_legal_lock_on_stem_cells (last visited June 30, 2007).

[59] Wisconsin Alumni Research Foundation, WARF Changes Stem Cell Policies to Encourage Greater Academic, Industry Collaboration (January 23, 2007), http://www.warf.org/news/news.jsp?news_id=209 (last visited June 30, 2007).

[60] Loring & Campbell, *supra* note 55 at 1716; Washburn, *supra* note 58.

[61] Nicol, *supra* note 51, at 140; Constance Holding, *U.S. Patent Office Casts Doubt on Wisconsin Stem Cell Patents*, 316(5822) Science, 182 (2007).

[62] Loring & Campbell, *supra* note 55 at 1717.

[63] Washburn, *supra* note, 58.

[64] Rai, *supra* note 36, at 135.

[65] Merrill Goozner, *supra* note 30.

[66] Taymor, Scott & Greely, supra note 46, at 411.

consequence paying for the use of, one of the above patents.

To summarize, with respect to the field of stem cell research, the patent system's main negative consequence of limiting access to technology is manifested in two different ways: the patenting of foundational research tools and the overly broad scope of stem cell patents both raise significant issues of access to technology and could therefore justify the need for alternatives to the standard business model of patenting stem cell technologies. The academic controversy surrounding the WARF patents suggests that the issue of overly broad patents is the most compelling argument against the patenting of stem cell technologies.

3. STEM CELL RESEARCH PRACTICES IN LIGHT OF THE WARF PATENTS

A) Stem Cell Research in the US

The American legal community has reacted strongly to WARF's assertion of property rights over all human stem cells and the techniques used to isolate them. There is an impressive amount of literature that purports that the patents may be impeding stem cell research in the US.[67] However, there seem to be nearly as many articles that describe methods that are currently being used, or could be used, to counter the effects these patents may have on the development of research. For example, it has been claimed that, instead of negotiating licences with WARF in order to pursue research, American scientists "have sent research monies abroad where they can avoid paying royalties to WARF"[68]. Also, as in the field of biotechnological research more generally, stem cell scientists could be using other "working solutions"[69] to pursue their work. Thus, scientists are not only criticizing the WARF patents but are also proactively attempting to circumvent the potential negative effects they may be having on the development of research.

The measures taken to dodge the effects of the WARF patents do not end there: not only has stem cell research been carried outside of the US, but legal challenges have also been officially filed against the validity of these patents.[70] In July of 2006, several non-profit organizations, namely the Foundation for Taxpayer and Consumer Rights and the Public Patent Foundation, called on the US Patent and Trademark Office (PTO) to "re-examine and revoke" the WARF patents based on the allegation that the processes used to isolate the human stem cells were obvious in light of the existing knowledge and, by consequence, not

[67] For example: Cathy Tran, WARF Stem Cell Patents Challenged (October 11, 2006), http://www.the-scientist.com/news/display/25037/ (last visited June 30, 2007); Alison McCook, Stem Cell Patents Loosened (January 23, 2007), http://www.the-scientist.com/news/display/43099/ (last visited June 30, 2007); Michael C. Mireles Jr., *States as Innovation System Laboratories: California, Patents, and Stem Cell Technology*, 28 Cardozo Law Review, 1133 (2006).

[68] Public Patent Foundation, Groups Challenge Stem Cell Patents that Loot Taxpayer Funds and Force Research Overseas: University of Wisconsin Affiliate Claims Rights to all Embryonic Stem Cells Used for Research (July 18, 2006), http://www.pubpat.org/warfstemcellsfiled.htm (last visited June 30, 2007).

[69] See section 2B

[70] Tran, *supra* note 67.

patentable.[71] In April 2007, the PTO found that the patents were indeed obvious, but the WARF has since appealed the merits of this decision.[72]

The theoretical criticism that WARF has received and the research community's proactive attempts to evade the research-restricting effects of the WARF patents suggest that there is an unyielding determination to continue doing stem cell research despite the practical obstacles that the WARF patents may present. In fact, even though this field is still quite new and even if not all researchers automatically seek patent protection for their inventions, as of April 2007, the PTO will have granted 1724 patents and will have received 3711 patent applications "covering any and all 'uses, methods, or compositions involving human or animal stem cells' ".[73] These numbers again suggest that, despite the disincentives to research that the WARF patents may create, the scientific community is nonetheless interested in pursuing stem cell research. However, the fact that researchers are trying to find alternative solutions bears witness to the negative effect of the WARF patents on research. As such, in order to sustain this high level of interest in stem cell research, it is important to create a research environment that would not further hinder the field's timely development.

B) Stem Cell Research in Europe

In Europe, there are legislated bars to patentability based on morality in the Directive on the Legal Protection of Biotechnological Inventions 98/44/EC (the Directive). Although the interpretation of the Directive's morality clause is far from being uniform in all European jurisdictions, there are nonetheless two watershed European Patent Office (EPO) decisions that discuss the patentability of stem cell technologies. In the University of Edinburgh and the WARF cases, the EPO ruled that since inventions involving hESC necessarily required the use of embryos, then these claims were not patentable pursuant to the Directive[74] which states that "[…] European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following: […] (c) uses of human embryos for industrial or commercial purposes […]"[75] Although it would seem that multipotent and unipotent stem cells that are extracted directly from the adult are not caught by this Rule, hESC *per se* and the processes used for their isolation are unpatentable.[76] Unlike the

[71] Constance Holding, *Prominent Researchers Join the Attack on Stem Cell Patents,* 317 Science, 187 (2007).

[72] Alison McCook, Key Stem Cell Patents Rejected (April 3, 2007), http://www.the-scientist.com/news/home/53051/ (last visited June 30, 2007) ; Erika Check, *Patenting the Obvious,* 447 Nature, 16-17 (2007); Ryan J. Foley, Wis. Foundation Challenges Decision to Reject Stem Cell Patents (June 1, 2007), http://www.gazetteextra.com/stemcellpatents060107.asp (last visited June 30, 2007).

[73] Karl Bergman & Gregory D. Graff, *The Global Stem Cell Patent Landscape: Implications for Efficient Technology Transfer and Commercial Development*, 25(4) Nature Biotechnology, 420 (2007).

[74] Nador & Loucaides, *supra* note 13.

[75] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions, art. 6(c), 1998, O.J. EPO; Munzer & Korobkin, *supra* note 9, at 56.

[76] Joe Vanden Plas, WARF Stem Cell Patent Faces Long and Winding Road (May 31, 2006), http://

American context, it is not WARF's patent, in and of itself, that could be problematic for the advancement of stem cell research. Rather, given the research incentives that patents create, it is the broad interpretation of the morality clause in light of the WARF patent that may be creating a disincentive to undertake such research. Thus, it is not just the granting of overly broad patents that could hinder progress in the field of stem cell research because the outright barring of stem cell technologies from patentability is equally capable of slowing such research.

The EPO's interpretation of the morality clause has caused some researchers to employ creative wording techniques in their stem cell related patent applications in order to ensure the validity of their claims: potential patent holders have made sure not to extend their claims to hESC by, for instance, adding the term "nonhuman" before "embryonic stem cell".[77] Another way of circumventing the ruling of the University of Edinburgh and WARF cases is to funnel patent claims through national patent offices rather than the EPO in order to obtain protection for hESC technologies.[78] These state patent offices have the authority to grant patents that are valid within their respective countries.[79] Scientists hope that countries' individual interpretations of the European Patent Convention will be more lenient than the EPO's with respect to the patentability of hESC technologies.[80] Thus, the EPO's interpretation of the morality clause might not necessarily cause scientists to lose interest in stem cell research. Instead, it has simply caused the research community to make use of alternate routes for acquiring protection for hESC technologies.

Thus, regardless of the suggestion that the University of Edinburgh and the WARF cases may be disincentives to research, the existence of alternate patenting strategies suggests that the motivation to engage in stem cell research is still obviously present. Moreover, as of April 2007, the EPO will have granted 421 patents and received another 560 patent applications "covering any and all 'uses, methods, or compositions involving human or animal stem cells' ".[81] Thus, similarly to the American context, the process of technology transfer must be low cost and uncomplicated in order to maintain this momentum in the development of stem cell research.

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wistechnology.com/article.php?id=3006 (last visited June 30, 2007). Note that Both the University of Edinburgh and the WARF have appealed these decisions based on the argument that only the use of embryos as raw materials are excluded from patentability. This would mean that while embryos themselves are unpatentable, patent claims that make use of them at some stage are valid.

[77] G. Porter, A. Denning, A. Plomer, J. Sinden & P. Torremans, *The Patentability of Human Embryonic Stem Cells in Europe*, 24(6) Nature Biotechnology, 654 (2006).

[78] *Id.*

[79] Vanden Plas, *supra* note 76.

[80] UK Intellectual Property Office, Inventions Involving Human Embryoninc Stem Cells, http://www.ipo.gov.uk/patent/p-decisionmaking/p-law/p-law-notice/p-law-notice-stemcells.htm (last visited June 30, 2007). For example: The UK Patent Office in particular has issued a Practice Notice to the effect that pluripotent hESC-related technologies are patentable (provided they meet all other patentability criteria) because they do not have the potential to develop into a full human being like totipotent stem cells do.

[81] Bergman & Graff, *supra* note 73.

C) Stem Cell Research in Canada

Canada's stem cell research regulatory framework is comparatively permissive because there seems to be only one bright line prohibition: all forms of cloning are prohibited. All other stem cell research practices, although highly regulated by various legislative documents, are tolerated.[82] However, despite the theoretical possibility of patenting stem cells, in practice, the Canadian Intellectual Property Office (CIPO) has yet to grant the WARF patents.[83] One author has noted that, should these patents be granted, the stem cell research-friendly environment that researchers currently benefit from is likely to disappear: "Canadian researchers' unfettered freedom to pursue certain avenues of stem cell research is in danger" because WARF's patents are expected to protect hESC *per se* and just about all related downstream inventions.[84] Practically speaking, "if the blurred line between commercial and non-commercial research is transgressed without WARF's prior permission, an action for patent infringement is likely to follow".[85] Much like what is currently being discussed in American academic circles, the WARF patents are seen as potential threats to the timely progress of stem cell research because of the scope of protection awarded to WARF.

However, if this is the case, then if/when the WARF patents are awarded, Canada is likely to follow the Americans' lead in resolving problems of patent scope. As the Americans have done, Canadians may engage in proactive attempts to circumvent the use of the WARF patents to continue stem cell research by conducting research overseas where WARF has not yet been granted exclusive rights over hESC or by mounting legal challenges to the validity of the Canadian WARF patents. Moreover, in light of the relatively liberal structure governing stem cell research in Canada, researchers may perhaps pursue these WARF avoidance measures even more aggressively than American researchers to re-establish their freedom of scientific inquiry. Thus, effective technology transfer processes must be elaborated to ensure that broad patents on upstream stem cell technologies such as WARF's do not hinder this anticipated enthusiasm for research.

In short, since the use of patent law is currently the most widespread way of protecting the interests of inventors, then researchers must address the potential difficulties associated with patent law

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[82] Canadian Biotechnology Advisory Committee, Patenting of Higher Life Forms and Related Issues: Report to the Government of Canada Biotechnology Ministerial Coordinating Committee (June 2002), http://cbac-cccb.ca/epic/site/cbac-cccb.nsf/en/ah00188e.html#sec2b (last visited June 30, 2007); *Assisted Human Reproduction Act*, S.C. 2004, c.2, *available at* http://www.canlii.org/ca/sta/a-13.4/whole.html; Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, ***Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans 9.4, (Public Works and Government Services Canada 2005)*** (1998 (with 2000, 2002 and 2005 amendments)); Canadian Institutes of Health Research, Updated Guidelines for Human Pluripotent Stem Cell Research (June 28 2006), http://www.cihr-irsc.gc.ca/e/31488.html (last visited June 30, 2007).

[83] Canadian Intellectual Property Office, Patents Database, http://patents1.ic.gc.ca/fcgi-bin/patquery_eo_el (last visited June 30, 2007).

[84] Herder, *supra* note 21.

[85] *Id.*

(ethical, philosophical, legal, and otherwise) in order to effectively continue their research. What remains to be explored is the extent to which open and collaborative models of technology transfer can be appropriate alternatives or complements to the patent system in the field of biotechnology.

4. ORIGINS OF OPEN SOURCE

Open models of collaboration take root in the computer programming concept of free software. In the 1960s and 1970s, a "hacker" culture developed whereby technicians tended to freely exchange software and source codes, codes that humans use to read and modify software.[86] Then, in the 1980s, the industry's focus shifted to privatization with the advent of new and more powerful computers: computer firms started protecting, until then, uncopyrighted software, thereby restricting the possibility of free duplication. In addition, private companies withheld the distribution of source codes and subjected end-users to non-disclosure agreements whereby the software transferred could not be shared or modified.[87] Thus, the increasingly proprietary mindset of the 1980s computer programming community put the "hacker" cooperative ethos under pressure.

In response to this ideological shift, Richard Stallman decided to create a "free" operating system, the key piece of software computers use to run. This software, called GNU, was released under a GNU Public Licence (GPL) that allowed people to run, copy, modify, improve, and redistribute the software at will (i.e. access to source codes was permitted).[88] This GPL, also commonly referred to as a classic "copyleft", also required that if modifications were made to the program, the modified version must be published under the same conditions as the original software.[89] Thus the copyleft is, in direct opposition to a copyright, created to ensure that users have the "freedom" to duplicate and improve a program.[90]

Unsurprisingly, the business community's response to Stallman's free software concept was lukewarm due to the movement's total rejection of exclusively owned software. By consequence, "open source" rhetoric started being used to appeal to a more commercial audience by drawing attention away from the moral "sharing" aspect of free software, but retaining the concept of freedom to run, copy, and modify software. [91] The "Open Source Initiative" was therefore launched to promote essentially the same principles as free software, but not under the moral rubric of sharing and community.[92]

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[86] Rai, *supra* note 36, at 137.

[87] Geoff Mulgan, Tom Steinberg & Omar Salem, Wide Open: Open Source Methods and Their Future Potential 12, (Demos) (2005); Richard Stallman, *The GNU Operating System and the Free Software Movement*, *in* Open Sources: Voices from the Open Source Revolution (O'Reilly Media, Inc) (1999);

[88] Joly, *supra* note 23; Mulgan, Steinberg & Salem, *supra* note 87, at 13; Stallman, *supra* note 87.

[89] Josh Lerner & Jean Tirole, *The Economics of Technology Sharing: Open Source and Beyond*, 19(2) Journal of Economic Perspectives, 99 (2005).

[90] Stallman, *supra* note 87. The "free software" movement was founded on the assumption that "the proprietary software social system […] is antisocial, it is unethical, […] it is simply wrong."

[91] Herder, *supra* note 21, at 26-27; Joly, *supra* note 23, at 392.

[92] Stallman, *supra* note 87; Herder, *id.*

There are two benefits of open source projects that are most commonly seized upon to justify its use in the field of computer programming: open source projects can generate high-quality output and at a low cost.[93] Firstly, the work produced is of good quality because participants are able to vet each other's contributions such that flaws and can be effectively and quickly weeded out. Eric Raymond has been quoted a number of times on this matter: "given enough eyes, all bugs are shallow".[94] In fact, several studies that compared the technical aspects of open source software such as Linux, Apache, and GCC with closed source software found that the former were technically superior.[95]

The second point that is often brought up to justify the use of open source projects is that it can produce results at a low price. To obtain open sourced software (and thereby participate in the software improvement process), a participant need only have access to a computer and internet access. Then, beyond these basic costs, the acquisition of the software costs only what the copyleft licensing fees, if any, cost. For instance, obtaining Linux software costs nothing beyond the basic outlays of a computer and an internet connection.[96] In addition, authors have identified other strengths of open source software such as transparency, existence of a legal structure and an enforcement mechanism, incrementalist, presence of powerful non-monetary incentives.[97]

The drawbacks of open source are not as widely discussed as the advantages, but academics have nevertheless briefly noted a few.[98] For example, open source projects may be susceptible to "minority capture" because they are vulnerable to being used to channel a group's interests. Because these projects allow anyone to access them, any organized lobbyist faction would be able to manipulate and distribute the software for its own purposes. Also, there is the risk of "diversion and dissension": because open source projects allow anyone to access them, they may suffer from contradictory contributions. Third, there is restricted access to funding. Open source

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[93] Rai, *supra* note 36, at 138; Mulgan, Steinberg & Salem, *supra* note 87 at 16ff.

[94] For example: Mulgan, Steinberg & Salem, *supra* note 87, at 20.

[95] Rai, *supra* note 36, at 139.

[96] Mulgan, Steinberg & Salem, *supra* note 87, at 17.

[97] Mulgan, Steinberg & Salem, *supra* note 87, at 23ff; Rai, *supra* note 36, at 145ff.

Transparency: open source projects thrive on being open about their internal functioning. By consequence, contributors are aware of how all innovation is created.

A legal structure and enforcement mechanism: copyleft ensures that others cannot appropriate the work of others for themselves because it requires that any improvements made to the open sourced software be made available. Thus, participants will not be deterred from contributing their ideas.

Incrementalist: improvements to software can be made by anyone, with any type of background. All modifications, no matter how small, contribute to the ongoing improvement process.

Powerful non-monetary incentives: participants in open source projects are often motivated non-monetary factors. For instance, they will contribute because of the desire to be recognized and respected for their work. Or, they may contribute because they need a computer program to accomplish a specific task and the easiest and cheapest way to achieve that goal is to modify open source software.

[98] Stephen Shankland, Is Open Source Fading Away? (November 21, 2001) http://www.zdnet.com.au/news/software/soa/Is-open-source-fading-away-/0,130061733,120261963,00.htm (last visited June 30, 2007).

projects have difficulty with attracting investment because the "goods" (the source codes) are made available to anyone who wants them. Fourth, it is believed that without an initial temporary monopoly over a product, nobody would have the incentive to develop it because the investments required to successfully market the good outweigh the potential benefits of open sourcing it. Note that this is the classic argument used to justify the patenting of inventions. Fifth, some argue that good ideas need to be isolated in order to thrive. Directed criticism in an open source project could have the effect of eliminating a good idea that was perhaps not yet fully developed.[99] Finally, open projects may have a reduced ability for generating revenues from main products. Instead of purchasing propertied computer programs, consumers can simply copy them due to the open availability of source codes. This in turn can decrease a computer company's revenues.[100] However, it should be noted that this decrease could be offset by the company's ability to increase its revenues from complementary, and propertied, goods and services.[101]

Despite these weaknesses, given the steadily increasing number of open source projects being launched in the technology context, it would nonetheless seem that the strengths of open source eclipse the weaknesses. For instance, in 2005, 91,000 such projects were recorded and authors note that this number continues to grow today. [102]

Although software is the most obvious use of open source, the principles that underlie the open source method have increasingly been adapted to other areas of invention.[103] What remains to be seen is whether such open source notions can be adapted to the field of biotechnology, generally, and to stem cell research, in particular. It should also be noted that since the expression "open source" can only properly be used in connection with source codes (i.e. software),[104] the authors will refer to the adaptation of the open source method to other fields of knowledge as "open models" of technology transfer.

5. OPEN MODELS IN BIOTECHNOLOGY

A) Why Use Open Models in Biotechnology?

Biotechnology is a cumulative science and in order for this field to progress, researchers must have access to a spectrum of "enabling technologies"[105] or upstream inventions. But, the patenting of key upstream inventions and overly broad patent claims may hinder downstream innovation. This means that the hindrance to the advancement of biotechnology lies in the tension between downstream inventors who need access to enabling technologies on the one hand, and

[99] Mulgan, Steinberg & Salem, *supra* note 87, at 23ff.

[100] Shankland, *supra* note 98.

[101] Joly, *supra* note 23, at 400.

[102] Herder, *supra* note 21, at 28.

[103] Rai, *supra* note 36, at 139.

[104] Andres Guadamuz Gonzalez, *Open Science: Open Source Licenses in Scientific Research,* 7(2) North Carolina Journal of Law & Technology, 321-366 (2006)

[105] Janet E. Hope, Open Source Biotechnology (December 23, 2004) (unpublished Ph.D. dissertation, The Australian National University), 62, *available at* http://opensource.mit.edu/papers/hope.pdf.

the owners or patentees who want to control access to these technologies on the other hand. Thus, in order to ensure that biotechnological research progresses effectively, what is needed is affordable and unfettered access to enabling technologies, all while protecting the interests of inventors.[106] Since the guiding principle of open models of technology transfer is unrestricted access to technology at a low cost, this article suggests that the targeted use of such models for the generation and transfer of biotechnological innovation may help pave the way to this objective. More importantly, there are also other benefits to using open approaches in biotechnology. Beyond having the potential of effectively addressing the perceived problems associated with the patent system, authors have discussed the numerous scientific, economic, and social advantages that are associated with the use of open approaches in biotechnology.[107]

B) Practical Applications of Open and other Collaborative Models of Technology Transfer in Biotechnology

So-called "open" models have already begun to make their mark in the biotechnology industry. However, the reader should note that, to date, there do not seem to have been any specific attempts at defining what exactly constitutes an "open" project. The authors suggest that, similarly to open source, open models of collaboration are characterized by four basic features: freedom to access, copy, and modify information, and most importantly, an obligation to publish downstream work under the same conditions (whether manifested through intellectual property rights or contracts). However, as will be seen, some existing biotechnological projects, although they do not incorporate copyleft-like restrictions, have nevertheless been characterized as "open" by the literature. These projects, although collaborative in certain respects, probably should not have been identified as such.

The authors believe that copyleft-like restrictions are critical to open models of collaboration even if it has been argued that such clauses are not necessarily needed to ensure that information remains freely available. One author suggests that putting certain research findings (such as the gene sequences that were mapped by the HGP) in the public domain "effectively excludes the patenting option until some additional step [is] taken":[108] since the research results are widely published, the invention does not satisfy the novelty requirement of patentability.[109] Moreover, since information in the public domain is accessible to all, then there is also a good chance that inventions building upon this information could be obvious and thus again ineligible for patentability.[110] However, the fact remains that the possibility of appropriating the work of upstream researchers, even if slight, still

[106] Nicol, *supra* note 51, at 142.

[107] See Joly, *supra* note 23, at 398-405.

[108] Nicol, *supra* note 51, at 148.

[109] Gonzalez, *supra* note 104.

[110] Jinseok Park, *Evolution of Industry Knowledge in the Public Domain: Prior Art Searching for Software Patents*, 2(1) SCRIPT-ed, 47 (2005), *available at* http://www.law.ed.ac.uk/ahrc/script-ed/vol2-1/park.asp (last visited June 30, 2007).

exists.[111] For example, in 1998, Craig Venter founded Celera Genomics, a private research lab with the goal of sequencing the human genome. One notes that the birth of this biotech company coincides in time with the HGP's efforts to do the same. However, whereas the HGP's goal was to make research findings publicly available on internet, Celera wanted to "[reap] the rewards of its investments": it aimed to create a database that users could access, but only in exchange for a fee.[112] Indeed, both projects were engaged in a veritable race to decode the genome because each tried to outdo the other's attempt to privatise/publicize the data. For our purposes, what is important to note is that it has been suggested that Celera's work "made extensive and inextricable use of the HGP genome information and thus [was] not an independent assembly of the human genome".[113] In other words, Celera could have, even if ultimately it was unable to, privatised the HGP's openly published research findings for its own purposes.[114] Thus, this risk of unfair appropriation of information placed in the public domain suggests that copyleft-like mechanisms are central elements of open models of collaboration in the field of biotechnological, and therefore stem cell, research.

It should also be noted that open models are but one specific subset of collaborative methods of technology transfer and since they have yet to be widely adopted in biotechnology, the following is an examination of other collaborative models of technology transfer and how they differentiate, or resemble, open models.

Public Databases and/or the Public Domain

Putting information in the public domain means that anyone can access, use, and modify the information without permission and free of charge. It thus also follows that the information can be used for whatever purposes, proprietary or not.[115] The public domain is more commonly considered to be a forum for materials that are, for whatever reason, ineligible for intellectual property protection; for instance, facts that lack the required level of originality for copyright protection and inventions whose patents have expired are placed in the public domain. However, it is possible to place copyrightable or patentable information in the public domain by renouncing to all intellectual property rights,[116] such was the case for biotechnology projects such as the HGP.

As previously discussed, there is a risk of private appropriation of information that was initially free. This situation is particularly

[111] Arti K. Rai & Rebecca Eisenberg, *Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California's Stem Cell Initiative* (Duke Science, Technology & Innovation Paper No. 11), 21 Berkeley Technology Law Journal, 1207 (2006).

[112] RTD info: Magazine for European Research, Accelerating into a New Age, http://ec.europa.eu/research/rtdinfo/en/27/genome01.html (last visited June 30, 2007).

[113] Robert H. Waterston, Eric S. Lander & John E. Sulston, *More on the Sequencing of the Human Genome*, 100(6) Proceedings of the National Academy of Sciences of the United Stated of America, 3022-3024 (2003).

[114] Gonzalez, *supra* note 104.

[115] University of California, UCCopyright, http://www.universityofcalifornia.edu/copyright/publicdomain.html (last visisted June 30, 2007).

[116] *Id.*

worrisome in the context of stem cell research because of the capital intensive nature of R&D: self-interested downstream researchers could effectively rob upstream inventors of their considerable monetary investments by patenting an improvement of the foundational research results that were initially placed in the public domain. Thus, the public domain may not be ideally suited to harbour upstream information that costs a significant amount to generate, such as upstream stem cell inventions.

Patent Pools and Cross-Licensing

A patent pool is "an agreement among patent owners to licence a set of their patents to one another or to a third party":[117] when multiple licences must be obtained in order to produce a final good, patent owners can come together and agree to cross-licence their patents to each other or licence them as "package" out to third parties.[118] Such an arrangement would be desirable in a field of knowledge that develops cumulatively because, instead of having to negotiate licences and pay royalties for each added "layer" of innovation, the pooling of patents reduces the costs of technology transfer not only by streamlining or standardizing the negotiations process but also lessening the amount of licence fees to be paid.[119] However, although patent holders benefit from these pools, consumers of the final product may be adversely affected if the participants of the patent pool collude and engage in anticompetitive practices so as to set the cost of the good unduly (and illegally) high. Past situations of antitrust put aside, patent pools have nevertheless been effectively used to commercialize many products.[120]

In the context of stem cell research, patent pools have been proposed as solutions to the alleged anticommons problem.[121] However, the field of stem cell research is characterized by a few broad patents like WARF's, rather than many concurrent patents, such that an anticommons is not necessarily a problem that has actually arisen. In any case, if these few patent holders were to form a patent pool, then only their research initiatives (or those of third parties who agree to pay for the "package" of licences) would benefit from the collaboration. But, when it comes to scientific progress in the field of stem cell research, many heads are probably better than just a few:[122] according to Sornberger, "what's

[117] Josh Lerner & Jean Tirole , *Efficient Patent Pools,* 94 American Economic Review, 691(2004); C. Shapiro, *Navigating the Patent Thicket: Cross Licence, Patent Pools and Standard-Setting*, *in* Innovation Policy and the Economy, Volume I (A. Jaffe, J. Lerner & S. Stern eds., MIT Press) (2001).

[118] Patrick Gaulé, *Towards Patent Pools in Biotechnology?*, École polytechnique fédérale de Lausane, CDM Working Papers Serie, 2 (2006).

[119] Chris Dent, Paul Jensen, Sophie Waller & Beth Webster, A Research Use of Patented Knowledge: A Review, (OECD Directorate for Science, Technology and Industry) (2006).

[120] Jeanne Clark, Joe Piccolo, Brian Stanton & Karin Tyson, Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?, (United States Patent and Trademark Office) (2000).

[121] Goozner, *supra* note 30.

[122] The Steering Committee of the International Stem Cell Initiative, *The International Stem Cell Initiative: Toward Benchmarks for Human Embryonic Stem Cell Research,* 23(7) *Nature Biotechnology,* 796 (2005); Stem Cell Network, Catalyzing: Commercialization (August 24, 2005), http://www.stemcellnetwork.ca/success/commercial.php (last visited June 30, 2007).

needed right now in stem cell biology is co-operation".[123] Therefore, to maximize innovation, as many scientists as possible should be brought into the picture, not just the few who are either members of the patent pool or wealthy enough to afford the license fees. Moreover, patent pools, in and of themselves, lack copyleft-like mechanisms. Hence, theoretically, improvements to upstream information could be patented and subsequently withheld from the pool. Should this be the case, we would still be faced with the potential patent-related problems of hampering research.[124] In light of the two research impediments presented above, patent pools might not be ideal models for the transfer of stem cell technologies

Clearinghouse Mechanisms

A clearinghouse is described as a system that simplifies the process of finding and negotiating licences by providing a platform for matching providers and users of patented inventions, based on a number of different criteria.[125] Potential licensees can pick and choose from a clearinghouse those patents which are most relevant for their purposes. Moreover, "a clearinghouse could perform one or more of the following functions: facilitating the search for technology that is available for licensing or free use; smoothing the progress of negotiations; and monitoring or enforcing negotiated agreements."[126]

Clearinghouses have been proposed as mechanisms that could alleviate the possible research impediments associated with the presence of concurrent patents in the field of stem cell research (i.e. an anticommons): since clearinghouses allow researchers to navigate the "thicket" with relative ease, the risk of the development of an anticommons is diminished.[127] However, we have established that an anticommons is not a serious threat to the timely progression of stem cell research because such a situation presupposes the existence of many fragmented and concurrent patents whereas this field of knowledge is, in reality, characterized by a few broad patents. Thus, that clearinghouses have the potential for remedying an anticommons, would not justify their use in the context of stem cell research.

It is also argued that the creation of clearinghouses can lead to an overly strict enforcement of intellectual property rights, including rights that are of uncertain validity, and thereby hinder downstream research efforts.[128] For example, the validity of the American WARF patents has yet to be unequivocally determined. If a clearinghouse grouping hESC related patents were to be created, the WARF patents would undoubtedly be listed in it. But, the fact that the patents are listed would also suggest that they are valid; by consequence, a downstream

[123] Joe Sornberger, *Critical Mass,* 5(1) *Stem Cell Network*, 7 (2006).

[124] See section 2B on "Patenting Key Upstream Inventions" and "Patent Scope".

[125] Esther van Zimmeren, Birgit Verbeure, Gert Matthijs & Geertrui Van Overwalle, *A Clearing House for Diagnostic Testing: The Solution to Ensure Access to and Use of Patented Genetic Inventions?,* 84(5) Bulletin of the World Health Organization, 352 (2006).

[126] Nicol, *supra* note 51, at 145.

[127] Karl & Graff, *supra* note 73, at 422.

[128] Nicol, *supra* note 51, at 145.

inventor could be deterred from engaging in any further research because of the expected transaction costs associated with negotiating a licence. In other words, clearinghouses could restrict the timely development of a field of knowledge because, by assuming the validity of the patents they inventory, they can mislead downstream inventors into wanting to avoid the licensing headaches that presumably accompany a validly patented invention.

Open models, the public domain, patent pools, and clearinghouses all present advantages and disadvantages regarding their ability to assist in, or conversely their potential to hinder, the advancement of stem cell research. However, of all these collaborative models, open models seem most suited to the aforementioned goal because of their unparalleled ability to spread and generate high-quality information, quickly, all while protecting it from being unfairly appropriated by downstream users.

Indeed, in light of this research field's relatively early stage of development, open models seem to be especially appropriate. Under a traditional proprietary regime, due to licensing complexities and potential resistance to collaboration among scientists (in order to maintain novelty in would-be patent applications)[129], it could take decades before basic stem cell research can be developed into something clinically useful. In addition, with respect to industry, currently, investing in biotechnological R&D is quite risky due to the high levels of capital required and the low chances of successfully producing a marketable product.[130] But, open models diffuse the risk among many contributors, thus allowing for further investment into biotechnological research, and thereby increasing the significance of the other benefits linked to open models of technology transfer. Hence, in stem cell research, whether one considers their ability to maintain the pace of research development or the benefits they confer to the corporate community, open modes of technology transfer may, in certain circumstances, be preferable to classic proprietary schemes for the management of intellectual innovation. Indeed, the biotechnological research sector has begun to recognize the benefits of collaborative models: the following biotechnology projects, although not purely open models, have all successfully incorporated certain elements of open models to achieve their research goals.

The Human Genome Project (HGP)

The HGP was launched to, among other objectives, identify all the genes in human DNA. It spanned thirteen years from 1995 to 2003 and was administered by the US Department of Energy and the National Institutes of Health. Since the completion of the mapping in 2003, several "in-depth analyses of complete chromosomes" have been published. [131]

[129] Yann Joly, Flora Wahnon & Bartha M. Knoppers, *Impact of Commercialization in Biotechnology Research: North American Perspective*, 8:1 *Harvard Health Policy Review*, 71.

[130] Resnik, *supra* note 25, at 130; Basheer, *supra* note 25.

[131] The Human Genome Program of US Department of Energy Office of Science, Human Genome Project Information, http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml (last visited June 30, 2007).

The HGP was an international endeavour lead by five major sequencing centers: the Sanger Institute, the Washington University Genome Sequencing Center, the Whitehead Institute, the Baylor College of Medicine, and the Joint Genome Institute.[132] The participants did not patent their findings and instead shared them by placing the information in the public domain.[133] The success of the HGP has often been attributed to the collaborative spirit of the participants.[134]

The International Haplotype Mapping Project (HapMap)

HapMap describes itself as a "partnership" between Canada, China, Japan, Nigeria, the United Kingdom, and the US with the goal of uncovering associations between specific diseases, genes, pharmaceutical products, and environmental factors.[135] The project was launched in 2002 and completed in 2005 when a "comprehensive catalogue of human genetic variation" outlined the most common differences in the human genome.[136] This effort has been heralded as a catalyst for personalized disease treatment because the identification of the different variations will reduce the cost of carrying out research into the genetic causes of disease.[137]

All the information generated was released into the public domain.[138] However, similarly to the copyleft principle, HapMap also implemented a click-wrap licence whereby anyone who accessed and used the data in their own work had to first agree (1) not to restrict the access of others and (2) not to patent the work.[139] Interestingly, in December 2004, the International HapMap Consortium decided that enough raw data had been produced to justify the removal of the click-wrap and thereby permit unrestricted access

[132] Wellcome Trust Sanger Institute, Historic Overview of the HGP up to 2003, http://www.sanger.ac.uk/HGP/overview.shtml (last visited June 30, 2007).

[133] Rai, *supra* note 36, at 142; Human Genome Research Institute, National Institutes of Health, Department of Health and Human Services, Office of Science US Department of Energy, Human Genome Project Information: Genetics and Patenting, http://www.ornl.gov/sci/techresources/Human_Genome/elsi/patents.shtml#7 (last visited June 30, 2007).

[134] For example: F. Collins & D. Galas, *A New Five-Year Plan for the US Human Genome Project*, 262 Science, 43-46 (1993); U.S. Department of Energy Office of Science, Office of Biological and Environmental Research, Human Genome Program, Human Genome Project Information: Revised 5-Year Research Goals of the U.S. Human Genome Project, http://www.ornl.gov/sci/techresources/Human_Genome/project/5yrplan/5yrplanrev.shtml (last visited June 30, 2007); National Human Genome Research Institute, National Institutes of Health, Department of Health and Human Services, Office of Science US Department of Energy, International Consortium Completes Human Genome Project: All Goals Achieved; New Vision for Genome Research Unveiled, http://genome.gov/11006929 (last visited June 30 2007).

[135] International HapMap Project, International HapMap Project, http://www.hapmap.org/index.html.en (last visited June 30, 2007).

[136] Massachussetts Institute of Technology, HapMap Provides 'Catalog' of Human Genetic Variation (October 27, 2005), http://web.mit.edu/newsoffice/2005/hapmap.html (last visited June 30, 2007).

[137] BBC News, Gene Map Points to Personal Drugs (26 October 2005), http://news.bbc.co.uk/1/hi/health/4378624.stm (last visited June 30, 2007).

[138] International HapMap Projectm International HapMap Project: Home, http://www.hapmap.org/index.html.en (last visited June 30, 2007).

[139] Herder, *supra* note 21, at 35; Rai, *supra* note 36, at 142-143; Mulgan, Steinberg & Salem, *supra* note 87, at 61.

to research results.[140] Much like the HGP, HapMap has been hailed as landmark project in medicine and commended for its use of collaborative methods.[141]

The Biological Innovation for Open Society (BIOS)

The BIOS initiative is aimed at developing innovation systems for disadvantaged communities and neglected priorities. It is funded by CAMBIA, an international, non-profit research institute with the same goals as its subsidiary BIOS.

To attain its goal, BIOS will produce and publish research with respect to three types of biotechnological research tools in a "protected, universally-accessible commons": the Patent Lens is a database to archive patents; the BioForge is a platform to support the open communication of innovation; and the Bios Foundation will consider the successes achieved, or the obstacles encountered, to create a model framework for the "democratization" of innovation. [142]

The Bioforge is managed in a copyleft-like spirit:[143] those who wish to participate in the project agree that generated data can be patented provided that "improvements are shared, and that licensees cannot appropriate the fundamental 'kernel' of the technology and improvements exclusively for themselves".[144] The BioForge currently has twelve ongoing projects, in a variety of different subjects.[145]

6. OPEN MODELS IN STEM CELL RESEARCH

A) Potential Obstacles to the Implementation of Open Models in Biotechnological and Stem Cell Research

The software writing context is very different from the stem cell research context, and as such, it is important to discuss in what ways the two fields of knowledge differ in order to determine whether the open source method could be successfully adapted to stem cell research.

Nature of Research Tools

In computing, raw materials are intangible data contained in the source codes whereas in biotechnology, research materials are often tangible objects such as embryos or stem

[140] Wellcome Trust Sanger Institute, International HapMap Consortium Releases All Data to the Public: HapMap Will Help Identify Genetic Contributions to Disease (August 2, 2007) http://www.sanger.ac.uk/Info/Press/2004/041213.shtml?;decor=printable (last visited September 30, 2007).

[141] For example: Bartha M. Knoppers & Yann Joly, *Our Social Genome?*, 25(7) Trends in Biotechnology, 284-288 (2007); Wellcome Trust, International Consortium Completes Map of Human Genetic Variation, http://www.wellcome.ac.uk/doc_WTX027367.html (last visited June 30, 2007).

[142] The CAMBIA BIOS Initiative: Biological Innovation for Open Society, Implementation Phase 2006-2008, (The CAMBIA BIOS Initiative) (2006), *available at* http://www.bios.net/daisy/bios/2029/version/default/part/AttachmentData/data/BiOS%20Initiative%20Phase%202006-2008.pdf.

[143] Gonzalez, *supra* note 104.

[144] CAMBIA, About BIOS (Biological Open Source) Licenses, http://www.bios.net/daisy/bios/398 (last visited June 30, 2007); Mulgan, Steinberg & Salem, *supra* note 87, at 60.

[145] BioForge: Biological Innovation, BioForge: An Online Community for Biological Innovation, http://www.bioforge.net/forge/kbcategory.jspa?categoryID=2 (last visited June 30, 2007).

cells. With respect to the adoption of open models in the field of stem cell research, the problems that may eventuate due to this discrepancy are significant.

First of all, while source codes can be protected by, among other forms of protection, copyright, biotechnological inventions are most often protected by patent. Copyrights can be obtained and maintained free of charge or very cheaply, patents are expensive legal tools. For example, it has been said that in the US, a patent application can cost 7,500 USD and defending a patent can cost up to 1.6 million USD.[146] These discrepancies in costs with respect to obtaining and maintaining protection of the research tools in computing on the one hand, and in biotechnology on the other hand, means that patent owners may be more reticent to the idea of giving open access to their inventions than source codes developers are.[147] It has also been noted that, as compared to copylefts that deal with copyrightable material, the corresponding copyleft-like licences for patentable materials can be extremely complex due to the nature of the innovation in question; for instance, the BIOS open licence, although still a work in progress, is described by one observer as being riddled with ambiguity and technicalities.[148] Confusing and complex licences could discourage researchers from adopting open methods of technology transfer.

Secondly, it is noted that software data is "modular and compartmentalised" such that it is easier to make improvements to certain parts of the program with only minimal and/or foreseeable repercussions on the rest of the program. In contrast, making modifications to biotech "hardware" can have unpredictable effects. [149] Moreover, since biotech research tools are not modular and compartmentalised, subsequent researchers may not be able to rely on previous output without some sort of standardization of the data.[150]

Third, the development and production of hardware in the field of biotechnology is much more capital intensive than for software. The amount of financial commitment to bring a biotechnological stem cell project to term is substantial whereas start-up and development outlays for software development are minimal.[151] Due to this difference in capital costs, it is said that biotechnology researchers would be less inclined to adopt open attitudes with respect to access to their work.[152] However, in response to this argument, scholars submit that the emphasis on the glaring difference in costs in the computing field versus the biotechnology field is exaggerated; it is argued that with contemporary advances in technology, the cost of doing wet lab or biotechnological research is rapidly decreasing such that the reluctance to adopt an open model in biotech cannot be entirely justified based on the capital costs of research.[153]

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[146] Gonzalez, *supra* note 104; Joly, *supra* note 23, at 388.

[147] Nicol, *supra* note 51, at 147.

[148] Gonzalez, *supra* note 104.

[149] Janet Hope, Open Source Biotechnology?, http://rrss.anu.edu.au/~janeth/OSBiotech.html (last visited June 30, 2007).

[150] Rai, *supra* note 36, at 149.

[151] Mulgan, Steinberg & Salem, *supra* note 87, at 17; Nicol, *supra* note 51, at 147.

[152] Rai, *supra* note 36, at 148ff; Hope, *supra* note 149.

[153] Hope, *supra* note 149.

Effects of Open Biotechnology on Public Health and Safety

Unlike with software, biotechnology researchers must abide by biosafety and biosecurity regulations having to do with, for instance food, drugs, tissue, or the isolation of stem cells. It has been argued that these regulated obligations may complicate the task of doing collaborative biotechnological research and consequently diminish the appeal of open models. A counter-argument is that software developers must comply with export laws and this has not stopped them from open sourcing programs.[154]

Thus, what is perhaps at the root of this issue is that, with respect to biotechnological research and unlike open sourced software, there is a fear that permitting open access to biotech innovations may pose threats to public health.[155] For example, if anyone can access the recipe for a very powerful drug or uncover the process for cloning human beings, then the careless or malevolent handling of this information could potentially put an uninformed population at risk. Of course, it is also said that no matter how much sensitive biotech information is protected, individuals with enough bad intent will find a way to access it. In any case, since in open biotechnological research the public's health and safety seem to be more vulnerable than in open source computing, it is argued that open models of collaboration may be less suitable for the former field.

Lack of Infrastructure to Support Open Models of Collaboration in Biotechnology

Another issue that computer software developers need not concern themselves with is infrastructure. Although the copyleft concept has been institutionalized in the open source software context (for example, the GPL), these types of legal mechanisms are not yet fully developed in biomedical research.[156] Although some open initiatives such as HapMap and BIOS have made use of copyleft-like principles to prevent the appropriation and patenting of public information, there is still a need for a more robust framework to ensure the viability of open models in biotechnological research.

The Importance of "Being Published"

In open sourced computing, innovation is uniformly disseminated through the public disclosure of source codes. Thus, the choice of "channel" of publication of information is a non-issue. Conversely, in the field of biotechnology, research results that are published in scientific journals or reviews are regarded with higher esteem than information that is informally published via, for instance, the internet. However, the problem lies in the fact that scientific journals or reviews may be reluctant to publish studies that rely on data that have already been informally disseminated: [157] if journals refuse to publish research based on openly disseminated

[154] *Id.*

[155] *Id.*

[156] Yochai Benkler, The Wealth of Networks: How Social Production Transforms Markets and Freedom, Chapter 9, (Yale University Press) (2006).

[157] Rai, *supra* note 36, at 144.

information, then such research, albeit valuable, may be ignored by the scientific community thereby defeating the purpose of using open approaches (i.e. to help research progress). However, since journals are likely to be sensitive to the need for open models of technology transfer, the right amount of pressure from researchers could convince them to publish work that has already been disseminated.

Conflicts of Interests between Technology Transfer Offices (TTOs) and Biotechnology Researchers

A final difference between software writing and biotechnology that may prevent the successful implementation of open models is the presence of conflicts of interests between TTOs and biotechnology researchers. TTOs are responsible for transferring intellectual property between universities, companies, and other organizations. These offices will often want to enforce intellectual property rights to maximize revenues from patent licence royalties.[158] This may conflict with scientists' interests in obtaining income from consulting fees.[159] In other words, if individual biotechnology researchers receive revenue by sharing their expertise with other users of the technology in question, then they will want to adopt an open model of collaboration to maximize their potential number of clients. However, this may clash with the university's/company's/organization's interest in obtaining royalties, in which case proprietary frameworks will be favoured. Should these two parties fail to agree on a primary goal, this conflict of interests could prevent the effective implementation of open models of collaboration in the context of biotechnological research.

The differences that exist between open source computing versus open biotechnology may complicate the adoption of open approaches in stem cell research. Moreover, to date, such models do not seem to have been widely used in the field of stem cell research such that it is difficult to assess their applicability and effectiveness. However, despite these uncertainties, some believe that the patent-related access to technology problems could be successfully resolved by open approaches of technology transfer due to their emphasis on "commons-based strategies".[160] The authors also suggest considering the use of open models of collaboration based on the benefits that they can bring to the field of stem cell research. Indeed, in addition to the benefits of open approaches enumerated previously, there are further advantages that would flow from the adoption of open approaches in the stem cell research environment.

B) Benefits of Open Models in Stem Cell Research

Economic Benefits

The literature has identified six main economic benefits of using open models in stem cell research. First, it could help lower

[158] Matthew Herder & Jennifer Dyck Brian, *Canada's Stem Cell Corporation: Aggregate Concerns and the Question of Public Trust*, 77(1) Journal of Business Ethics, 73-84 (2007).

[159] Rai, *supra* note 36, at 146.

[160] Herder, *supra* note 21.

the costs of technology transfer. Since R&D outlays are diminished and since research does not necessarily need to be patented, the costs of transferring technologies from one researcher to another can be much lower. Second, the open dissemination of projects will allow individual researchers to be more quickly and easily aware of what information has already been made available. Thus, scientists will know not to duplicate research on issues that have already been explored by others. Third, there may be a development of a market for complementary goods and services. By openly publishing stem cell research results, companies could bolster the marketability of their complementary proprietary goods.[161] Fourth, the use of open models could improve a company's reputation. Allowing fellow scientists free access to research results could strengthen a company's social and technical reputation[162] in turn increasing its overall appeal to consumers. Fifth, since the research burden is spread out among a group of contributors, open approaches have the ability to keep R&D costs low.[163] It should be noted that R&D outlays also include the costs of taking the risk of investing in expensive and potentially unprofitable projects. Sixth, open source could eliminate or significantly diminish the need for negotiations. It has been argued that patents slow the transfer of technology partly because obtaining licences involves negotiation.[164] In open models, since there are often no patents, obtaining necessary upstream information does not require any time-consuming negotiations.[165]

Social Benefits

The social reasons for adopting open models of technology transfer are also compelling. Since open models of collaboration allow researchers to view and vet each other's work more quickly and accurately, individual scientists may earn greater respect for their work from their peers because many people will have had the opportunity to appraise its quality.[166] Moreover, since open projects allow everyone to view each other's work, participants may feel encouraged to work harder in order to gain recognition from their target audience (i.e., peers, the labour market, venture capital communities).[167] Finally, open models could assist in promoting healthcare in developing countries; because the research burden is spread out among a group of contributors, open approaches have the ability to keep R&D costs low.[168] This being said, open models of collaboration that encourage the participation of developing countries will

[161] Janet E. Hope, *A New Way to Manage Scientific Intellectual Property*, 18(1) GeneWatch Magazine, (2005), *available at* http://www.gene-watch.org/genewatch/articles/18-1Hope.html (last visited June 30, 2007).

[162] Hope, *id.*

[163] Rai, *supra* note 36, at 138; Mulgan, Mulgan, Steinberg & Salem, *supra* note 87, at 16ff.

[164] Constance Holden, *US Patent Office Casts Doubt on Wisconsin Stem Cell Patents*, 316(5822) Science, 182 (2007).

[165] Hope, *supra* note 105, at 99.

[166] Josh Lerner & Jean Tirole, *The Economics of Technology Sharing: Open Source and Beyond*, 19 Journal of Economic Perspectives, 104 (2005).

[167] Joly, *supra* note 23, at 402-404.

[168] Rai, *supra* note 36, at 138; Mulgan, Steinberg & Salem, *supra* note 87, at page 16ff.

allow these countries to build upon their own medical research at a low cost.[169]

7. CASE STUDIES OF CONTEMPORARY COLLABORATIVE MODELS IN STEM CELL RESEARCH

This analysis will seek to gather empirical evidence on the successes and failures of collaborative projects in order to gauge the extent to which the introduction of open models would be beneficial to this field.

A) Aggregate Therapeutics Inc. (ATI) (originally called StemNetCo)

Year of Creation: 2005

Current Stage of Development: Operational

Type of Funding: Formally public funding, now a mix of public and private funding

General Description: ATI used to be the Stem Cell Network's for-profit commercialization arm. The Stem Cell Network is part of Canada's Networks of Centres of Excellence, collaborative science and technology research enterprise. The Stem Cell Network has recently partnered with the MaRS Discovery District[170], a non-profit networking corporation whose mission is to encourage collaboration between the science, business, and capital communities. The Stem Cell Network has in effect relinquished control of ATI to MaRS who now ensures its continued funding and management.[171]

ATI holds exclusive first commercialization rights to development-stage stem cell therapies from thirty-seven Canadian scientists at sixteen universities and research centres in exchange for making these contributors company shareholders. The company then streamlines the process of developing stem cell therapies by "aggregating complementary technologies and leveraging them across a common development platform, management team and source of capital."[172] Finally, it licences these bundles of rights out to industry. All technologies remain available for research purposes by scientists of the Network.[173]

Method of Technology Transfer: ATI is an intermediary between researchers, their institutions, and the market place. It contributes to the relationship by adding commercialisation

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[169] For example: Maurer, Rai & Sali, *Finding Cures for Tropical Diseases: Is Open Source an Answer?*, 1(3) PLoS Medicine December, e56 (2004).

[170] MaRS, About MaRS (2007), http://www.marsdd.com/About-MaRS.html (last visited September 30, 2007).

[171] MaRS Discovery District, New Partnership Leverages Promising Canadian Stem Cell IP: MaRS and Canadian Stem Cell Network Partners in Transnational Development Company Focused in High Growth Area of Regenerative Medicine (April 11, 2007), http://www.marsdd.com/News/Press-Releases/2007/Stem-Cell-Partnership20070411.html April 11 2007 (last visited September 30, 2007).

[172] *Id.*

[173] Networks of Centres of Excellence Canada, Stem Cell Network: NCE Spin Off Company Partners with Investigators and Universities to Bring Regenerative Medicine to Market (December 7 2006), http://www.nce.gc.ca/pubs/ncenet-telerce/dec2006/scn-dec06_e.htm (last visited September 30, 2007); Stem Cell Network, Catalyzing: Commercialization (August 25 2005), http://www.stemcellnetwork.ca/success/commercial.php (last visited September 30, 2007); MaRS Discovery District, *Stem Cell Network Teaming with MaRs to Accelerate Commercialization Efforts*, 21(7) Research Money, 3 (2007); Aggregate Therapeutics Inc. *License Agreement Template* (Aggregate Therapeutics Inc.: Ottawa, 2005-2007).

expertise and by helping to leverage and aggregate promising technologies. In certain respects, ATI is similar to a patent pool: ATI collaborators bundle their patents and agree to let other members of industry use and improve upon their bundled technologies in consideration for a percentage of the licensing fees.

Benefits Provided to the Scientific Community and the Public at Large: To date, the Networks for Centres of Excellence and ATI account that the project has identified over sixty-five new technologies[174] based on stem cells from the skin, pancreas, retina, and bone marrow and has optioned or licensed out eight of them. The ATI team reports that two of these discoveries in particular, namely skin-derived precursor cells and new treatments for diabetes, are "breakthroughs".[175] Moreover, it is looking to secure between ten and twenty million USD to finance further commercialization efforts and expects to launch its first regenerative medicine product within five years.[176]

Finally, ATI is also playing an important role in supporting the members of the scientific community in their endeavours by informing them of the different aspects of the commercialisation process and by lending expertise to university technology transfer offices.

However, as vibrant as the company seems, others are not convinced of the benefits of this new technology transfer model. Herder and Brian contend that ATI's commercialization activities are problematic because they benefit the company's *share*holders, i.e. the contributing researchers, but at the expense of its *stake*holders, the Canadian public that expects to benefit from new stem cell therapies. Herder and Brian explain that this "breach of public trust" occurs for three reasons: first, conflicts of interests may arise because whereas the public is anticipating great medical benefits for society at large, ATI only has an interest in developing the technologies that will generate the most income; these interests will obviously not always necessarily coincide. Secondly, and as a consequence of the first point, a breach of public trust may arise because of the corporate-driven nature of research. Since ATI's research efforts will be spurred by the financing of corporate venture financiers, the technologies produced with these patented tools will only be those that can recoup high profits. In other words, the products developed using technologies licensed from ATI might not be amenable to distribution in a publicly-funded healthcare system, the system that most citizens depend on for care. Thirdly, it is contended that the taxpayer will be forced to pay twice for the same end-product; once to fund the research and again to obtain the actual technology. In short, according to Herder and Brian, the combination of these three issues could result in a perception that ATI is breaching the Canadian public's trust.[177]

[174] Aggregate Therapeutics Inc., Portfolio (2007) http://www.aggregatetx.com/ (last visited September 30, 2007).

[175] Aggregate Therapeutics Inc., Featured Technologies (2007) http://www.aggregatetx.com/ (last visited September 30, 2007).

[176] Networks of Centres of Excellence Canada, Stem Cell Network: NCE Spin Off Company Partners with Investigators and Universities to Bring Regenerative Medicine to Market (December 7, 2006), http://www.nce.gc.ca/pubs/ncenet-telerce/dec2006/scn-dec06_e.htm (last visited September 30, 2007).

[177] Herder & Brian, *supra* note 158.

However, this negative review of ATI has been contested. Indeed, one author contends that government funded initiatives do not normally guarantee "a specific return on that public investment"; thus, expecting ATI to produce stem cell therapies to benefit the entire Canadian public is unreasonable.[178] This debate illustrates the difficulty of promoting commercially sustainable models of stem cell technology development all while avoiding the ethical pitfalls attributed to research commercialisation. However, with respect to public institutions involved in fundamental stem cell research, ATI's system of technology transfer is nevertheless a model worth exploring and perfecting.

B) The International Stem Cell Forum (ISCF) and the International Stem Cell Initiative

Year of Creation: 2003

Current Stage of Development: Operational

Type of Funding: Mix of public and private international organizations

General Description: The United Kingdom ISCF consists of fourteen funding organizations that are committed to the advancement of stem cell research through collaboration and funding support. Since its inception, the ISCF has launched four major projects to address key issues: (1) the standardisation of criteria for characterisation (i.e. identification) of stem cell lines; (2) an analysis of the different national ethical policies relating to stem cell research; (3) an analysis of the different national intellectual property regimes; and (4) the development of the ISCF website to facilitate the diffusion of information on stem cell research.[179] The parameters of research objective (1), otherwise known as the International Stem Cell Initiative, seem most akin to a collaborative model of technology transfer because, unlike the other three projects, the characterisation project involves scientists from six different countries contributing research results in order to draw up globally agreed criteria for characterising stem cell lines

Method of Technology Transfer: All the information produced by the project will be made publicly available on the ISCF internet registry.[180] One of the other Initiative's leaders has stated that "our central aims are to provide openness and reliability; and to enable scientists to reproduce and extend each other's work." [181] Indeed, the Initiative has already "established a comprehensive registry of cell lines and their molecular characteristics which is soon to be made freely available to the wider scientific community."[182] In other words, it seems that the Initiative

[178] Chris Macdonald, The Business Ethics Blog: Aggregate Therapeutics and profit for Publicly Funded Research (March 1 2007), http://www.businessethics.ca/blog/2007/03/aggregate-therapeutics-and-profit-from.html (last visited September 30, 2007).

[179] International Stem Cell Forum, Forum Initiatives (2007), http://www.stemcellforum.org.uk/about_the_iscf/forum_initiatives.cfm (last visited September 30, 2007).

[180] International Stem Cell Forum, Project Overview (2007), http://www.stemcellforum.org.uk/registries_&_banks/characterising_cell_lines/project_overview.cfm (last visited September 30, 2007).

[181] Medical Research Council, Agreeing What Makes a Stem Cell (February 3, 2007), http://www.mrc.ac.uk/NewsViewsAndEvents/News/MRC003489 (last visited September 30, 2007).

[182] *Id.*

will rely on the public domain to disseminate its findings.

Benefits Provided to the Scientific Community and the Public at Large: The ISCF reports that the Initiative has already completed phase one of five phases in the characterisation project: (1) UK Stem Cell Bank acquires and prepares antibodies for distribution to participating laboratories; (2) Recruitment of participant laboratories; (3) Experimental work; (4) Analysis of results; (5) ISCF workshop to discuss results and reach consensus on conclusions, followed by publication on ISCF online registry. Moreover, according to the ISCF's chair, funding organizations are continually joining the Forum in a concerted effort to advance stem cell research.[183]

However, the fact that this project uses the public domain to transfer its technology can be problematic because of the risk of the appropriation of upstream work by a downstream scientist. The concern is that,

with publicly available databases, commercial providers would find large sections of readily available information that can be repackaged and resold as part of a commercial database. [Release of information into the public domain] is extremely useful for future researchers, but it does little to curb the further commercialization of the data.[184]

In other words, the downstream user looking to make financial gain from this freely available information need only make an improvement of any type to the data, and then impose restrictions on the entire block of information by way of contractual clauses (or a *sui generis* right in Europe); anyone viewing this new database must agree not to copy the information for their own purposes. However, if the use of the improvement is crucial for further research, these clauses could potentially halt the chain of progress. Therefore, the use of the public domain may not be the best vehicle for the dissemination of ISCF's because profiteering individuals could slow the Initiative's progress in identifying universal criteria for the characterisation of stem cell lines.

C) The WiCell Research Institute and the National Stem Cell Bank

Date of Creation: 2005

Current Stage of Development: Operational

Type of Funding: Federally funded

General Description: The US WiCell Research Institute is a subsidiary of the WARF and is committed to studying the scientific and medicinal potential of stem cells. In 2005, the National Institutes of Health (the primary federal agency for conducting and supporting medical research in the US) awarded the Institute the "National Stem Cell Bank" contract which made it the country's only repository for hESC that are listed on the NIH's Registry and therefore eligible for federal funding. The patent holders of these stem cell lines are located all over the globe but the National Stem Cell Bank inventories thirteen of the twenty-one hESC lines eligible for federal funding in the US.[185]

[183] *Id.*

[184] Gonzalez, *supra* note 104, at 324.

[185] Jill Ladwig, A Scientific Treasure for the Future, WiCell Journal of Stem Cell Discovery, 7-11 (Winter

The National Stem Cell Bank's mandate is to:

> acquire, characterize and distribute the 21 cell lines on the NIH Registry, and to provide technical support to researchers who work with the cells at academic and non-profit institutions. […The goal is], with the agreement of the cell owners, to maintain, produce and distribute these lines to the research community.[186]

To do so, the Bank aggregates the cell lines, performs sophisticated characterization research on them, and subsequently standardizes the results for further use by other scientists.[187]

Method of Technology Transfer: The National Stem Cell Bank incorporates the characteristics of a clearinghouse. Among other roles, it catalogues stem cell lines in view of simplifying the process of finding and negotiating stem cell licences. By consolidating the majority of hESC lines that are eligible for federal funding and by standardizing characterization protocols, the Bank is effectively performing the functions of a clearinghouse for academic or non-profit inventors seeking to perform downstream stem cell research.

Benefits Provided to the Scientific Community and the Public at Large: In fulfilling its mandate, the Bank has been commended for lowering the transaction costs associated with, and thereby facilitating the process of, transferring stem cells to scientists.[188] Moreover, in February 2007, the Bank teamed up with the U.K. Stem Cell Bank to maximize efforts in creating international standards for the isolation of hESC and in distributing the stem cell lines.[189]

D) Possible Applications of Open Models in Stem Cell Research

These case studies are a tribute to the relative success of collaborative models of technology transfer in the field of stem cell research. To be sure, several issues must be addressed in order to maximize progress in each of the aforementioned projects. But, given the current successes of these endeavours, it nevertheless seems that both the scientific and lay communities would be receptive to the introduction of another technology transfer model that is perhaps the most collaborative of them all, the open model.

That is not to say that open models should completely replace intellectual property rights in stem cell research. On the contrary, property rights should still have an important role to play. However, these traditional proprietary schemes ought to be reconsidered from a collaborative point of view so that each project's respective goals may be effectively achieved all while maintaining the

2006), *available at* http://www.wicell.org/index.php?option=com_content&task=category&sectionid=7&id=233&Itemid=240; University of Wisconsin-Madison, National Stem Cell Bank Announces Addition of New Cell Lines (September 19, 2006), http://www.news.wisc.edu/12890 (last visited September 30, 2007).

[186] Ladwig, *supra* note 185.

[187] *Id.*

[188] National Institutes of Health, NIH Awards a National Stem Cell Bank and New Centers of Excellence in Translational Human Stem Cell Research (October 3, 2005), http://www.nih.gov/news/pr/oct2005/od-03.htm (last visited June 30, 2007).

[189] Medical News Today, US, U.K. Embryonic Stem Cell Banks to Announce Partnership to Promote Research, Create Standards (February 16 2007), http://www.medicalnewstoday.com/medicalnews.php?newsid=63078 (last visited June 30, 2007).

free flow of new and valuable information. From this perspective, the commercial goals of industry and the scientific goals of academia can be more effectively balanced. For instance, one could conceive using open models at the early development stages of stem cell technologies and proprietary schemes once the basic technology has been perfected. In this way, the entire scientific community would be able to both access the basic technology and then profit from individual improvements made to it. By the same token, the crucial foundational research would not be delayed thereby allowing clinical adaptations of the technologies to be released in a timely manner. Or, another possibility is a hybrid technology transfer scheme: maintain traditional property rights but incorporate certain "open" elements into the licenses. In other words, although a stem cell invention would be subject to a patent (for the financial benefit of the inventor), the inventor would allow unrestricted access and use of it on the condition that any subsequent improvements be made publicly available (for the academic benefit of the research community).

CONCLUSION

This article explored the interplay between proprietary and open technology management mechanisms and their respective effects on the advancement of stem cell research. It was seen that the conventional intellectual property rights scheme is currently under fire because of the potentially negative effect it may be having on technology transfer and thus, on scientific progress. However, due to the unconfirmed nature of these critiques, the collaborative technology transfer solutions put forth by some scholars to address these concerns could be somewhat premature and misdirected.

This article posits that collaborative models of technology transfer should be considered for their remarkable ability to maintain or increase the pace and quality of scientific development in stem cell research rather than for their potential to fix problems that do not empirically exist. In light of this scientific field's logistical constraints and its current stage of development, the open model appears to be a particularly suitable collaborative method of technology management for stem cell research. Moreover, case studies of successful ongoing collaborative projects suggest that an eventual introduction of open models could yield more positive results. In retrospect, although not an outright substitute for the proprietary protection regime, open models could be used in conjunction with traditional intellectual property rights to ensure that society will reap the benefits of this potent field of knowledge. Integrating open models in the field of stem cell research could also revive the humanitarian approach to academic sciences that has, of late, been weakened by commercial pressures. Indeed, an over reliance on the patent system in key medical research fields could result in more than foundational innovation being lost down the rabbit hole.

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