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Canada's Science: An Ethnography of Ethics and Expertise in Stem Cell Biology

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CANADA'S SCIENCE: AN ETHNOGRAPHY OF ETHICS AND EXPERTISE IN STEM CELL BIOLOGY

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A DISSERTATION
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OF DOCTOR OF PHILOSOPHY

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ABSTRACT

In a series of experiments performed at the Princess Margaret Hospital in Toronto in 1961, Drs. James Till and Ernest McCulloch, a physicist and a hematologist, first demonstrated the existence of stem cells. The advent of human embryonic stem cell research in 1998 spurred Canadian scientists and the Canadian government to build on the country's research capacity in the field. At the same time, the government put in place a policy framework which criminalizes certain human embryonic stem cell experiments. Canadian stem cell science is currently a vibrant research field involving different types of cells and many different lines of research and it remains a funding priority, despite this relatively strict policy on human embryonic stem cell research. Drawing on two years of fieldwork, this dissertation traces the experiences and practices of stem cell scientists, policy researchers and institutional experts in research review and in commercialization as they make and remake the meaning and legitimacy of stem cell science. I explore their morally inflected experiences and modes of analysis as they work to turn stem cell science to medical benefit. To understand how Canadian stem cell science has maintained government and public support, I investigate the conditions in which stem cell research is conducted and shaped in four domains of meaning and practice: that of scientists engaged in research who are concerned with the scientific validity of their results and the credibility of their visions, that of the institutional ethics bureaucracy which certifies research as conforming to Canadian values, that of policy experts trying to steer stem cell science away from potential controversies and, lastly, that of commercialization experts working to move research out of the academy to the benefit of patients without activating public concerns over commercial agendas and profits.

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This dissertation builds on the coursework completed within and without the Anthropology Department under the direction of Jim Boon, Abdellah Hammoudi, Carol Greenhouse, Carolyn Rouse, Rena Lederman and João Biehl in Anthropology, Amy Borovoy in East Asian Studies and Angela Creager in History of Science, professors who will remain an intellectual guide throughout my career.

For first introducing me as an undergraduate in Princeton's Anthropology Department to the possibilities in the study of science for an anthropologist, I thank Emily Martin. Working as an M.Phil. student under the supervision of Marilyn Strathern at the time of Dolly the sheep was a stimulating experience that continues to inform my work.

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Table of Contents

Abstract iii
Acknowledgements iv
List of Abbreviations vii

Introduction.
Researching Researchers 1
Contextualizing Stem Cell Science 11
"Stuck North of the 49th" 16
The politics of Stem Cell Science 19
Anthropology of Emerging Sciences 22
Outline of the Chapters 25
A Methodology for Culturally Complex Systems 27
Methods 30
A Future-Oriented Enterprise 38

Chapter 1.
Becoming Regulated: Beyond National Policy 41
Realizing a Concept, Introducing a Paradigm 45
The "Promise" of Stem Cells and the Excitement of Discovery 47
Dr. Franks 53
Experiments and "Exceptional Oversight" 57
"Science Moves Where the Data Lead You" 60
"We do not Feel These Constraints" 63
"You Never Know Until You're There" 67

Chapter 2.
Becoming Innovative: Multiple Temporalities and Measurable Outcomes 79
A biology of Time 82
Visiting the Lab 84
Return to the Lab 87
(Not) Growing, Differentiating, Proliferating 91
"The Whole Science is Changing:" Growing Knowledge, Growing a Field 95
The Tempo of Innovation 100
"Deliverables" 101

Chapter 3.
Becoming Ethical: Research Review and Bioethical Rationalities 107
Obtaining Ethics Approval 113
Studying the REB 120
"Bad Science is Unethical Science": Research Review as Common Sense 126
Dr. Patel: "Science Done Well" 136
Science in Society, Society in Science 140
Global Others 145

Chapter 4.
Becoming Custodians: Foresight and the Shifting Practices of Procurement 151
The ISCF.....156
Cellular Models.....163
"Who's Working on Your Disease? You Want to Know, Right?".....170
Anticipation, Consent and the Limits of Risk.....172
Bureaucratic Anticipation.....178

Chapter 5.
Becoming Entrepreneurial: Strategizing, Collaborating and Recognizing Value 180
Technology transfer: Between the Academy and the Market.....182
Patenting: Navigating "Muddy Waters".....189
Comparisons: Technology transfer, Health Canada, REB.....194
The CCRM and John Hu.....200

Conclusion.
"Canada's Science".....212

References.....217

List of Abbreviations

AHR Assisted Human Reproduction Act
CCRM Centre for the Commercialization of Regenerative Medicine
CECR Centres for the Commercialization of Research
CIHR Canadian Institutes of Health Research
ELSI Ethical, Legal, Social Implications of Science
EWP Ethics Working Party
FDA Food and Drug Administration
hES Human Embryonic Stem
IPS Induced Pluripotent Stem
IRB Institutional Review Board
ISCF International Stem Cell Forum
IVF In Vitro Fertilization
MTA Material Transfer Agreement
NCE Networks of Centres of Excellence
NIH National Institutes of Health
PI Principal Investigator
REB Research Ethics Board
SCOC Stem Cell Oversight Committee
TCPS2 Tri-Council Policy Statement, 2nd Edition
WHO World Health Organization

Introduction

Researching Researchers

On the morning of day three of the World Stem Cell Summit in Pasadena, California in 2011, I sat in a small room in the Pasadena Convention Center, listening to a panel discussion. The Summit's agenda that morning was broken into several concurrent sessions labelled "Society," "Science," "Progress" (for science on the path to clinical application) and "Industry". I was at the "Society" session and it was on stem cell tourism, the phenomenon of people traveling to "foreign" unregulated clinics to receive unproven stem cell treatments. The room and audience were small, the atmosphere more informal than the ballroom addresses. The session was well-attended. Led by the Scientific Director of a large international organization for the promotion of stem cell research and an American professor of bioethics, the panel discussed how best to combat the proliferation of clinics operating outside of the mainstream of scientific research and regulatory oversight and offering ineffective and potentially dangerous treatments. When the discussion was thrown open to questions, a man stood up and challenged the speakers. His daughter was seriously ill. - "We are considering various options," he told them. He asked how the panel's scientists knew that these clinics' claims were fraudulent. There was a brief bemused silence as the panelists struggled to understand and respond to the question.

Expressions of concern over unregulated clinics from bioethics and policy quarters frame their emergence as a problem created by unethical mavericks and shysters exploiting vulnerable patients with bogus treatments but that implicates legitimate

scientists who could do more to educate the public and combat the dangers of stem cell "hype". (Bharadwaj 2012: 312) Implicit in the comments of the panel were notions of legitimate, mainstream stem cell research and one of its Others – the suspect science of "snake oil salesmen". To the panel, the difference between the two was obvious. One cannot assume that scientists at unregulated clinics adhere to basic epistemic scientific norms in their research and this makes the odds of their producing good science and effective therapies vanishingly small. Watching from the audience, what I saw in that moment of challenge was a close affinity of the expert knowledges - biomedical science, ethics and policy - on view and an apparently shared sense of moral order.

This was one of the few moments of fieldwork in which deeply conflicting understandings of the world were made visible; indeed, it was the only lay challenge to expert knowledge that I witnessed. Yet the most recent period of stem cell science began with intense controversy when, in 1998, American developmental biologist James Thomson developed a technique for creating human embryonic stem (hES) cells by removing cells from inside 6-day old embryos and culturing them (growing them in the laboratory in a nutrient substance and under controlled conditions). Thomson used embryos left over from IVF treatments under informed consent. (As congressional restrictions on federal funding for any research use of embryos were in place at the time, his research used private funds.) hES cell research quickly became a publicly contentious issue in many countries because it relies on destroyed human embryos and debate largely centred on the embryo's moral status.

In the years following Thomson's creation of hES cells, research involving human embryos has been subject to particular social and bioethical scrutiny. Many countries put

laws or policies in place to control or ban certain research practices. Although there is considerable variation among countries, some national policies are relatively liberal (and permit most technologies), some more restrictive (with prohibitions on hES cell research or allowing research only on imported hES cell lines) and some, like Canada, take an intermediate approach allowing hES cell creation and research but with restrictions and state oversight (Isasi and Knoppers 2006).

In the US, there are widely varying state policies on hES cell research from restrictive to permissive, as in California which famously responded to the federal restrictions in place in the US in 2004 by putting stem cell science to the vote. The people of the state voted yes, thereby authorizing an amendment of the state constitution and the allocation of three billion dollars of public bonds for stem cell research. Despite state differences, legal challenges and a tumultuous history of policy reversals (in 2009, President Obama signed an executive order overturning Bush's ban on federal funding for new human ES cell lines), the US is the leader in the stem cell field, with American stem cell research currently supported by federal and private funding, philanthropic donations and some state funding. Without a federal policy, where there are no state laws, privately funded stem cell research is unregulated in the US. The other countries that are most often cited as leaders in stem cell research include the UK, Canada, Israel, Australia, Japan, Singapore and South Korea. All of these countries have a more permissive approach to stem cell science except for Canada. Canada has a federal law addressing embryo research and using criminal sanctions which makes its policy relatively strict.

The kind of policy regime in place in Canada does not seem to correlate

particularly closely with its degree of research activity. Despite the country's relatively stringent policy framework, by all measures, the Canadian academic stem cell field is a vital and ongoing concern. Graduate programs in stem cells and regenerative medicine are on the increase, as are the number of students entering the field. Stem cell science is a focus of significant government investment and newspapers regularly report new funding announcements. In 2014, for example, the Ontario government announced its support for a new provincial institute of regenerative medicine (Drinjakovic 2014). Most recently, in January 2016, Prime Minister Trudeau has promised twenty million in funding over ten years to create a stem cell therapy development institute (Canadian Press 2016). Canada appears to be holding its own on the global stage. An industry briefing on Canadian regenerative medicine from 2009 places Canada in the top five countries for number of Principal Investigators (PIs) (researchers leading funded lab projects) working on hES and adult stem cells, with the Toronto area comparable to Boston or to California (MaRS 2009). A 2011 Industry Canada publication counts 416 researchers working in stem cell science in Canada (Industry Canada 2011). Of those almost one half were in Ontario and the majority of those were at one large research university, the University of Toronto. While a significant presence internationally, Canadian stem cell scientists are small enough in number to have met many of their peers.

The impression that stem cell science is currently thriving in Canada was borne out in interviews with scientists who referred to it as a hot field and Toronto as a hotbed for stem cell science. One young researcher, Dr. Peter Wallace whom I interviewed in 2012, told me that he had seen an increase in the numbers of scientists trained in areas other than stem cell biology adopting stem cells as their cell model of choice. Peter had

completed his Ph.D. in a dedicated stem cell biology program in Toronto two years before our interview, working primarily with embryonic mouse stem cells, and had observed increasing numbers of biomedical researchers switching from model organisms like yeast or bacteria to stem cells.

Scientists think that stem cells will be useful for medical therapies because they are cells that can both replicate themselves and develop into other specialized cell types. Some kinds of stem cells can make only one or a few specialized cell types and some, like embryonic stem cells, are pluripotent which means that they can make all the cell types of the body. Researchers are exploring the potential use of all types of stem cells as therapies for a broad range of diseases and conditions including some of the most common like cancer, heart disease and Alzheimer's. In the most optimistic of visions, stem cell biology has the potential to revolutionize medical care. An increasing number of stem cell research projects in the countries most heavily involved in stem cell science are reaching early stage clinical trials. However, at the moment, stem cell research has not yet started to repay the hopes and funding invested in it; there have been few actual therapies produced. Bone marrow transplants that contain stem cells for patients with Leukemia have been in use since 1968. The last few years have seen stem cell therapies for other cancers and blood disorders and the use of stem cells for skin grafts. The Canadian public has seen the rise of stem cell banks like the Stem Cell and Marrow Network run by Canadian Blood Services as well as private cord blood banks charging parents thousands of dollars for their services. Press stories about the public stem cell banks encourage donations so that the banks might have the genetic matches needed to serve a diverse Canadian population. Overall, however, the medical benefits have not

appeared. An awareness of the lack of results pervaded my interviews with stem cell scientists. In a 2013 interview with a university commercialization expert, for example, when the discussion turned to the California public bond that funded stem cell research in the state, he spoke of the dangers of overpromising. The proponents of stem cell science in California, he told me, "are dealing now with the fact that they promised cures and they're still a long way off."

Another perceived drawback to stem cell research, frequently mentioned in financial literature, is uncertainty surrounding the regulation by the US Food and Drug Administration (FDA) and Health Canada of experimental therapies. A recent survey of Canadian stem cell scientists found that this was a recurring theme among researchers who felt that there was a need to better adapt regulatory requirements, such as those for clinical trials, to stem cell therapies (von Tigerstrom, Nguyen, and Knoppers 2012). My fieldwork also took place under the shadow of Geron, a California biotechnology company which began the first ever clinical trial involving a hES cell product for spinal cord injury. It was rumored amongst the scientists that Geron had submitted a forty-thousand-page new drug application to the FDA, the longest ever, and spent sixty million dollars to get their trial approved. It was front-page news when Geron, having survived safety concerns, abruptly discontinued its trial in 2011 citing lack of money and later sold its stem cell program.

Why then with its controversial beginnings, extraordinary oversight procedures and criminal sanctions, its few therapeutic successes and regulatory uncertainties, is Canadian stem cell science as healthy an endeavor as it is? Why does it today appear practically indistinguishable from other forms of biomedical research? Why has there

been little public controversy of late?

To answer these questions, I follow ethnographically the fates of notions and practices of ethics and of various types of expert knowledge as certain actors, procedures and species of disciplined reflection make and remake the field. For example, Canadian bioethicists and policy experts are discussing the effect on stem cell science of the stress on commercialization of academic research with the proprietary claims that this entails. They worry that commercial practices may be having a detrimental effect on sharing materials and information (Caulfield and Ogbogu 2015). Policy and legal experts are currently also paying particular attention to the intersection of stem cells, genetics and bio-banking – the practice of depositing donated patient data or biological samples into a central repository (Caulfield 2007; Knoppers and Zawati 2012). Cell lines can be made from donated patient samples and banked for research purposes. Banks are an important locus of both research and medical care. Their research use is understood to implicate the notion of patient privacy and to be putting pressure on traditional research ethics mechanisms like informed consent which are being viewed as increasingly unworkable for biobank research projects (Caulfield and Knoppers 2010; Dove et al. 2013). Legal and social science scholars are discussing how best to structure biobank governance which has emerged as the favored oversight mechanism in this context (Caulfield and Knoppers 2010; Gottweis and Zatloukal 2007).

This is a dissertation about how those working in Canadian stem cell research understand and creatively reconstruct the appeal and legitimacy of their field. It charts the current political and ethical contours of stem cell research as they are taking shape in publicly funded Canadian institutions. In this context, I have approached stem cell

research as an international endeavor that takes specific local forms as shaped by a range of global, national and institutional forces as well as by the personalities, imaginations and passions of the people involved. Stem cell science is an excellent phenomenon for anthropological study as it exists at the intersection of institutionalized knowledge practices, market forces and various regimes of research regulation and is freighted with bioethical sensitivities and imaginings of the future that are playing a formative role in the emergence of the field. Therapeutic visions, ethics regulations and commercial landscapes are influencing funding priorities and resulting in self-conscious experimentations with forms of governing stem cell science and with organizations that bring together infrastructure, expertise, and public and private actors in novel ways. This research sheds light on some of the key actors in Canadian stem cell science, their expertise, imaginaries and sensibilities, and the institutional structures which shape them and which they, in turn, help to shape.

Through interviews, I have explored the ways in which my interlocutors understand stem cells and science and society, their shifting ethical anxieties, experiences of bureaucratic temporalities and imagined futures. This research has also examined institutional actors' styles of reasoning and evaluating scientific knowledge as they are played out in two areas of "research management" - research review, the primary oversight mechanism for regulation of biomedical research and a practical application of bioethics, and technology transfer, the activity involved in facilitating research collaboration and commercialization. Bioethics I take to refer to a field of expertise on biomedical research and health care that is amenable to policy uptake and that is applied in various institutional settings where it principally involves decision-making. The

heightened scrutiny that stem cell research continues to receive makes stem cell research a particularly interesting corner of biomedicine in which to explore the articulation of bioethics with mechanisms of regulation and forms of governing.

It is crucial to attend to the role of institutions in mediating the many complex regulatory, cultural and political-economic forces that come to bear on stem cell science. In my analysis, I explore the links between the subjectivity of stem cell scientists and the institutional and bureaucratic contexts in which they live their professional lives and to bring into view a quasi-legal field that enables and subtends stem cell research. A critical ethnographic analysis suggests that the taken-for-granted could always be otherwise; in highlighting the contingent and the diversity of views and experiences amongst Canadian stem cell scientists, this analysis decenters dominant narratives of progress and humanitarian benefit and policy framings.

These were some of the guiding questions of my research: How are national and international regulatory mechanisms mediated by research management practices in universities and hospitals? How are they translated into local practices and with what effects on the stem cell research enterprise? What can attention to this bureaucracy reveal about contemporary institutional knowledge production on the one hand and the kinds of science taking shape on the other? How are bioethical paradigms shaping an emerging politics of stem cell research? If political processes addressing stem cell science shine a spotlight on basic questions of inclusion, how does institutional knowledge bureaucracy answer or reframe these questions?

I was motivated to concentrate on the research review scenario and technology

transfer practices because I was interested in the question of if and how regulatory mechanisms and associated institutional practices contribute to "shaping" science. Research review mediates regulations for the protection of human subjects in biomedical research and technology transfer, the endeavor to move knowledge “out the door” of the university or institute, is at the intersection of various regulatory mechanisms, primarily patenting and the decisions of regulatory agencies like Health Canada or the FDA. And these two areas of academic research management are the offices within institutions that engage most directly with the content and specificities of particular research projects. I was also responding to the realities of stem cell research today, much of which is at the level of basic science (whose goal is the understanding of phenomena and in contrast to applied science whose goal is the application of knowledge to practical problems). There are many regulations, policies and codes of conduct involved in managing knowledge production in today's research institutions; clearly such things as financial regulations and health and safety policies are vital to laboratory research. In choosing these two areas, I bring into the same frame distinct domains involving very different types of regulatory mechanisms in a juxtaposition that, I believe, illuminates the complexity of forces brought to bear on life sciences research as it moves into and out of university and hospital labs. Both forms of practice involve assessments, expertise, values and codified rules and depend crucially on ongoing human relationships. This makes them conducive to an anthropological enquiry attendant to meaning and the ways in which personality, understandings and experiences influence the course of events. This dissertation thus contributes to an understanding of bureaucracies experienced in a mode of collaboration rather than in encounter or resistance.

Contextualizing stem cell science

The development of the Canadian government's national policy framework for stem cell research dates to events in the field of reproductive technologies inaugurated by the first IVF baby (born in England in 1978) and to the concern of women's groups, religious groups and advocacy groups (Norris and Tiedemann 2011). The government created a Canadian Royal Commission on Reproductive Technologies in 1989 which eventually recommended statutory prohibitions on several specific practices relevant to hES cell research including the pursuit of human cloning, buying and selling of eggs, sperm and embryos and the creation of animal/human hybrids.

The legislative process started down a somewhat complicated path that was ultimately to include dead ends, advisory groups and varying degrees of public consultation. In 1997, the creation by cloning of Dolly, the sheep, added a sense of urgency to the process. In 2004, an Act Addressing Assisted Human Reproduction and Related Research (the AHR Act) was finally passed. It attempted to provide a comprehensive legislative framework for technologies related to reproduction that in some sense reflected Canadian society's values. It put into place the recommendations of the Royal Commission prohibiting the creation of embryos specifically for research but allowing hES cell research on donated supernumerary embryos left over from infertility treatments. It also prohibited human cloning under all circumstances and the creation of embryo chimeras. The prohibitions carry a potential prison sentence of up to ten years (Baylis and Herder 2009). The AHR Act's stance on hES cell research positioned Canada somewhere between the US at the time and the UK. In 2001 President Bush had restricted federal funding to research on cell lines that already existed and the UK had allowed the

creation of embryos for research up to 14 days after conception (and before the "primitive streak," an early developmental stage that happens on day fifteen in humans.) (Wertz 2002). All research on hES cells in Canada is subject to the AHR Act.

The AHR Act came into effect before the advent of reprogramming technology. Reprogramming technology makes specialized adult cells behave as though they were pluripotent embryonic stem cells. The reprogrammed cells are called induced pluripotent stem (iPS) cells. The first successful reprogramming technique of this kind was introduced in 2006 by Japanese biologist Shinya Yamanako (who, along with British scientist John Gurdon, received a Nobel prize in 2012 for his iPS work). Many scientists have since incorporated iPS cells into their research programs.

Policy positions and academic writing on science in Canada as elsewhere are dominated by the view that scientific innovation will bring social benefit and economic value and that the best way to encourage innovation is through encouraging the public and private sectors to work together. To this end, the Canadian government has been encouraging commercialization in publicly-funded science since the 1990s. Stem cell science is no exception; in Canadian universities and research institutes, particular stem cell research programs may be very far from therapeutic application, but the field as a whole is oriented towards medical benefit and actors are looking to industry for help in turning research into therapies.

The shifting relations of universities and industry are a perennial issue in scholarly studies of science, both those that take a normative approach and those that seek to describe analytically the workings and effects of such shifts. Social scientists have

been charting the various ways in which industry and commercial interests are increasingly playing a role in publicly-funded science (Fleising and Mather 2005; Rabinow 1999; Rabinow and Dan-Cohen 2005; Shapin 2008; Sunder Rajan 2006). In Canada, the ubiquitous rhetoric of innovation and entrepreneurialism has accompanied a flatlining of federal funding for basic research and there are perennial calls for increased funding for basic science. The Canadian Association of University Teachers' "Get Science Right" campaign, for example, opposes the government strategy of encouraging the convergence of academic research and industry and, specifically, what it views as corporate influence on the funding decisions of the three granting agencies. Advocates of basic research point to a 2015 budget analysis by a consulting firm that finds that the grant money available to academic researchers from the country's three funding agencies has not risen with inflation since 2009 (Semeniuk 2015). While the government is the main source of funding for research, as it has become scarcer, in particular for fundamental research with no immediate application in sight, competitions have become increasingly competitive and researchers apply for targeted funding grants, encouraging opportunistic applications. In this environment, academic scientists may be more willing to consider accepting industry funding of their research. Science commentators have also highlighted examples of the "muzzling" of federal scientists by the federal Conservative government (which was succeeded by a Liberal government under Justin Trudeau in 2015) and called it a "war on science." They worry that science is being compromised by corporate interests or political agendas.

In 1989, the Canadian government reorganized the structure of science funding, moving away from central organization in favour of "networks" of research institutions

(called the Networks of Centers of Excellence (NCE) Program) and emphasizing commercialization of research. In 2001, it created the Stem Cell Network as the country's organization for the funding and support of its stem cell community. The Stem Cell Network was understood to represent the interests and views of Canadian stem cell scientists, particularly in relation to the federal government with members giving testimony to the Parliamentary Standing Committee on Health during the years in which legislation on stem cell research was being debated. (The act passed in 2004). From its inception, the Network acted on its mandate to "translate" stem cell science to the benefit of Canadians not only by funding research on stem cells – biomedical and ethical, legal and policy research - but also by training young researchers, encouraging commercialization, promoting the field, creating technical consortia and databases, writing policy statements and providing expert advice, most recently, in testifying to the need for a national public cord blood bank.

The federal emphasis on commercialization and industry involvement continued in 2007 with the government's creation of non-profit Centres of Excellence for Commercialization and Research (CECR) of which there are currently twenty funded, including the Centre for the Commercialization of Regenerative Medicine (CCRM), created in 2011, where I also did research. An Industry Canada publication from 2007 summarizing the government's science and technology strategy cites a widening "productivity gap" between Canada and its largest trading partner, the United States, as evidence of a need to increase competitiveness through scientific and technological innovation, a theme continued in its most recent message on Canada's standing in the "global innovation race" (Industry Canada 2007: 8; Industry Canada 2016: 4). Like other

countries working towards strengthening their position within the "knowledge economy," the Canadian government emphasizes drawing the private sector into science and technology to commercialize basic research discoveries and innovate for economic and social benefit.

The Stem Cell Network's annual general meeting is the main stem cell scientific meeting in Canada and is called the Till and McCulloch Meetings after James Till, a biophysicist specializing in radiation biology and Ernest McCulloch, a medical doctor specializing in blood cells and leukemia who together demonstrated the existence of stem cells in mice. As I learned, almost every description of stem cell science in Canada contains a reference to Till and McCulloch. Till and McCulloch have become a rhetorical grounding for a narrative of a Canadian "founding" of the current stem cell field and bolster claims by organizations like the Stem Cell Network that Canada could and should be a current leader in the field. I had understood this to be nationalist rhetoric until I heard a Canadian stem cell scientist at the 2014 Till and McCulloch meetings describe a memorable moment that he had witnessed at a previous meeting when Alan Bernstein, a cancer and stem cell researcher who led the Canadian Institutes for Health Research (CIHR) from 2000 to 2007 and a former student of Till and McCulloch, looked around a room of researchers and asked "How many of you were taught by Till and McCulloch? Now, how many of you were taught by his students?" At this point, the scientist told us, almost everyone in the room had their hand raised. For many researchers, Till and McCulloch are forefathers who continue to influence stem cell science in Canada through their influence on successive generations of researchers.

"Stuck North of the 49th"

In 2012, a small controversy erupted in *Nature* over access to two hES cell lines created in Canada by stem cell scientist, Andras Nagy. Dr. Nagy was the first Canadian researcher to create hES cell lines which he did using donated surplus eggs from a Toronto fertility centre in 2003. The National Institutes of Health (NIH) have been keeping a registry of hES cell lines approved for use in US federally-funded research since the days when President George W. Bush authorized the use of 21 hES cell lines in 2001. So, Nagy applied to have his cell lines, called CA1 and CA2, added to the registry, submitting, amongst the documentation, a material transfer agreement (MTA) specifying terms under which other researchers could use the cell lines. Common in biomedical research, MTAs are legally enforceable contracts that accompany the transfer of research materials or data and that address rights, responsibilities, risks and benefits with regard to the researchers and institutions involved. In 2011, the NIH accepted Nagy's submission and added his cell lines to their registry which meant that they could be used by researchers with NIH funding. However, the MTA that Nagy had sent the NIH relied on the consent forms that he had used with the fertility centre patients in 2003 when he created the cell lines and those consent forms had a sentence stipulating that the cell lines could be distributed to other Canadian laboratories affiliated with the Canadian Stem Cell Network, a sentence which the NIH interpreted to mean that the cell lines would be eligible for NIH funding *only* at laboratories affiliated with the Canadian Stem Cell Network. This reading effectively restricted their use to Canadian scientists (2% of NIH funded research takes place in Canadian labs). The *Nature* report of the controversy featured a picture of CA1 stem cells with the caption "Stuck north of the 49th" (Dolgin

2012: 325).

The flap over Nagy's embryonic stem cell lines and the NIH registry might seem technical and bureaucratic but it draws attention to an administrative, legal and ethical apparatus that subtends biomedical research and involves researchers, staff, experts in knowledge management and documents like consent forms and MTAs which are used throughout biomedical research. Consent forms are the product of research review practices. The use of informed consent became established as one of the primary norms for ethical research involving humans over the course of the twentieth century. It is now the cornerstone of national and international ethics guidelines and has become prerequisite in a variety of institutional contexts. Before federally funded researchers can receive the funds and begin their work at a Canadian university or hospital, the institution requires them to obtain ethics approval. Informed consent terms attach to human biological materials, potentially constraining their research uses (to investigation of a specific disease, for example) regardless of their broader scientific or commercial potential, as Nagy's lines were initially understood to do.

Dr. McKenzie, a technology transfer officer at the research institute in which Nagy worked, had helped him create the MTA that had led to the NIH's restriction of the Canadian cell lines' availability. He agreed to be interviewed and we met in his office at the institute in 2013. Dr. McKenzie is an articulate, bespectacled fifty-year old with a background in cancer cell biology and over a decade of experience in technology transfer at the institute. It was not uncommon for my discussions with technology transfer staff during my fieldwork to remain largely hypothetical where stem cells were concerned. Dr. McKenzie, in contrast, had considerable experience assisting stem cell researchers at the

institute with their collaborations, industry partnerships and patent applications.

When we met, I had already interviewed Dr. Nagy the previous month and he had given little indication of the challenges and controversies he had faced while creating the country's first hES cell lines, preferring more general reflection on the relation of science and society. Dr. McKenzie offered a glimpse of the behind-the-scenes activity of Nagy's laboratory research and the institutional practices, documents and expert knowledges that accompany and enable biomedical research. It was Dr. McKenzie who told me about the kerfuffle over the NIH registry that he and Nagy had, he said, unintentionally started. McKenzie explained that the institute had carefully examined the process by which Nagy had obtained the eggs and that he and Nagy had worked out the terms of the MTA that accompanied the submission to the NIH such that it would meet the stipulations of the consent forms signed by the fertility centre patients and follow what rules and guidelines existed in Canada at the time. He pointed out that Nagy created his embryonic stem cell lines prior to the implementation of a national regulatory framework for stem cell research, when there was very little guidance available as to what to include in the consent forms. (In 2003 the AHR Act was being read by Parliament and consent regulations subsequently added to the Act were not in place until 2007.) They were, he told me, trying to make the two cell lines broadly available, not restricting access to Canadian researchers only.

To *Nature* readers, the idea that the Canadians were deliberately preventing US researchers from using Nagy's cell lines was a breach of the norms of sharing amongst scientific colleagues. The Nagy incident illuminates how central the research ethics apparatus is to biomedical science and just how sensitive the issue of sharing/excluding is

among researchers.

The politics of stem cell science

In a recent interview, British stem cell scientist Robin Franklin asserts a close connection between biology and politics and characterizes stem cell science as an heir to a left-leaning biology that privileges the environment over an essentializing understanding of genes. Pointing to evolutionary biologist Stephen Jay Gould as a forerunner of his own approach, he states that Gould emphasized biological potentiality and the role of the environment in response to the rise of sociobiology, the controversial application of evolutionary theory to human social behavior – "There are so many parallels between Stephen Jay Gould's work and what I do in my work now. Stem cells are similar in the sense that they have a whole diversity of possible things they can become, and the environment determines which of those possibilities the cells proceed along" (Wollenberg 2014: 45). I find Franklin's statements interesting because he is referring to his stem cell research as political in a way that the scientists of my fieldwork never did. The scientists that I spoke to never attributed to biological processes or properties political significance. (Nor did they ever mention stem cells in relation to evolution.) Their discourse was dominated by an instrumental view of stem cells, of how they could be manipulated for better health. Franklin contextualizes his work in a long-standing debate about genes vs. the environment which was absent from my fieldwork. As members of a field that has "growth", "paths" and "choice" as technical terms, Canadian stem cell scientists apprehended their research in terms of temporality and

complexity. Taking my cue from them, I use the notion of 'becoming' as developed by anthropologists João Biehl and Peter Locke– "the plastic power of people, worlds, and thought" (Biehl and Locke 2017; see also Biehl and Locke 2010) -- to analyze evolving dynamics of knowledge production and the politics of Canadian stem cell science as it is emerging through the efforts of scientists and others in the face of great uncertainty.

Reading Franklin's interview, I realized that for most people, when they think about the politics of stem cell science, they are thinking about political processes and entrenched and divisive positions, particularly in the US where stem cell science tends to be a partisan issue and linked to abortion in the public debate (Wertz 2002). I think of the Bush-era restrictions, legal challenges, pro-life language and high-profile research advocates of the US scene.

In this sense of "political", stem cell research has been less politicized in Canada than in the US. Although for some in Canada, embryonic stem cell research illustrates the need to protect the most vulnerable Canadians in the embryos imagined as potential citizens, at the same time, Canada's political make-up, as Michael Ignatieff, historian and scholar of human rights policy, has argued, results from a distinctive balancing act of the rights of national and minority groups on the one hand, and individual rights on the other (Ignatieff 2007). The discourse of individual rights that marks American debate about embryos – the right of the unborn child, a woman's right to choose, intellectual property rights, patients' rights – is inflected in a different way in Canada. In this regard, Canada is an interesting national setting for this project; despite its close cultural and economic ties to the US there has been much less public opposition to stem cell research.

Still, researchers saw their field as having been politicized by external groups concerned about embryo research. For example, while in Calgary in October 2011 to meet with stem cell researchers associated with the university, I interviewed Dr. Marks, a scientist at one of the few Canadian stem cell companies in existence at the time and whom I had heard speak at the World Stem Cell Summit in California not long before. A soft-spoken man in his 40s who spoke slowly and thoughtfully, choosing his words with care, Dr. Marks distinguished between ethics, which he considered a valid part of science, and religious or political convictions that should have no part in directing research. When I asked him about the AHR, he told me that political and religious will had been inappropriately injected into the Act: "It's probably not the right place to inject those opinions. Ethically, yes, but not morally or based on the will of the people, in a sense." I responded, "but it's still important to have ethical considerations included?" and he said, "essential, yeah, but ethics and religion are two different things, right?" I answered, "but the will of the people and ethics - aren't the ethical boundaries drawn by the people?" to which he replied: "Ah, no. Legislation and acts are historical. We see things like abortion law in the US turned and overturned and shifting every election. One could argue that that is not the will of the people. That is the will of whatever populous, sub-portion of the population drags it in one direction or another." This exchange suggests a notion of ethics independent of social or political history and raises various questions: who should make ethical decisions in a liberal democracy? What concepts of people and population are at play here? What kind of ethics is this, with what kind of temporality and what kind of politics does it imply? As the beginning of an answer to these questions, I will suggest that there is a dominant "evidence-based" notion of ethics

shared by scientists and bioethicists.

Anthropology of Emerging Sciences

Studies of science have long been pursued against a backdrop of larger questions about the place of science in liberal democracies with attendant questions of scientific governance and expertise in decision-making (Jasanoff 1994, 2005). Philosophers of science have turned to a recognition and normative analysis of values in science as epistemic, guiding methodological choices and evaluation of evidence (Douglas 2009). In my analysis, I have engaged scholars forming a strand of recent anthropological work that focuses on the entwined moral, political and epistemic in scientists' own contextualizations of their research and understandings of its significance by empirically exploring notions and practices of "good" science (Fortun and Fortun 2005; Hayden 2003; McCarthy and Kelty 2010; Sleeboom-Faulkner 2010; Thompson 2013). This work is part of a turn to the ethical in the production of scientific knowledge (Fischer 2003, 2005, 2007; Petryna 2005, 2009). These ethnographies approach the ethical as dialogically constituted amongst multiple actors and involving the creation of new institutional and infrastructural technologies like biobanks and databases.

This strand of ethnographies converges with a recent anthropological deployment of an analytic of uncertainty for emerging technocratic phenomena involving shifting forms of governing and new modes of assessment and prior decision-making that go beyond risk management (Collier and Lakoff 2008; Rabinow and Samimian-Darash 2015). Anthropologists Elise McCarthy and Chris Kelty, in a related study of

nanotechnologists, have charted the emergence of new conceptions and practices of collective responsibility as the much less studied complement to risk (McCarthy and Kelty 2010). Despite the cultural salience of responsibility and the fact that for scientists, "today, one must be responsible; one cannot dissent from the demand and still be considered a good scientist," they observe that "there has been little attempt to empirically specify the diverse practices emerging around it" (McCarthy and Kelty 2010: 426, 406).

Despite such ethnographies illustrating the way in which various actors are thinking about and acting on ideas of ethical practice in "emerging sciences," this can be overshadowed by bioethics practices which can appear in social science literature as a way of neutralizing public controversy around contentious practices in order to facilitate research (Stevens 2000; Thompson 2013: 64). Building on this ethnographic work, I attend to risk/benefit thinking as articulated by stem cell scientists and law and policy scholars and as deployed by research review boards and technology transfer professionals. My juxtaposition of bioethics and commercialization decision-making draws out the commonalities in their styles of reasoning, despite what is, organizationally, the siloing of expert knowledge in these different offices. I also attend to the ways in which the various actors articulate ways of being responsible such as to society for producing value and upholding Canadian values, to students for providing a safe and productive work environment and to human subjects for mitigating harm. The concept of responsibility is integral to ways of governing science as in the ideas of (individual) responsibility that inform national policies such as Canada's Responsible Conduct of Research (as its policy document on research misconduct was renamed in

2011) which addresses falsification of data and other breaches of research norms.

Anthropologist Sarah Franklin has pointed out the paradoxical ways in which stem cell research is both global and local, taking place in a transnational research space, generating universal findings, and provoking ethical governance in universal terms like human dignity at the same time that it is organized in specific places and has local forms (Franklin 2005: 61). She describes stem cells as a "global biological," in that they are part of the global enterprise of biotechnology but also because they are folded into totalizing narratives about identity and future cures. At the same time, she writes, stem cell technologies "demonstrate how biological properties are increasingly not only being 'discovered,' but are being created, in ways that reveal specific national and economic priorities, moral and civic values, and technoscientific institutional cultures" (Franklin 2005: 61).

This dissertation builds on such insights on global technoscience as it is subtended by institutionally specific policies and laboratory practices. It also engages with two further key paradoxes, the unremarkable, business-as-usual nature of current stem cell research after widespread controversy and morally irreconcilable positions and the malleability of embryonic stem cells which inspires great therapeutic hopes for the stem cell community while, at the same time, driving anxieties over the feasibility of those therapies and how Health Canada and other regulators will handle them. In the process, it describes exchanges of materials that are simultaneously collegial and legally defined through a written agreement and a move towards "personalized" research in the face of anonymizing, individualizing research ethics paradigms. I found the research questions and approaches in the stem cell field much more diverse than I had anticipated and the

ethics and politics of stem cell science form a different topography from the one that I had expected to find.

Outline of the chapters

As I quickly discovered, the "exceptional" Canadian federal policy response to hES cell science does not loom large in the lives of stem cell scientists and an analysis of state solutions to the question of how science should be governed in liberal democracies does not seem adequately to account for the "normalization" of Canadian stem cell research. Instead, the dissertation begins in Chapter One with a consideration of how my stem cell scientist informants understand the significance of stem cell science and their views of the national regulatory framework for stem cell research. Since the policy debate around the world on the topic of human stem cell research focused strongly on the creation of embryonic stem cells, I chart the range and variety of research projects and approaches currently using different types of stem cells. I analyze the appeal of stem cells for scientists and the kinds of manipulations of patient bodies that they are envisioning. Introducing an analytic of becoming, the chapter shows that scientists' ethical anxieties are clustering around how to satisfy general regulatory requirements covering the move from animals to humans rather than the regulations specific to human stem cell research. In Chapter Two, I use scientists' discursive uses of time and the various temporal registers of their research practices as a window on the norms of academic stem cell researchers and on the material realities of working with stem cells. The chapter explores the tensions in academic science between teaching and research and between

instrumental and exploratory research through a cultural study of scientists' experiences of time.

My fieldwork revealed that regulatory decisions of institutional experts about stem cell research are, in many ways, more consequential that those of state actors. The remainder of the dissertation therefore focuses on domains of expert representations and practices surrounding mechanisms of institutional knowledge bureaucracies that shape what and how stem cell science happens and how far towards the clinic it gets. Chapter Three focuses on my observations of research ethics board (REB) meetings as the primary institutional site of research regulation and legitimation. I argue that REBs deploy a characteristic mode of evaluation, a bioethics rationality of sorts that sees ethical implications as always already inherent to scientific experiments involving humans. At the same time, stem cell scientists and board members use notions of society and the public to articulate an outside or other to science. Chapter Four takes up the central issue of procurement of human materials. It explores the way in which bioethical concerns around the use of human materials in stem cell research have been addressed by the International Stem Cell Federation to elaborate on the idea that there is an impetus for scientists to align scientific knowledge, pragmatic values and bioethical concerns. The chapter introduces Canadian stem cell law and policy experts and innovations around the ethics of procurement which are leading to tensions with research ethics actors over the norms of informed consent. Chapter Five examines the activities of technology transfer staff as an understudied onsite location of consequential decision-making on research and of regulation through patenting and illustrates ways in which stem cell science has been inflected by a Canadian distinctness. It presents Dr. John Hu, a high-level executive at

CCRM, the organization designed to fulfill the role of technology transfer for stem cell discoveries.

In exploring the institutional practices and actors identified by stem cell scientists as affecting their work, the dissertation sheds light on what new configurations of stem cell science, government, bioethics, the university and the market are emerging today. Bureaucratic practices embody government, bioethical and market imperatives. At the same time, stem cell science is a site of experimentation with forms of governing science that rely on and pull away from the existing bureaucratic status quo.

A methodology for culturally complex systems

My analysis builds on the attention that critical anthropological thought gives to the human work and the contingent human choices that go into the making of science and to the social, cultural and political forces in which science is enmeshed (Hess 1995). In this dissertation, I understand scientific knowledge as contingent and socially produced in this sense. Anthropologists have also significantly rethought (or rejected) the "science and society" dyad (eg. Martin 1998) in ways that are sometimes echoed, sometimes countered in the analyses and reflections on science that informants offered me during fieldwork.

I also return to the notion of culture in my analysis. While some anthropologists have argued that traditional anthropological categories like culture are insufficient or need to be radically rethought to address complex biotechnological phenomena (Fischer 2009: Rabinow 1999: 181), culture continues to act, at the very least, as a heuristic

opening up areas of technical expertise like science, a challenging topic because of the privileged status of its knowledge and its technical nature. Anthropological analyses of reproductive and genetic technologies inspired my 1997 M.Phil. thesis, supervised by Marilyn Strathern, on Dolly the sheep as a technical event that was simultaneously a cultural phenomenon (Bonaccorso 2004; Carsten 2000; Edwards 2000; Edwards et al. 1999; Franklin 1997; Franklin et al. 1998; Thompson 2005). I found the anthropological concept of culture allowed for an insightful exploration of the event without privileging scientists' expert knowledge over lay understandings. It allowed me to approach both the scientists who created Dolly and the public who reacted to the news as reflective of shared cultural views. I have been interested since in technologically-mediated shifts in lay and scientific understandings of human reproduction and life and in the dualisms associated with nature/culture and science/society.

Two anthropologists whose work I have found most helpful for approaching "science as culture" are Emily Martin and Marilyn Strathern. In my reading of their work, Martin's analyses of the medical management of childbirth and of the cultural idiom of flexibility as it appeared in biomedical views of the immune system demonstrated that cultural assumptions could be excavated from scientific thinking and language (Martin 1989, 1994). Culture appeared as a repertoire of tropes and images. Methodologically, she approached science as part of a larger society and culture which meant that to understand biomedical views of the immune system involved multiple sites outside the lab in which the same sets of ideas echoed. In the work of Marilyn Strathern, culture referred to a technique of meaning making that relied on analogy and, more broadly, the manipulation of ideas in relation to one another. The act of comparing, she wrote,

"constitutes a making of connections, and evokes a metaphorical relationship" (Strathern 2004: 51). These uses of culture foreground the conceptual. They reveal knowledge as contingent, relational and situated.

Work in this vein is also reflexively implicated in the exercise. Indeed, that anthropologists share so many of the conditions and practices of knowledge production of science, law and other areas of rational-technical endeavor has recently become a point of departure for studies exploring institutional settings and bureaucratic knowledge and informational practices. While Latour and Woolgar in their famous ethnography of a laboratory emphasized the "inscriptions" of laboratory practice (Latour and Woolgar 1986), Donald Brenneis and others are focusing on bureaucratic practices like those of conference organizers, research ethics committees and grant reviewers that tend to form the unexamined background of research activities (Brenneis 2004, 2009, 2012; Meneley and Young 2005).[1]

In this project, I continue along the anthropological path of attending to the ways in which culture can elucidate the project of science and combine it with attention to the knowledge bureaucracy that generates REB applications, informed consent documents and MTAs. Anthropologists have recently explored the role of documents in a variety of bureaucratic contexts, from knowledge practices in academic institutions to state government (Cabot 2012; Riles 2006; Strathern 2004). Anthropologists approach documents not only as technologies that bring about particular ends but also as implicated in various forms of reasoning and as having their own aesthetic. Annelise Riles has

[1] Anthropological reflections on research ethics review include contributions to a 2006 issue of *American Ethnologist* and to a 2007 issue of *Political and Legal Anthropology Review*.

argued that documents are challenging to study because they are the material products of knowledge practices already too familiar to the anthropologist but can be made amenable to anthropological analysis through an analytic of aesthetics and form (2001). Similarly, to anthropologist Bill Maurer, ethical knowledge forms are difficult to analyze because they seem too familiar, too much like peer review, for example (Maurer 2005). Attention to documentary practices and an alertness to the specificity and agency of institutional technologies is a way to decenter the kinds of universalizing, naturalizing and depoliticizing claims made by bioethics.

It is perhaps not so much the familiarity of certain documents and practices that is a challenge but the quality of sameness in which they share. Anthropologists have traditionally defined their enterprise as the exploration of cultural difference and the presence of difference allows their relativizing tactics to generate insight. The challenge in studying science is as Michael Fischer puts it "to develop translation and mediation tools for making visible the difference of interests, access, power, needs, desires, anxieties, and philosophical perspectives" without necessarily approaching sameness as something to be revealed as actually difference. (2005: 55) Ethical and political logics lead to governing solutions emphasizing scientific integrity, accountability and transparency that look very similar wherever they appear.

Methods

Since Canadian stem cell scientists are geographically dispersed around the country, the fieldwork from which this dissertation draws took place in multiple

locations. From my home base of Toronto, I visited Ottawa, university towns in Southern Ontario, Calgary and Banff in Alberta and Montreal, Quebec. My field research took place roughly from the summer of 2011 to the summer of 2013 and had three main components.

I began my research in Ottawa investigating the federal regulatory response to assisted human reproduction and stem cell technologies and exploring the records of Parliamentary debates during the legislative process. With this background on the national policy framework for Canadian stem cell research and on the terms of the public and political debate of the time, I then made contact with Canadian stem cell scientists working in publicly-funded research institutions and with other academics prominent in the field of stem cell law and policy. I started with the Canadian Stem Cell Network, the country's primary organization and funding arm for stem cell researchers, and widened my sphere of contacts from there. This component therefore involved semi-structured interviews and ultimately included stem cell scientists (including one doing stem cell research for a company and one for a government agency), regulators, lawyers and research management actors specializing in such areas as (industry) “partnerships,” “commercialization” or “research ethics”. It included a teleconference interview with employees of Health Canada, and one former and one current member of the Stem Cell Oversight Committee (known as SCOC) at CIHR. Several Canadian stem cell scientists played an active role in the development of policy and regulation. Together with researchers in the legality, ethics and social effects of stem cell research, they bring their expertise to matters of “science and society” and are important advisers, consultants and committee members in a variety of policy contexts. Several of my interviewees had

provided expert testimony in Ottawa during the generation of the AHR Act. Some took part in educational and outreach initiatives, such as StemCellTalks, started by young scientists to introduce high school students to stem cell science.

When beginning research for this project, I focused on the most ethically controversial and high-profile aspect of stem cell science, embryonic stem cell research. Learning that Canada had exceptionally used the criminal code to prohibit certain experiments involving embryos made me want to explore stem cell scientists' views of the government's policy response to embryonic stem cell research. Learning then that the regulatory framework in place in Canada had gaps, overlaps, inconsistencies and confusions, that the statute had ambiguous wording[2] and that the province of Quebec was challenging large sections of it on the grounds of being unconstitutional made the problem I hoped to study one of how stem cell science had become "normalized" and continued apace in such a regulatory environment.[3]

[2] The AHR Act's treatment of cloning provides an example of ambiguities in the language for stem cell researchers. Cloning through somatic cell nuclear transfer is the transfer of a body cell into an egg cell from which the nucleus has been removed and which is then made to grow as if it were a fertilized egg. Creating human embryos in this way would allow stem cell scientists to take a cell from a patient and produce an embryo from which they could extract stem cells specific to that patient; in other words, it could prove to be a method that brings scientists closer to the goal of individualized medicine. Yet cloning is one of the activities prohibited by the AHR Act and carries a potential prison sentence of five to ten years. However, if a non-human egg cell is used as the receptacle for a human body cell, the result is classed by the Act as a hybrid, not an embryo, and is not regulated at all even though it has human content, so creating a hybrid in this way could be interpreted as legal. This seeming contradiction suggests that at the time Parliament was drafting the Act, scientists were not thinking about human-animal hybrids as a method of deriving stem cells.

[3] The constitutional challenge to the Act brought by the province of Quebec was, after a lengthy wait, decided by the Supreme Court of Canada in December 2010 in favour of the province. The Supreme Court ruled that much of the Act was unconstitutional as it was instantiating a federal ban of health care matters that were within the purview of the provinces. In agreeing that the federal government had overstepped its bounds in legislating on healthcare-related issues and that the provinces have authority to make their own decisions on issues such as the reimbursement of embryo donors or the licensing of stem cell research, the Court's ruling created some confusion and left the government agency designed to implement the legislation and regulations of the Act with very little to do.

I found that many of the stem cell scientists that I interviewed had opinions on the specific prohibitions of the AHR Act or on the governing of scientific research by law and policy. They described experiments that they thought might be interesting or eventually necessary to conduct but are either banned by the current regulations or fall through the cracks. Many commented on the current lack of regulation for iPS cells or the regulatory challenges on the horizon as they move toward therapeutic applications. However, I expected it to loom large in their lives and that I would tap into a vein of resentment and frustration. Instead, I found a more complex reality, one in which the path to clinical trials and the scientific interest of stem cells are more salient than the restrictions and additional oversight applied to the research. I soon learned that, on the whole, they do not feel that their own research has been adversely affected by Canada's stem cell research policy. As we discussed their workplace, they spoke instead of arranging for MTAs, filling out grant applications, thinking about the standards for pre-clinical evidence and working with students and industrial partners, all practices in which the institutional environment of their research plays a significant role. What emerged as particularly salient was the temporal shaping of their work life that many of these experiences engendered. I came to see stem cell researchers' experiences of their work as structured by multiple temporalities and in a way that inflected their sense of identity as a research community. Their experiences were also shaped by a range of emotions and desires which affected their understandings of regulatory mechanisms in complex ways. In an interview, one academic stem cell scientist spoke in turn of the desperation and suffering of patients and of enjoying the challenge of basic science, of liking “complex systems.” He objected to restrictions on his research whether from regulation or from

industrial partners and appreciated the relative lack of regulatory attention to iPS cells compared to hES cells as this had enabled him to forge far more international research collaborations. At the same time, he believed in the importance of talking about stem cell science with the public and expressed interest in what kinds of ethical and regulatory responses certain imminent technological developments in the field would receive. His views of regulatory mechanisms were therefore coloured by his enjoyment of research, their effect on his career, his belief in the moral imperative of stem cell science and a social analytic attuned to changing social mores.

While stem cell research has been "exceptionalized" within biomedical research and treated to an extra layer of oversight in Canada, increasingly the debate over the most salient ethical issues is moving beyond the use of embryos to issues shared with other fields of biomedical research. The regulatory environment has become clearer in the realm of basic research but has displaced the uncertainty to the commercialization path where confusion or a state of standards-in-the-making marks patenting, clinical trials and manufacturing of cell therapies. Debates take place over access to knowledge, the ethics of intellectual property and distributive justice. As more successful therapies are produced, more issues surrounding access and disbursement will surely emerge.

The second component of my research involved attending conferences, workshops, classes and lectures, primarily in Toronto and large, annual, international courses and conferences that took place across the country (such as the Stem Cell Network's course on the social, ethical and legal implications of stem cell research offered in 2011 in Calgary and again in 2013 in Montreal, the 2011 ISSCR (International Society for Stem Cell Research) annual meeting in Toronto, the 2011 World Stem Cell

Summit in Palo Alto, California or the Stem Cell Network's Till and McCulloch Meetings in Montreal in 2012 and Banff in 2013). At conferences, scientists communicated their laboratory's latest findings and discussed issues considered of particular salience to the field as a whole usually falling under such rubrics as “ethics,” “clinical translation” (the movement from lab to patient or “bench to bedside”). or “commercialization”. The utility of attending conferences was in no small part due to the fact that, being large and inter-disciplinary or “multi-sectoral,” audiences were composed of scientists from various disciplinary backgrounds as well as social scientists, regulators and other “stakeholders.” Speakers thus had to articulate views and assumptions that they would otherwise not have made explicit. Furthermore, conferences predominately attended by Canadian scientists provided formal and informal opportunities for face-to-face communication between researchers and representatives of national agencies like CIHR or Health Canada and were used by the latter to provide "updates" on proposed guideline changes or to solicit feedback. International conferences made partially visible the contours of a Canadian stem cell “community” and policy framework, particularly vis-a-vis the US. US-focused policy sessions at conferences tended to focus on “the state of the states” or the variety of state government responses to stem cell research and on legal challenges to policies (as in a case filed in 2009 against the NIH challenging the allowance of federal funding of hES cell research, subsequent to President Obama’s reversal of the Bush-era restrictions.) Canada’s federal response to stem cell research was also met with a court challenge but the substance of the challenge was about the jurisdiction of assisted reproduction clinics not stem cell research. The state variation and the judicial challenges to hES cell research in the US made Canadian stem cell

researchers appear a more unified community working in a less politically contentious environment in comparison.

Following up on a tip from a university director of research ethics, I spent the final months of fieldwork, the summer and fall of 2013, attending seven research review meetings. In Canada, any institution that receives funding from one of the country's federal granting agencies must abide by their policies for human participation in research and review all research proposals for compliance with the policies. Institutional review is performed by REBs.[4] This third component involved observation of full board meetings of health sciences REBs covering such areas as biomedicine, public health, social work, nursing and pharmacology, and including boards for a community-based hospital, an academic research hospital, university faculties of medicine and integrated hospital systems. This complemented my own experiences of taking this project through the Canadian REB process.

Every PI has either an institutional web page or laboratory web site describing his/her research interests. Finding Canadian stem cell scientists was easy, convincing them to donate their time to be interviewed (and by a student from a non-scientific discipline and another institution) was more of a challenge. Those who answered my emails about the possibility of an interview often answered with a version of "I'm not really the best person to talk to..." They referred me to journal articles or white papers on policy questions, associating the subject of my study with codified regulations and

[4] Similarly, in the US, federally funded research involving human participants is subject to the Common Rule (Federal Policy for the Protection of Human Subjects) and subject to Institutional Review Board (IRB) review. Technically, US institutions could decline to apply the Common Rule to research that is not federally funded but relatively few do so (Millum 2012).

written argument. One prominent stem cell scientist very active in the policy scene whom I contacted early in my fieldwork recommended that I acquaint myself with the work of the Canadian law and policy academics working under the aegis of the Stem Cell Network and think about how to carve out a niche for myself. For those informants, like her, active in the Stem Cell Network, the tendency was to associate my project with the work of the legal scholars who dominate the Network's funded research on the ethical, legal and social implications of stem cell research. These researchers tend to use quantitative approaches to questions about the stem cell research community and aim to devise metrics to gauge the effectiveness of the current research system. The idea of an ethnographic study, more descriptive than normative, and attuned to mundane bureaucratic and laboratory practices seemed somewhat foreign to most of the people with whom I spoke.

The bioethicists and ethics officers (involved with REBs or research use of animals) agreed to be interviewed the least of any of the institutional actors that I approached. This is perhaps because, as one bioethicist suggested to me, they are not used to being studied. Or perhaps, like those scientists who referred me to texts, they thought that what I needed to know was already written down. What they cited most often in emails to me were concerns over conflict of interest and confidentiality. To address the confidentiality of the scientists, research subjects and board members involved in REB meetings, I was asked to sign a confidentiality agreement before each meeting covering the discussions and information to which I was about to be privy. (On one occasion, the Chair asked me to supply him with an extra document addressing how I intended to protect the anonymity of the board members in my future ethnographic

writings.)

Paul Rabinow has recently called for attention to the "micro-practices" of knowledge production observing that anthropologists have paid attention "to the macro-scalar conditions of funding, institutional and bureaucratic inertia, the corporate shaping of agendas, as well as to our ever-increasing audit culture" but "how these macro-forces became anchored in practice, often tacitly, has been less explored" (Rabinow and Stavrianakis 2016: 405). As an effort in this direction, I look at stem cell science through the lenses of the institutional compliance scenario of research review and institutional mechanisms for the transfer of knowledge and materials and attempt to illuminate the interdependencies of bioethical and management reasoning and practices and their specific effects.

A future-oriented enterprise

In the course of fieldwork, I learned to think like an REB, to feel excitement over stem cell approaches to biology and to speak of the field as at a particular stage of development. I became increasingly aware of the temporal dimensions to my interlocutors' research and my own. A brief exchange with an expert in biomedical patenting at a Stem Cell Network run conference serves as illustration. In a break between sessions, I approached her table and introduced myself. I said that I had become interested in commercialization in relation to stem cell research. She responded that in that case there was really not much yet for me to study with the exception of the newly established Centre for the Commercialization of Regenerative Medicine. She herself had

earlier in the afternoon led a session precisely on commercialization and patenting of stem cell science. Many of my interlocutors work in this space, slightly ahead of the field in its current existence, hoping to help shape it in different ways - into something more productive, creative or equitable. I came to see part of my challenge as accurately presenting the field as it is now.

The ethnographic study of a phenomenon like stem cell science that gives the impression of being in the middle of its unfolding is a challenge. The apparently perpetual search for novelty and the over-determination of science and technology by the idea of progress make it difficult to escape notions of development or comparisons with other periods (particularly the recent past and near future). Like my interlocutors, my own research was shaped by academic time-frames and administrative processes like ethics review, itself a lengthy procedure. Where basic scientific research seems open, its eventual discoveries almost certain to be unexpected, bureaucratic processes are formalized and standardizing, the final product conforming to the rules. I started fieldwork hoping to find stem cell researchers preparing an REB application or getting ready to submit a new disclosure application to their technology transfer office so that I could follow their progress through the process as they engaged with their institution's offices and re-thought their submissions. Like the cellular manipulations of stem cell scientists, the timing would have to be just right. In the end, it proved too great a challenge to find scientists at these stages of their research. Anthropologists studying research are studying a system of which they are a part. Like my scientist-interlocutors, I found issues of access and timing shaping my project in ways I had not anticipated at the outset.

Annelise Riles has called for attention to technocratic bureaucratic temporalities in relation to "everyday temporalities" (Riles 2006: 18). I attend to the temporal in scientific and governing discourse and practices throughout this dissertation, from prior review to the permanence of documents, to notions of anticipation, to the "future anterior" of proprietary claims (Landecker 1999: 210). An analytic of becoming is suited to people whose work is animated by visions of the future(s) and who are faced with so many unknowns, wagering on particular paths with unforeseeable effects. It captures the agencies of cells, systems and knowledge workers and the entrenched yet provisional nature of structures and practices. Attending to uncertainty, openness and creativity in the field and in ethnographic analysis prevents a misleading sense of closure or completeness.

1. Becoming regulated: Beyond national policy

Stem cell science makes frequent appearances in the Canadian media, from reports of discoveries made by researchers in Canadian laboratories to stories about former hockey star Gordie Howe's treatments for stroke in Mexico, calls for greater genetic diversity in the public stem cell bank or advertisements for rejuvenating stem cell cosmetics (Favaro and St. Philip 2015, Teotonio 2014, Ubelacker 2015, Zerbisias 2014). The press coverage around stem cell science is today largely indistinguishable from that of other promising biomedical fields. It is dominated by research "breakthroughs" and a rather celebratory tenor.

The Stem Cell Network, one of the country's federally-funded organizations for the advancement of research in a specific "strategic" area, has contributed to these benign public representations of stem cells, creating a public outreach award in 2010 and supporting various stem cell-themed projects in art galleries, science museums and online, many of which rely on visual imagery. There was an art exhibit called Perceptions of Promise which I viewed in 2011 in Calgary's Glenbow Museum during the Network's first course on the social and ethical implications of stem cell research. Paintings, sculptures and multi-media installations imaginatively represented the fears and hopes associated with stem cell science as with biotechnology more generally. The Network began an annual photography contest for stem cell scientists in 2007. Called "Cells I See," it is about "the beauty of stem cells and biomaterials" with notable entries reproduced online. Images are full of light and saturated colours, the product of high-tech cameras and microscopes. The cells they depict are decontextualized from specific bodies

or locations, many appear to be floating in a beautiful, alien world as if in space or the ocean depths. A Network-funded museum exhibit for children called “Super Cells,” depicting stem cells as superheroes creating and repairing human tissues with their incredible powers, is currently travelling around North America. Another Network-funded project is a series of entertaining minute-long videos created by a doctoral student and post-doctoral researcher in stem cell science called Stem Cell Shorts. Narrated by leading Canadian investigators, each video features an animated explanation of a stem cell type (such as embryonic, iPS, neural or cancer) orienting what scientists believe to be the most medically promising research. The accompanying images feature animated petri dishes and lively cells.

A few Canadian stem cell scientists have been deeply involved in advising and policy development and the Stem Cell Network has also played a significant role in creating an avenue to bring researchers’ perspectives to regulators and the public. Many of the scientists that I interviewed had been involved in efforts to engage with the public or policy makers. For example, the first interviews of my fieldwork were at a hospital research institute where two stem cell scientists and the director of technology transfer agreed to speak with me and all three had been involved in education and advocacy. Dr. Bain, a leading researcher in cord blood stem cell applications, told me that he had been invited in 2006 to Ottawa to speak about his research to Supreme Court justices and that he was part of a lobbying group that promotes cord stem cell science to Congress and the American public. Science is in the news a lot, he said, and the public “are getting better educated.”

In the next office, Dr. Kim, a stem cell scientist who has made several high-

profile discoveries in the field, told me that many stem cell conferences now include an extra day for an open public forum where people ask questions of the researchers and that he takes this kind of public engagement seriously: “I think it is very important.” He continued: “There is a lot of misconception around this field. There are those who just don’t want this to be happening.” Then there are people who are sick who want stem cell research “to be happening much faster than what is really possible” and, in their desperation, are willing to try unsafe therapies.

Down the hall, the director of technology transfer also spoke of a “misconception” amongst the public, referring to the number of people who still equate stem cells with embryonic stem cells. He told me that he had chaired the Public Interest Forum of an organization for people working in biotechnology and had participated in a Café Scientifique, where the public discuss topics in science and technology with researchers, on research translation.

These diverse activities are premised on an information gap between experts and laypeople but they suggest that researchers have become attuned to differences among audiences. Researchers who told me of testifying in front of Parliament during the early 2000s when the AHR Act was being developed, were often, it seems, imparting the fundamentals of human stem cell research. For example, Dr. Smith, Head of the Stem Cell Network, told me that the Parliamentarians “thought [scientists] were taking babies and cutting them up to make stem cells; I mean, politicians actually thought that in Canada when the legislation was being crafted.” Today, the Stem Cell Network has initiatives in public, student and patient education, understood as discrete and differently situated groups. Outreach is as likely to involve communicating the appeal of stem cells

to high school students to attract them to the field or keeping patients apprised of their options.

With such stem cell science references in Canadian culture, this chapter explores the significance that stem cell researchers attribute to their research and how they understand themselves in a social and regulatory context. Their sense of themselves as scientists working towards the amelioration of health depends on their views of stem cell research and the medicine of the future. Their understanding of experiment as an inherently unpredictable enterprise shapes their view of the regulation of science. I examine scientists' narratives, teasing out the pragmatic, technical and bioethical logics.

In a study of US toxicologists, anthropologists Kim and Mike Fortun argue that how toxicologists think about what is good science affects how they understand their work as a public good and feeds into a particular understanding of toxicology as "civic science" (Fortun and Fortun 2005). Specifically, they argue that toxicology has been reconfigured by genomics and informatics with a resulting shift in toxicologists' sense of their relationship to regulators and in the focus of their ethical anxieties. They argue that toxicologists traditionally focused on testing, but now see their field as one of experiment and discovery. Of science more generally, they suggest that the tension between testing and experiment is a "double bind;" notions of good science emerge from it and decisions made within it "are where the ethics happen" (Fortun and Fortun 2005: 47). In contrast to toxicology in the Fortuns' analysis, stem cell science has been dominated by experimental research from the beginning and is now moving in the opposite direction, from experiment to testing. I suggest that the increase in numbers of stem cell researchers applying to run clinical trials is bringing researchers into a new regulatory domain,

tempering their excitement and reconfiguring their ethical anxieties.

Realizing a concept, introducing a paradigm

The first video of the Stem Cell Shorts series defines a stem cell as a cell that can both "self-renew," meaning "divide and give rise to more cells like itself" and "differentiate," meaning "divide and give rise to specialized cells." Scientific explanations of stem cells often then describe them as classified by source - adult stem cells found in organs and tissues of the body, fetal stem cells taken from discarded fetal tissue and embryonic stem cells taken from the inner cell mass of pre-implantation embryos - and by potency (the greater the range of cell types a stem cell can differentiate into, the greater its potency) - totipotent, multipotent or unipotent. Embryonic stem cells are pluripotent because they are able to form all the cells of an organism. This neat typology of stem cells reiterated in scientific textbooks and educational materials imparts, at the level of the definition, the idea that stem cell science is more than the science of embryos. It also creates a sense of stability in a field which has seen its own understandings of the limits of cellular plasticity repeatedly rewritten.

The first Stem Cell Shorts video is the only one of the series that refers to specific, historical experiments - a bone marrow transplant from one mouse to another. These experiments were performed by Till and McCulloch in 1961 at the Princess Margaret Hospital in Toronto (Sornberger 2011). They were doing research for the Ontario Cancer Institute on the effects of radiation on cells, part of a strand of research that applied nuclear medicine to diseases like cancer in the 1950s and '60s. Bone marrow

is particularly susceptible to the effects of radiation used as cancer treatment. It was known in the 1950s that bone marrow had a restorative effect on irradiated mice but how was unclear. Till and McCulloch's experiments showed that a transplanted marrow cell was producing colonies of thousands of blood-forming cells which they could count. The more transplanted cells, the more colonies (Sornberger 2011: 32). Canadian origin narratives situate stem cell research firmly in Till and McCulloch's medical research and the field remains today almost entirely dominated by medical goals.

To stem cell scientists, the Till and McCulloch experiments are significant because they are understood to have vindicated the 19th century notion of a cell that is a precursor to others, confirming the existence of stem cells and their two defining features, their ability to make copies of themselves and to differentiate into more specific cell types. Irving Weissman, a cancer stem cell biologist and Director of the Stanford Institute of Stem Cell Biology and Regenerative Medicine, told a Till and McCulloch biographer that bone marrow, at the time, was a "black box" (Sornberger 2011: 38). Till and McCulloch's work demonstrated the existence of self-renewing precursor cells and instantiated a new framework in which, as Weissman expressed it, "you don't think of bone marrow forming each of the blood cells individually from beginning to end; but you think of a hierarchy from stem cells to multi-potent progenitors, to various multiple-lineage progenitors" (Sornberger 2011: 40). He said, "Nobody had shown or even thought of a single cell having multiple blood potentials before that" (Sornberger 2011: 39). Till and McCulloch are understood to have instantiated both the conceptual paradigm in which today's researchers work and a quantitative approach to cell biology, a subject dominated by methods focusing on structure and function.

The "promise" of stem cells and the excitement of discovery

Janet Rossant is a UK-trained developmental biologist who moved to Canada in 1977 and has since become one of Canada's best known stem cell researchers both for her contributions to the science and for serving as adviser on the science, ethics and policy of stem cells in numerous contexts. Her area of expertise is genetic control of development in the early mouse embryo and embryonic stem cells.[1] In a CIHR regenerative medicine course lecture on stem cell science in the fall of 2013, she reviewed some of the "exciting" developments in the field, describing Till and McCulloch's blood stem cell as having an "amazing self-renewal capacity" and an "amazing capacity to spit off differentiated cells." Similarly, the stem cell scientists that I interviewed expressed excitement, even awe, at the way in which stem cells "have this beautiful ability to grow and differentiate" in ways that researchers can make use of and this excitement at the capacity and promise of stem cells often melded with their enjoyment of basic science. The way that researchers discuss the Till and McCulloch experiments today, for example, illustrates this double appeal. Alan Bernstein, a researcher who joined James Till's lab as a graduate student in 1968 and is a former president of CIHR, writes of the Till and McCulloch experiments and the "sense of wonder and excitement that I still get when I think about the stem cell story" (Bernstein

[1] Rossant is the most active of Canadian stem cell scientists in the policy domain. When CIHR convened a working group on stem cell research in 2000, Rossant was the chair. The working group was responsible for generating the guidelines that eventually became agency policy for human pluripotent stem cell research in Canada. She addressed Parliament on behalf of Canadian stem cell scientists during the consultation period leading up to the passage of the AHRA, drafted white papers as co-director of the Policy Unit of the Stem Cell Network, and worked with the National Academies of Science in the US as they developed guidelines for US stem cell research. She continues to play a role in stem cell policy and ethics debates both in Canada and internationally, such as Director of Toronto's Centre for Modeling Human Disease and ex officio member of the International Society for Stem Cell Research Board of Directors (She was its President in 2013). In 2015 Rossant won a Gairdner Award, a prestigious award for medical researchers and was widely praised for her work as an "ambassador" of stem cell science.

2011: xvi).

For Dr. Mick Bhatia, a Canadian cancer stem cell researcher who works in an Ontario university research institute, Till and McCulloch's work is a personal intellectual touchstone and he summarizes the methodological and aesthetic appeal of their work: "I still have those papers on my desk. The 1963 one in *Nature* and the 1961 paper that was the prelude to it. I look at [the *Nature* paper] all the time. It's a classic" (Sornberger, 2011: 38). He continued: "Their approach to the science, not knowing anything going in, and how they went at it in a completely non-biased fashion, it's just very artistic. I actually use it as a tool when I have postdocs and students who are venturing into new areas and asking new questions. That work transcends stem cells. It's about how to do everything right when you're exploring unknown biological systems" (Sornberger 2011: 38). One of the things that Till and McCulloch did was to define what they had discovered operationally; they called the transplanted cells "colony-forming units". Other researchers later connected these "units" with stem cells (Sornberger 2011: 32-33).

The scientists with whom I spoke believed firmly in the importance and ultimate utility of stem cell research for medicine and described to me many different visions of what future therapies emerging from stem cell research could look like. In her lecture on stem cells, Janet Rossant explained that their "broad potential" is why "pluripotent stem cells have become such a hot topic because if you can restrain and direct that potential then you have an endless source of cells to essentially make every cell type." Scientists working with this idea are hoping, for example, to one day be able to provide replacement tissues generated from a person's own or unrelated stem cells. Dr. Lorenz is a bioengineer at a large university in Southern Ontario who trained in chemical and

bioengineering at the University of British Columbia and at MIT in the 1990s. During an interview in January of 2012, he told me that he is working on ways to create tissues out of pluripotent stem cells. He told me that one of his projects is "trying to design technologies to grow stem cells outside the body better." In the light of the perennial problem of finding organ and tissue donors, the idea of replacement tissues is a seductive vision.

However, the scientists also flagged numerous technical and scientific questions raised by the idea of therapies involving replacement tissues or cell therapies in which cells are injected into the body, not least of which is the problem of immune rejection, as with transplant therapy more generally. With regard to replacement tissues, Dr. Kim told me that using animals to grow tissues is more likely to result in therapies than using stem cells: "I don't think that stem cell research is close to generating complex organs in the near future." A lecture at the 2013 World Stem Cell Summit had already impressed on me the technical difficulties involved in manufacturing cells for cell therapy. The lecturer had described how easily cells change in response to environmental conditions and how difficult this made it to "scale up" lab procedures to industrial-scale, mass-production of stable, safe, predictably-behaving cells.

In part in response to these challenges, there has been a shift in the ways in which people in the stem cell field envision stem cell therapies. Several of my interlocutors believed that developing drugs to modulate the patient's own stem cells was likely a more realistic strategy in the short-term. Industrial scientist Dr. Marks, whom I interviewed in Calgary in 2011, told me that this was the approach that his company was taking. Cell therapy has not so much been supplanted as it has been re-conceptualized. Early notions

of cell therapy expected that transplanted cells would directly regenerate cells and tissues. Today, some stem cells are understood to produce proteins and other substances and it is these substances that, it is hoped, will have a therapeutic effect such as tempering a damaging immune system response to a disorder or trauma to the body. Since autologous therapies (in which a person's cells are returned to her) avoid the risk of an immune reaction, hospitals may well remove and alter a person's stem cells and re-introduce them. The most obvious current practice in this mold is banking one's own blood. This is the idea of "personalized medicine" which a researcher told me would be something only the rich could afford as suggested by the fee-for-service model of cord blood banking.

Several of the scientists that I interviewed imagined the relationship between stem cell research and clinical applications as more indirect; as one researcher phrased it, increasingly the stem cell "is a research tool not an end in itself these days." Several researchers told me that embryonic stem cells may well end up making their biggest contribution to medicine through their use as a laboratory tool to generate knowledge through experiment, rather than being transformed into therapies. As a Director of technology transfer phrased it, in the race to produce therapies "embryonic stem cells will eventually be left behind."

One of the main appeals of human stem cells for scientists, particularly for those who have recently integrated them into their research, is that they are useful tools that allow the creation of better, humanized models of human tissues, processes and diseases. IPS cells can be used to model human systems or diseases in vitro, models on which drugs can then be tested. Discussing research to determine the effect of biological substances in eliciting regeneration in stem cells, Lorenz told me that this "is an exciting

area where stem cells are just a tool to screen for new molecules."

With iPS technology, scientists can now theoretically turn any human being into a pluripotent stem cell in a Petri dish. As Janet Rossant expressed it in the regenerative medicine course lecture - "That we have this amazing ability to get any human being and turn them into a stem cell in a petri dish means that we have unprecedented access to human biology". This is a dream of unfettered access to all of human genetic diversity, a complete picture of the human in biological terms, including all human diseases. (The kind of vision that led to the Human Genetic Diversity Project which, in actuality, quickly became mired in controversy and challenges to scientific constructions of race and the proprietary regime in which blood samples were taken.) iPS cells are exciting to researchers in three inextricable ways – because they can help answer questions about the human body in health and disease, because they may well result in therapies and because they solve practical and ethical problems of access, requiring adult cells like skin cells rather than embryos.

Although the researchers that I interviewed had their own predictions about which approaches were likely to bear fruit soonest, all approaches are being used as the emergent, experimental nature of the field currently makes it very unclear which, if any, of these imagined therapies will work. One of the few discursive differences among the researchers was found in the more careful choice of words of those who were undertaking clinical trials and who, unlike scientists at the bench, were representing their experiments to patient recruits as well as to funders. A hospital-based stem cell scientist who studies neural stem cells, for example, corrected himself from "cures" to "therapies", while describing his two, ongoing brain cancer clinical trials, saying, "we don't use the word

'cures'."

Whether trained in stem cell science or recent converts, publicly-funded scientists appear to be enjoying the current high profile of stem cells to pursue their intellectual interests. Several of the PIs that I interviewed described, with a certain relish and a number of metaphors, basic research as curiosity-driven and discovery oriented. One academic researcher told me, "we're out there charting uncharted coastlines and we change direction depending on where the coastline goes." Basic scientists, he said, "follow their nose;" they do not "color within the lines." He continued, "the unexpected is where the opportunities lie." Another scientist who worked on the commercialization of regenerative medicine research told me that the academic world is "driven by novelty and creating new ideas." A university basic researcher explained that science constantly "moves forward" into the unknown - Scientists may repeat themselves; they may be reluctant to change their practices; they may later be proved wrong, but "science never goes backwards".

In these kinds of depictions, scientists present themselves pursuing their interests as they lead in directions dictated by their research materials. It is a vision specific to basic research and it implicates ideas of academic freedom; it presents an image of scientific research that has room for knowledge for knowledge's sake, an image that scientists whose research involves patients are less likely to offer and one that fits better with the Weberian notion of a calling independent of questions of value (and bureaucratic attention to risks). The representational view of science in the metaphor of researchers following the coastline contrasts with that of science studies scholars who illustrate the considerable work that goes into separating research results from the specific and

controlled ways in which they are made to exist in laboratory conditions (Knorr-Cetina 1981; Dumit 2004; Latour and Woolgar 1986).

Dr. Franks

The story of Dr. Franks, a young stem cell scientist whom I interviewed in 2013 at a research institute in Ontario, illustrates the appeal and excitement of research on human materials. As he told the story of his career path, he expressed excitement about certain approaches and techniques, appreciation of how the biology works, pride in the products of his labor and desire to help patients. Franks described how he was working on a master's degree studying the biochemistry and cell biology of a topic unrelated to his later work in stem cell science when a serious car accident left him with major injuries, bone and cartilage damage in his joints and chronic pain. He moved into the stem cell field, he told me, in part to investigate its regenerative possibilities for himself.

When considering Ph.D. programs, Franks looked for labs that were working on the regeneration of bone and cartilage. It was, by his own account, a case of "physician, heal thyself." His Ph.D. research ended up being in the cell biology of cartilage development and on the use of drugs for the regeneration of cartilage. Dr. Franks describes how he felt about his work in those years, using a mouse model to test drugs: "I really enjoyed doing the bench work at the time. And the thing is that it was exciting because there were discoveries to be made so it was very discovery oriented. There wasn't necessarily a hypothesis. You could do a screen of thousands and thousands of drugs and see if they had a response on the system." This was a system "that you had

constructed from the ground up." He told me: "So the screen didn't exist prior to my work which is fantastic. There's a sense of ownership and pride as well associated with that."[2]

After his Ph.D., he joined the lab of a well-known Ontario-based stem cell scientist as a post-doc and began working with human iPS cells. This scientist was researching genes and their signals in networks in interaction with one another and studying the way in which stem cells differentiate into the various tissues. The work appealed to Dr. Franks. It was exciting; iPS cells were new. He said: "I'd seen him at conferences presenting and I was always blown away by his work. And so, I thought 'ah, this is a person that I would love to work for. He seems to have this global view." He continued: "And the induced pluripotent stem cell field was just taking off. I remember reading the initial papers and thinking 'Wow!' "The Fantastic Four" [four genes] as Mark Tomishima at the New York Stem Cell Foundation calls them… four genes can be over-expressed in a cell and turn back the clock."[3] Dr. Franks conveys the intellectual and emotional satisfaction of discovery, of using an integrative methodology that strives to apprehend some complexity and of being part of an emerging field and his appreciation

[2] The term "discovery science" is often used to describe the kinds of experiment that large amounts of genomic data combined with computing power have made possible in the biological sciences. Discovery research is generally considered a species of basic research which is research undertaken to increase scientific understanding, although the scientists that I interviewed appeared to use them interchangeably. For example, one scientist explained to me that "basic scientists do discovery research" although "there also can be clinicians in basic discovery research as well."

[3] Stem cell science is shot through with a narrative that pairs elegant simplicity with complexity. Discoveries of ever greater and unexpected plasticity generate expressions of awe. In much the same way that the deciphering of the structure of DNA elicited surprised commentary on the simplicity of the four nucleic acid base pairs (or the Human Genome Project's final tally of 10,000 genes, where many had estimated that the human genome would contain 100,000, was presented as much lower than expected), scientists refer to Yamanaka's reprogramming technique as surprisingly simple - and like Watson and Crick's discovery of DNA, it is told with a similar air of an origin story - it was found that four factors can set off a complicated cascade of changes within a cell.

of the efficacy of technical manipulation and the plasticity of cells.

Still living with the effects of his accident, Dr. Franks was attracted to iPS cells because of the kinds of exciting research that they made possible, in particular, the ways that they could be used to study tissues affected by injury and disease. With the advent of iPS technology, he discovered that, in his words: "Hey, the bone and cartilage work that I wanted to do I could do on patient samples. I could make these induced pluripotent stem cells from patients that had diseases such as Marfan's Syndrome and Ehlers-Danlos – so these are connective tissue disorders - and I could take samples from [the hospital] collected by a clinician, reprogram them to a pluripotent stem cell and then I could differentiate it back to cartilage." Marfan Syndrome, a genetic disorder that affects connective tissue, often ends up being fatal because it damages the aorta. His work, therefore, eventually led him towards the study of muscle. At this point, his lab was approached by an advocacy organization for a rare, cancer-like disease that affects women and involves an abnormal proliferation of muscle cells. Again with iPS cell technology, the lab worked on creating an in vitro model of the disease which they could use to understand the disease process better and to test drugs.

During this stage of his career, Dr. Franks was engaged in research on a rare lung disease that affects women and was funded by a grassroots Toronto-based foundation that raises money for research through public donations.[4] He came to know and admire the leader of the foundation, Anne, herself a patient, and was clearly inspired and motivated

[4] This was the only example that I came across in my research of an Ontario patient group raising awareness and funds for research on a disease studied by stem cell scientists. While there may well be others, I think it is fair to say that stem cell patient advocacy or activism is muted in Canada compared to the US. This may in part be due to President Bush's prohibition on the use of federal money to create new embryonic stem cell lines which led to the mobilization of some high-profile supporters of embryonic stem cell research such as Nancy Reagan, Christopher Reeve and Michael J. Fox.

by her story, her energy and her drive to learn all she could about the disease. As he described it, she had developed a personal relationship with the researchers working on her disease and would come to the lab, often bearing gifts, to encourage them. By virtue of her patient status and perhaps her acquired scientific expertise, the lab was open to her and she was apparently a welcome visitor. For Dr. Franks, the relationship with the foundation leader was much more than the by-product of a financial transaction. Speaking in the same breath of the leader and the in vitro cell models which he was developing he said, “She appreciated the work I was doing and it became a mission that I was on to try and develop these models.” He told me: “[the foundation] would raise money and they would fund the research on the disease and again we never took salary out of this at all. It was something that I was doing, the work. I would advertise this disease anywhere I went. This was what I was working on and I became very passionate about this.” After several years, he moved on to a new organization to reprogram cell samples for other researchers on a fee-for-service basis.

In his narrative, Dr. Franks’ impetus shifted from “patient heal thyself” to excitement over using actual patient samples to model “their” disease, rather than cells from a model cell line, and a desire to reprogram. His research was multiply personal. His biography was different from the other scientists that I interviewed in that a personal experience of the physical and emotional effects of bodily damage had so clearly influenced his research career, but his story offered an example of the kinds of varied and complex emotions and feelings of responsibility which can shape research choices. As he said to me of his time working on Anne’s disease: “She’s a fantastic lady who, despite her condition, is a ball of energy.” He continued, "She’s the champion of this disease and

she's pushing forward with it and she's an inspiration. I mean how can you not work hard on this disease?" She “doesn’t give up; she laughs as much as she can laugh… and you know I get pretty emotional about these things…”

Experiments and “exceptional oversight”

Federally-funded pluripotent stem cell research in Canada is subject not just to the AHR Act but also to Guidelines for Human Pluripotent Stem Cell Research first set out in 2002 by CIHR. The two main objects of regulatory focus in the Guidelines are cell lines and types of experiments. SCOC, a mandated CIHR oversight committee, reviews pluripotent stem cell research protocols by researchers applying for CIHR funding for conformity to the Guidelines. While every researcher that I interviewed agreed that some form of oversight was vital to their research, there was less consensus on whether or not the extra regulatory measures specific to human ES cells are necessary, are the most appropriate form of oversight, or directed at the right practices.

Dr. Lorenz, the bioengineer at a large university in Southern Ontario, described the period in which the national framework was being established as an uncertain time for Canadian stem cell researchers: “I've been working in this area for a long while and at first there were no regulations and then we weren't sure what the regulations were and then when the regulations first came in, there was a huge time delay and backlog in getting approval.” When there was “less clarity” on the regulations his research was “much more difficult.” He continued, “but thankfully those things have been sorted out… if you can justify the research as being, first of all, necessary and, secondly, ethically

sound and not in violation of any of the fundamental tenets of Canadian law, then applications generally get approved."

To Dr. Lorenz: "The regulations are something we need to work within and I think that they're the appropriate thing for Canada. In my mind, they've hit the right balance." He acknowledged that "some of the things that other researchers might want to do that are covered by regulations such as transplantation in embryos and these sorts of things are not things that we do," but concluded: "We've never had any issues getting regulatory approval for the work we're doing. I find it comforting that there's something in place, actually." Similarly, a bioethicist described the AHR Act as "very Canadian, very balanced in its approach."

In an interview in his office in October 2012, Dr. Smith, a Senior scientist at a hospital-based stem cell research institute and head of the Stem Cell Network, was much more critical of the Canadian framework which he depicted as the "exceptionalization" of human ES cell research for political reasons: that CIHR-funded research with human ES cells must be submitted to SCOC means that "in order to do an experiment with human embryonic stem cells you need special approval from the national body so that's really an exceptional level of oversight."

Dr. Smith strongly opposed Canada's use of criminal sanctions. Invoking Trofim Lysenko, the infamous Soviet scientist who, with Stalin's support, suppressed scientific dissent to his anti-Mendelian ideas about inheritance and whose name has become a byword for state interference in science, Dr. Smith condemned the use of criminal law "to reach into labs": "In the secular participative democracy where scientific advances have a

value where scholarly and free thinking is valued this is, I think, a really retrogressive way of doing things." Speaking of the AHR Act's stance on cloning, for example, he pointed out that it prohibits all forms of human cloning rather than using what he implicitly acknowledges as a (technically and ethically) justifiable distinction, between creating a person through cloning and using cloning as a research technique: "Doing nuclear transfer experiments to explore epigenetic regulation or molecular mechanisms of genetic control in early embryonic cells in the human context is illegal, just as illegal as nuclear cloning to create a person." Prohibiting the use of cloning to create a person is "more reasonable." As Dr. Smith phrased it, "the law is a blunt instrument;" it does not make the kinds of distinctions that he would like to see.

Dr. Kim has been working with embryonic stem cells since the 1980s, originally in mice. Since the emergence of hES cell science, he has repeatedly made international headlines with technical and scientific advances in the field. In an interview in September 2011 in his office in the hospital research institute where he works, he identified the prohibition on putting "human pluripotent stem cells into developing non-human embryos" as "the biggest restriction in Canada." There will be times, he continued, "when this will be the best way to prove normality of human stem cells." As several scientists told me during interviews, demonstration of the capacity of pluripotent stem cells to make all the cell types of the body is considered the best proof of their potency.

While SCOC ensures that researchers use only cell lines that the committee has established were created under ethically acceptable conditions, several of the scientists whom I interviewed situated stem cells in a different ethical realm, that of responsible workplace practices. They referred to stem cells as useful lab tools or, as one scientist

referred to them in our interview, as “a particularly promising reagent.” Dr. Smith, for example, listed a number of cell types commonly used by researchers - “HeLa cells, 293 cells, hec 2 cells, a whole pile of human cell lines that are tumor-derived, growing in a lab.” Stem cells are ordered from a supplier or a bank “like any other cell line.” And a researcher does not “need to go to a national body or even an REB” to use any of these other cells in the lab. He concluded that these cell types “are the tool kit that we use to do experiments.” The regulatory focus for many of these cell types, as it affects researchers, is on safety. Assimilating stem cells, then, to other lab materials, Dr. Smith asked, “What is the potential harm that can come from doing an experiment in a petri dish, in a laboratory, from working with embryonic stem cells?” Since “there are no threats to other humans, no threat to the person handling the cells; it’s not like you’re growing the SARS virus… the question is what is so dangerous about embryonic stem cells that warrants a national approval?” This is a bioethics language of harm and proportionality but focused on the potential harm to those working in the lab.

Dr. Lorenz, similarly, talked of stem cells in the context of establishing a safe laboratory work environment, part of his responsibility as the PI: “For me, it's like biosafety in the lab. This is something you have to do, running a safe environment. You have to show that you're running an ethical, approved, safe environment. It's just another aspect of the job...” The demonstration is key.

“Science moves where the data lead you”

The unquestioned mission of stem cell researchers in the discourse of the

Canadian scientists and researchers in the ethics, law and policy of stem cell science who were the subjects of my fieldwork is improving health care. Even basic scientists whose work does not involve trials with patients framed their critique of Canada's use of the law in terms of delay in getting therapies to patients. For example, concerned about the prohibition of certain laboratory experiments, Dr. Kim invoked the suffering of patients to criticize the use of the law to govern scientific research, telling me, "obviously we do this because we want to help humans and eliminate or decrease the level of suffering in humans and if this is the only thing that we are looking at, any law type of regulation is going to have the potential to be restrictive and slow down this process and lots of people will die."[5]

My interviewees' criticisms of Canada's use of the law often focused on the perceived time lag between the science and the policy response. Dr. Marks arranged to meet me at the hotel where I was staying just off campus. In the hotel's crowded cafeteria, he told me that laws "are by nature static" where "science moves where the data lead you." As a result, "you can anticipate that something's going to happen but it may never because you may not at that time perceive the technical hurdle" or you "may not have the tools to say that it can't happen." Dr. Marks continued "[Acts] are sometimes based on the science, sometimes based on our prediction of the future. If the prediction is dire, the act reflects that. If it's laissez-faire the act anticipates that."

[5] At times, the figure of the suffering patient was a powerful rhetorical presence. At the second Stem Cell Network course on the social, legal and ethical ramifications of stem cell science, for example, a researcher began his presentation on clinical trials with a Power Point image of a long hand-written letter that he had received from a patient begging to be allowed to try the experimental multiple sclerosis therapy that this scientist and his team were working on. At the time, they had already recruited all the patients that they needed for their clinical trial. The researcher framed his work and translational science in general in terms of urgent need.

Several researchers made versions of this argument in our interviews. Indeed, it is commonplace to point out that law-makers could not have imagined the development of reprogramming technology and the advent of iPS cell technology. In this view, science has built-in constraints because it responds to the natural world. - As scientists' knowledge deepens, they better understand what is and is not technically possible and this is not something that can be predicted. Nature is unpredictable wrong-footing scientists with the unexpected. In an article published in 2009 on the AHR, stem cell scientists Janet Rossant and Peter Rugg-Gunn and legal scholars Ubaka Ogbogu and Timothy Caulfield depict legislation as a "clumsy" tool that can create "unintended hurdles" in front of science because it cannot possibly predict the direction in which science will go (Rugg-Gunn et al. 2009: 285). Similarly, Dan Monroe, the President of the Stem Cell Network from its inception in 2001 until October 2013, argued that the unpredictable nature of the basic science discovery process fated the AHR Act to have little impact on the research practices of Canadian stem cell scientists once many of them switched from embryonic stem cells to iPS cells. Where Dr. Smith thought that the AHR did not make fine enough discriminations, for Dan, the problem with the law was that it attempted to be too specific. In identifying specific experiments that were already possible or might be soon and that would be unethical to attempt, the law fated itself to be ambiguous or irrelevant when research moved in different directions: He said, "They kind of boxed themselves into a corner somewhat by trying to imagine every possible scenario."

To Dr. Smith, the unpredictable nature of basic research makes the most appropriate way to regulate more controversial research activities to be a permit-granting

regulatory body: “What one does is create a regulatory framework that allows progressive, particular types of experiments after consideration by an authoritative body, so for example I would not go to jail for doing a particular experiment with uranium or plutonium, I would get into trouble because I didn't have the permits to do it.” He would prefer guidelines which he sees as more flexible, more responsive to the science and more easily updated as scientific understanding changes: “Science advances so fast you can't anticipate what the next experiment might be so creating a regulatory framework is a smarter way of dealing with this.” Dr. Smith understood appropriate regulation as proportionate and consistent, a system that is neither too much (“overkill”) nor too little (which is represented by the checkbox. As he said of his own work with animal stem cells: “You just check off a few boxes and away you go.”).

“We do not feel these constraints”

For younger scientists, the controversy surrounding hES cells and the political processes that resulted in Canada’s policy framework were history. The regulations for pluripotent stem cell research were in place; they were no longer particularly interesting and in the immediacy of their work, they were no more remarkable than any of the other national and institutional regulations and guidelines which require approvals and agreements prior to the start of research. Exemplary of this perspective was the young researcher, Dr. Peter Wallace, whom I met at the Network's courses on the social, ethical and regulatory issues of stem cell science.

I interviewed Peter in October 2012 together with Stem Cell Network President,

Dan Monroe, in the Ottawa offices of the Stem Cell Network. The Network's premises were secreted on a floor of the Ottawa Hospital Research Institute behind unmarked doors and I had to ask two people for help finding it. At the time of our interview Peter was the Scientist-in-Residence at the Network overseeing educational events for network trainees. Peter held leadership positions at the Stem Cell Network from 2012 to 2015. He is interested in stem cell science policy and outreach and was one of the founding members of StemCellTalks which brings researchers to speak to high school students about stem cell science, a subject about which most students know little. Peter had completed his Ph.D. in Toronto working primarily with embryonic mouse stem cells in the laboratory of a prominent Canadian stem cell scientist and worked for a year at a large pharmaceutical company. I asked him to what degree he had been conscious of the regulations for the use of hES cells during his years of laboratory work. He told me that for scientists working on the bench, stem cell regulatory issues seem a far remove from their daily research: "as a researcher, you're focused on your project." This is, in part, a reflection of professional roles within a lab. He explained that his laboratory's PI and his administrators had handled the SCOC and REB applications: "Certainly any work that we did in the lab was in compliance with SCOC and that was handled by my PI". For younger scientists, obtaining SCOC approval to work with pluripotent stem cells is a routine laboratory practice.

Peter understood a question about regulation to be a question about research restrictions. He told me that the Canadian regulatory framework for pluripotent stem cell research is stricter than the US's because it prohibits certain practices at the federal level but, speaking for researchers, "at the bench level we do not feel these constraints so we are

able to do the research, effectively." Reflecting on his work as a graduate student using mouse and hES cells, he told me that, to the contrary, he associated human pluripotent stem cells with the excitement of being at the leading edge of research: "I didn't ever feel a constraint. Yeah, it was actually the opposite… we were pushing the envelope by using cells in a system that people weren't using before."

To Peter, a significant part of the appeal of stem cells to researchers, particularly those not trained in the field, was their ability to be differentiated into different cell types and used as a model. That iPS technology lets researchers take cells from someone with a disease and turn them into a model "that has all of the bits and pieces of that disease etiology," is "very attractive" to researchers, Peter said, and "very attractive from the commercial and industrial perspective as well." He continued: "When I was at Astra Zeneca, we were screening for analgesics, for pain meds, and we were using a hamster cell line that we would express the human gene into. Now you can see that's almost as artificial as it comes, with the exception of the human protein." iPS models are better models. For industry, more accurate models mean savings: "You've got to remember that for pharma, for example, if they could reduce the cost of development of any of these drugs, by one or two percent by having a better predictive toxicology report, you're talking about hundreds of millions of dollars that they can save collectively by doing that."

Sarah Franklin has traced some of the ways in which ethical concerns converge with logics of efficiency in the products of biotechnology which she has called "built-in ethics"; ethical positions are built into the biological in attempts to contain or pre-empt public concern (2003: 113). Peter not only illustrated this, he also described similar processes in academic research. Now that researchers can use human iPS cells, "it's always

nice," he said, "if you can do most of this work in a dish without having to go to a larger animal model" and without "having to make the investment and go into higher-level, more expensive studies." He concluded, "the focus really from the broader scientific community, not just stem cell researchers, is to do it in the most cost-effective and ethically responsible way."

Dan then pointed out that if I had asked the question seven years ago, in 2005, I would have received a very different answer. During his time as President of the Stem Cell Network Dan had witnessed (and testified in) the prelegislative debates in Parliament, the establishment of SCOC and the considerable scientific and policy activity of Stem Cell Network members. Dan had read Politics, Philosophy and Economics at Oxford and had a business degree from Stanford. He had worked as a researcher in the UK House of Commons and as a management consultant and CFO of two start-up companies. Unaffected in manner, he had red hair and a noticeably Scottish accent. Dan had been a helpful early contact when I first began fieldwork and I frequently saw him at Stem Cell Network events, often the product of his behind-the-scenes work. He contextualized Peter's comments by narrating how the AHR Act and its regulations initially had the effect of preventing almost all Canadian scientists from deriving hES cell lines: "The way the legislation was written was, if you wanted to derive new human embryonic stem cell lines, you had to have been working on derivation at the time the bill was passed and given CIHR hadn't been flowing any funds for that, that kind of left a very limited number of people." In fact, he told me, "there were just three researchers which we had funded through a project and CIHR's oversight committee had approved just prior to the legislation coming into force." Very quickly, "it just came down to one

researcher who did a couple of lines almost just to prove he could do it." This meant that, in the immediate aftermath of the passage of the AHR, it could be argued that it had a particularly restrictive effect on the practice of hES cell line derivation.

However, Dan continued, the effect was short-lived as events in the US effectively made derivation unnecessary for Canadian researchers: "By that time, there were standard lines being developed for use by the world" - in particular, the hES cell lines developed by James Thomson at the University of Wisconsin, Madison. Already, the majority of the world's researchers were favoring two of Thomson's lines, H1 and H9. This meant that by the time Canadian researchers had a regulatory framework that allowed derivation of hES cell lines, there was "tremendous incentive" to use Thomson's lines instead, "because everybody wants to be able to compare their results to everybody else." Researchers then came to CIHR "saying 'we want to use H1 and H9,'" and CIHR "set up a process within six to twelve months to pre-approve those lines for everybody" so that researchers did not have to "come forward and demonstrate all the consent forms all over again." At first, for a researcher proposing to work with one of those approved lines, Dan concluded: "the turnaround time for the researcher getting that work approved" was "a year for the first ones" where "now it is almost at administrative review at this point and you're talking weeks."

"You never know until you're there"

The excitement of scientists about stem cells evident in my fieldwork was accompanied by expressions of uncertainty about the likelihood of certain envisioned

therapies ever coming to be and anxiety about the risks to humans in the clinical trials ahead. In presentations and interviews, scientists pointed to a range of scientific and technical issues that are immediately evident and will need to be solved before stem cells can be used in health care. Success in cell therapies modeled on drugs, for example, would depend on therapy providers being able to produce vast quantities of cells that could be maintained in cultured conditions, packaged and shipped around the world and on scientists figuring out how to put stem cells in the right place in the patient, keep them there and get them to function in a way that treats disease. As Rossant put it, if you want to use stem cells as a cell therapy, "clinical protocols to implant those cells are really, in many cases, a huge challenge."

In their study of toxicologists, Kim and Mike Fortun, using a distinction between experimentation and testing which they attribute to Hans-Jorg Rheinberger, describe the kinds of research that toxicologists traditionally performed as focused on testing the effects of chemicals on living systems, on providing practical data that regulators involved in environmental protection could use where now the field has become more heavily experimental, complex and attuned to patterns over large sets of data. Stem cell scientists are increasingly moving from experimental research to the kinds of testing that go into clinical trials and product development. They are now attempting to provide the kind of practical data needed by regulators concerned with protecting the public's health.

This means that research institutes and companies preparing for stem cell clinical trials must assess their evidence and the risks involved in moving into humans and present their findings to Health Canada. They have studies that demonstrate that the proposed intervention has some biological effect and animal studies that demonstrate an

effect in vivo in animal models. The burden of proof is on them to demonstrate that they are now ready to try their intervention in humans. To approve a clinical trial application, regulatory agencies need to see enough evidence to suggest that there is a scientific rationale for the proposed intervention, that it will have a measurable effect and that it is unlikely to be harmful in humans, but the standards for this evidence have not yet been fully established.

The question of what kinds of pre-clinical evidence scientists should be required to present to Health Canada emerged from my research as, in the words of one of my interviewees, "a huge issue… an evolving issue," at least among researchers. Several scientists in the course of my fieldwork told me that they thought that it was still unclear what evidence they should provide regulatory bodies in order to take transplanted stem cell interventions into clinical trials. Cell therapies often differ in important ways from the molecules which shaped the drug development model. As a result, concepts like placebo or measures such as toxicity which have been defined and delimited for clinical trials involving drugs need to be rethought for such therapies. In such cases, it is unclear whether old concepts can be pressed into new service, what they might then mean or what might count as a measure, making the elaboration and refinement of specific standards a challenge. In my interview with Dan and Peter, this issue prompted Dan to tell me that during his tenure at the Stem Cell Network, scientists who had engaged with Health Canada had experienced a lack of fit between their proposed cell-based interventions and the clinical trial application, largely written with drug therapies in mind. Peter compared my experience as an applicant of the REB process (I had been commenting on the difficulty of presenting a social science project in the terms of the

biomedical model used in the applications that I had been filling out) to stem cell scientists' experiences with Health Canada: "A lot of the times […] stem cell researchers kind of find themselves in a tough situation where regulatory issues surrounding biologics or drugs are applied to stem cells and that's a real contentious issue I'd say right now, how to move past regulation and move cell therapies into the clinic. ...The frustrations that you are feeling on the regulatory side are shared by scientists alike." This is, of necessity, a time in which standards for stem cell clinical trial interventions are in the process of emerging.

In February 2013, I interviewed Dr. Vargas, a stem cell scientist and adviser on bringing cell therapy clinical trials to regulatory agencies and head of a cell therapy program at a busy city hospital that specializes in cancer research. We met in the area of the hospital that houses the cell therapy program and a manufacturing facility. Dr. Vargas ushered me into a small office. Like many of the researchers whom I interviewed she wore many hats and the office looked as though she was frequently elsewhere. We talked about her work helping clinicians and company scientists steer experimental cell therapies through the Health Canada clinical trial application process. I asked her to comment on the idea that the standards of evidence that stem cell scientists hoping to conduct clinical trials have to meet have not yet been entirely worked out. She responded: "Yeah, and you don't really want them to be worked out because the field is evolving and it's changing so fast that you don't want anything that you have to abide to that really doesn't make sense, so I think a case-by-case flexible approach is what most agencies, including Health Canada, have chosen, I think very wisely." She continued, "It's difficult to create standards and it really varies from indication to indication." Using the example

of cardiac interventions, she explained that a rodent model of the intervention "nobody's going to trust… because their physiology is completely different." Instead, a researcher should consider using "a pig model or a sheep model because there the anatomy and the physiology are much more relevant." For another disease "maybe a rodent model is completely sufficient and it captures the physiology or the disease progression quite adequately." Therefore, "you can't say 'well no this is what we're going to do for animal studies for stem cells.'" She continued, "I think the FDA has seen some of this and you'll see that there are guidelines for cardiac or for cartilage repair, or for cord blood. So they've come up with very specific subsets and I think that's how it's going to be."

Describing how different cell therapies are from drugs she continued: "It is difficult to set up standards for this but I think it'll happen gradually." As sets of animal studies turn out to be predictive for humans, those standards will gradually become entrenched in the research community and "then that will get taken up and become, if not a required standard, a *de facto* standard, anyway." She concluded, "so I don't know that the regulatory agencies are imposing standards nor should they be. I think it will evolve from the research that's taking place."

To Dr. Vargas, the uncertainty surrounding technical standards reflects current knowledge (which will deepen as scientists understand more) and is a sign of an appropriate regulatory posture in the face of significant differences among diseases and among treatment modalities such as cell therapies and drugs. The regulatory response that she considers appropriate to scientific progress is flexible - regulatory agencies need to be able to, for example, adapt their existing classificatory schemes, or when there are cross-cutting systems of classification, privilege one over the other (such as classification by

indication rather than by characteristics of the intervention), and it takes its cue from researchers. She suggests that Health Canada, in institutionalizing the scrutiny of scientific rationales from the perspective of safety, is formalizing the process of analyzing and standardizing pre-clinical evidence that scientists are themselves already doing. This is a view of regulation, informed not by external, "social" factors, but by biomedical research and its presumed shared goals of patient benefit. When it comes to regulating basic science experiments, regulatory imagination can fall wide of the mark. Researchers like Dr. Vargas view Health Canada's regulation as appropriate because its relation to the science is reactive not predictive.

What kind of results need to be demonstrable in pre-clinical studies involving animals is an important open question for stem cell interventions. Animal models are a crucial link in almost all translational research but the move from animal models to human participants is fraught with uncertainty and attendant risk. Results in animals need to be generalizable to humans but scientists have discovered that, in certain circumstances, some animal models are far more predictive of how humans will react to proposed interventions than others. In many interviews, it was made clear to me that there are significant differences between human biology and the biology of the various animal species most commonly used in stem cell research. One stem cell researcher, reflecting on the successful creation of completely embryonic stem cell-derived mice in the early '90s clarified that "there's no evidence that what we can do with a mouse embryonic stem cell can be done also with a human… Mouse embryonic stem cells and human embryonic stem cells are simply not the same…" Learning when and where animals are sufficiently similar to human biology to act as a predictive surrogate model and where they are not is

key in translational research. Even with increasingly "humanized" animal models, the limits to their usefulness are a key area of concern. As an ethicist told me, all you can do is choose the model that is most appropriate while acknowledging its limitations: "In the absence of something, all you can do, I think, morally, is not pretend that a model you know to be totally inapplicable is a meaningful model." While human iPS models are emerging as an important tool, currently animal models are and likely will remain necessary to basic and translational science and with them comes a degree of anxiety over the limits of the analogy.

Another source of anxiety about taking stem cells into patients is the threat of tumors. Pluripotent stem cells, in particular, with their ability to form different cell types, have been found to be "tumorogenic" in certain situations. Indeed, pluripotent stem cells have been shadowed by cancerous versions of themselves throughout their history. Scholars have described a genealogy of stem cell research that runs through the nineteenth century and includes both research on the self-renewal capacity of some cells and on the pathology of tumors, including cancer research in the mouse in the late 1950s (Blum and Benvenisty 2008, Maehle 2011, Solter 2006). That research led to the discovery of a strain of mouse prone to the spontaneous development of embryonic tumors and discovered that these embryonic mouse cancer cells were pluripotent. Their findings along with technical developments such as the generation of better culture conditions contributed to the isolation of mouse embryonic stem cells in 1981 (and began the field's experimental focus on this species). Similarly, in humans, there are cancerous embryonic cells thought to be close counterparts to normal human ES cells. They have come to be known as "the archetypal cancer stem cell" (Andrews and Gokhale 2011).

The close links between normal and cancerous stem cells are evident in the ways in which cancerous cells are used as a matter of routine laboratory practice. For example, human ES cells are cultured on a substrate made of a mixture of proteins secreted by a kind of mouse cancer cell. “This is still by far the most used method,” Dr. Martin, a PI working with stem cells at Southern Ontario University, told me. “We use something that’s called matrigel which is secreted by the mouse sarcoma cell. So, basically, they’re cancer cells…” Another common example is the teratoma assay which is the standard test for pluripotency. Teratomas are non-malignant tumors made up of disorganized masses of cells. Dr. Peter Wallace described the assay as “the most rigorous test, they say, for pluripotency” and explained: “You inject [cells] into the kidney capsule; so, it’s an immune-protected area of the mouse, and these cells kind of accumulate there and they begin to divide and they form this tumour called a teratoma. If the cells are actually pluripotent you should be able to dissect this teratoma and identify cells that were derived from all three of the germ layers [early embryonic cell layers that go on to form all the cell types of the fetal body].” The concept of pluripotency seems to contain within it an inextricable intertwining of the normal and the pathological, organized growth and uncontrolled proliferation. (It also suggests the conceptual and technical significance of timing to health and disease in biomedicine).

In an interview with an Ottawa hospital clinician-scientist, he underscored the inescapable element of risk and the attendant anxiety in clinical trials. He had set in motion two clinical trials involving stem cells, one for a disease involving the lungs, the other a genetically modified stem cell therapy for the heart. I asked him about his experiences with Health Canada and he responded: “They’ve been good. I mean, it’s not

an easy process but I can tell you, especially when you're doing something new as we have done, there is an anxiety, a concern about what you're doing." He continued "you're often second guessing yourself and saying, 'okay, is what I'm doing the right thing?' so I think that the process with Health Canada is... in a way it's welcome, especially when you're out in front of things and you don't know what's going to happen when you start a trial and it's never been done before." He concluded: "Giving these genetically engineered cells to patients with this terrible disease who knows what would happen, right? We could have terrible problems. We didn't think so, we'd done everything we could in terms of modeling it pre-clinically and looking at the safety issues and so forth, but you never know until you're there." As Dr. Vargas explained, many of the stem cell researchers and clinicians of her acquaintance are trying to help patients "some of whom are desperately ill and have no other outcome that they can rely on." In her view, "most of the researchers exact a much higher standard themselves because they don't want to be the one to cause some kind of death in their trial because of something that they didn't do."

Industrial scientist, Dr. Marks, made particularly vivid how scientists beginning clinical trials in any area of biomedicine are moving into areas rife with unknowns and invest intellectually and emotionally in a range of provisional answers. "As you transition from early animal studies into human studies," he told me, "you take the best evidence you have in another species and say it's going to be equally safe in people." Dr. Marks described the various stages of the process from early clinical trials, intended to provide evidence of safety, to later trials whose goal is to test efficacy, as pioneering. In the first stage trials, he explained: "You do an early study on volunteers around patients who are

very, very sick and try to understand if you're doing any harm. Identifying that you're not doing any harm is really the goal. That in itself is pioneering because you don't know in humans if you're going to do harm or not; you simply don't know…" He described some of the many types of unpredictable effects an intervention could have: "you can elicit immune responses, you can change the circulatory system in some ways that can be deleterious or change consciousness or other things that you just can't anticipate." Portraying biology as something of an art, he told me that "highly complicated" biological entities are made of integrated systems; with this complexity, "mechanistic demonstration" that one answer is the best, is the substitute for proof. This inevitably leaves clinical trial patients exposed to potential harms.

Like the double edge of cell growth, trial drugs, Dr. Marks told me, have the potential to be either harmful or beneficial but are not, in themselves, either: "Many of the drugs that we have are in fact just toxins that we've identified in nature and we give a dose that's therapeutic… but the reality is that they're a poison somewhere else; they just happen to be therapeutic at a certain dose." In safety studies, as Dr. Marks depicted them, researchers are disrupting a finely balanced system and the wellbeing of the trial participants depends on the researchers' skill in the art of application.

The second stage of clinical trials, where scientists are trying to demonstrate that their intervention works, he told me, again involves assumptions that the physiology of the trial participants will "act in a way that's similar to the pure population of inbred rats that you tested before" and about technical criteria like "placebo rate" and "absolute drug effect" that factor into the design of the trial. Of designing the trial, he said: "That's pioneering. It's like throwing a rock over the edge… There are many, many factors in the

design of trials that are educated guesses at best… and the whole industry is that way, because it has to be. Any time you pioneer you really have to test and tweak repeatedly and it's as much a game about perserverance as it is a game about getting it right the first time." For Dr. Marks, clinical trials seem to embody a mix of complex emotions including his hopes for helping the ill, excitement about breaking new ground and a sense of the systemic complexity of bodies.

Conclusion

In this chapter, we have seen some of the ways in which Canadian scientists frame the national regulatory framework for human stem cell research and how their ideas and emotions about "good science" are producing a vibrant stem cell field. I have argued that the relationship of stem cell researchers to regulatory authority is shifting as they increasingly take stem cell therapies into clinical trials. The instrumental ethical logics of the lab which see animals and models as tools to be made more accurate, more efficient, less wasteful (of money or animal lives) give way to anxieties over potential harm to patients as well as over the public and regulatory repercussions that a death would cause. Such anxieties lead the scientists to proceed with a heightened sense of caution. The standards-in-the-making nature of stem cell clinical trials amplifies what is already a site of unpredictable creativity and ongoing negotiation amongst biological entities, researchers, regulators and trial participants. In what follows, I look at the regulation of stem cell research through the lens of the temporalities that shape academic laboratory research. In the process, I approach stem cells as material, agentive entities

and explore what it means to researchers when they speak (as they unanimously did) about the challenges of working with hES cells.

2. Becoming Innovative: Multiple temporalities and measurable outcomes

In August 2011, my first summer of fieldwork, I discovered online that there was a small group of scientists working with stem cells at the University of Southern Ontario. With some interviews set up, I took a train to a mid-sized Ontario town on a beautiful October day. A bus from the downtown train station dropped me off on campus. Map in hand, I navigated my way around the university campus, an environment that felt familiar with its grassy swards and nineteenth century neo-gothic architecture. I met with Dr. Martin, a man of about forty-five with a Francophone accent. He is the PI of a Southern Ontario University laboratory using biochemical techniques to learn about hES cells' micro-environment. In an office in his laboratory, we discussed stem cell science as a field and his experience of day-to-day research with stem cells, Dr. Martin briefly explaining scientific concepts and lab techniques to me as we went.

While discussing the idea of deriving and growing stem cells as an artisanal practice, Dr. Martin depicted them as difficult materials to work with for students. Describing one particular student's efforts to get her human ES stem cells to grow, he told me: "Oh, she struggled. It took her a year and a half and every time it's money down the drain… but that's just part of it." Growing ES cells, he said, is not like "a chemical reaction that's published and [you] just follow it exactly and you should get exactly the same thing." He continued: "Here, no. So my colleague always says 'You have to love these cells. You have to go watch them several times a day. Make sure they're ok. Feed them.' You know almost like a little pet." He told me that "cell lines like H9 are now very well studied by a huge number of groups around the world, at least in North

America, and they work very well but it takes everybody about a year for them to at least grow enough [cells] to do a proper analysis, at least the one we want to do." The problem, he told me, is that "it fails after two weeks or something contaminates it." This problem is "not trivial," he said: "As opposed to yeast cells or the other model which is a cell of cancer… They reproduce constantly and it's easy. These cells die, or, worse, they differentiate." Working with stem cells in the lab puts researchers in a close relationship with a lively yet recalcitrant form of life.

Since Sharon Traweek's early ethnography of particle physicists (Traweek 1988), there has been a strand of ethnographic scholarship showing that scientists' subjectivity is constituted in relation to laboratory instruments, materials, routines and institutional structures (Fortun and Fortun 2005, Gusterson 1996, Rabinow 2005, Myers 2015). Influenced by the "practice turn" and Actor Network Theory, these ethnographies have provided descriptions of laboratory practices that rely on the embodied, craft knowledge of scientists, including a sense of rhythm and tempo, and the intimate and affective relations that can develop between scientists and their lab materials. (Fischer 2012, Hayward 2010, Myers 2015, Tousignant 2013).

Despite this attention to the indeterminate temporalities of laboratory materials, anthropological ethnographic scholarship on bioscience tends to dwell on biotech research and its temporal shaping by market forces (Franklin 2003, Rabinow 1996, 2005, Sunder Rajan 2003). Sunder Rajan, for example, analyzes the life sciences in US-style biotech companies as structured by the temporality of capital (Sunder Rajan 2003). Sarah Franklin discusses developments such as cloning and stem cell technologies in the context of biotechnology companies' market strategies in which ethical decisions become

smart anticipatory business strategies (Franklin 2005). Paul Rabinow explores the inner workings of biotech companies, charting the personalities, relations and biographies of company members as they form part of emergent "assemblages" of technical, ethical, regulatory and market structures (Rabinow 1996, 2005). Traweek remains the scholar who has focused most on scientists' understanding of the various temporal dimensions of their research, illustrating ethnographically that a significant part of the culture of particle physics and of the subjectivity of the physicists is a particular experience of time (Traweek 1988).

In this chapter, I consider what it is like to work with stem cells, particularly human ES stem cells, in the lab, and some of the temporalities of publicly-funded stem cell research that shape their experiences of daily lab research – Stem cell scientists experience their work as marked by the rhythms and tempo of lab work and innovation, different historical scales, the cycles of academe and of government funding and ideologically entrenched understandings of progress. They use notions of progressive science, of the development of stem cell research as a field, of efficiency in the face of delay and waste and of the succession of cohorts of students. Issues of timing are one of the ways in which they distinguish academic from industrial research. I consider scientists' experiences of time to distinguish what is specific to stem cell science compared to other "cutting-edge" research and to draw out some of the links among academic science, temporality and subjectivity.

I suggest that an important dimension of the temporality of science is mutually constituted by academic practices, some of which align with practices of commercialization (such as patenting), some of which do not (like the training of

students). I describe two visits to Janet Rossant's lab and draw on discussions with PIs and with young researchers to shade in some of the specificities of pluripotent stem cells as researchers experience them. Dr. Martin was a talkative and generous interviewee who raised many of the aspects of the temporalities of academic stem cell research that emerged in my fieldwork. He therefore plays a prominent role in this chapter. At stake with regard to forms of governing science are the ideas of progress, continuity and utility of research projects on which funding depends.

A Biology of Time

To begin with, stem cell science could be considered a biology of time. Hannah Landecker has argued that the history of biotechnology since 1900 can be characterized as "the increasing realization and exploration of the plasticity of living matter" and that the dominant mode of intervention in living matter enacted by biotechnology is the operationalization of biological time (Landecker 2004). This history illustrates that the techniques involved in human ES cell and iPS cell research are dependent on and a continuation of cryobiology and cell synchrony technologies that are fundamental in cell biology. She argues that they have enabled research on living cells to manipulate their temporality with control of cellular processes and carefully timed interventions as cells are put into states of suspension, frozen and reanimated or synchronized en masse. Embryonic stem cells are in vitro constructs in this way, the product of manipulations inducing pluripotent cells to remain in a state of continuous potentiality where in the developing organism they exist for only a brief phase before differentiating into the

developing tissues of the body. Landecker writes that cells keep appearing as ever more modifiable and malleable and that their plasticity is often manifested as their robustness in the face of techniques that disrupt their temporality. The result is living matter "living differently in time" (Landecker 2004).

Reprogramming techniques seem to take the malleability of cells even further, making specialized adult cells act like embryonic stem cells. Reprogramming experiments have challenged the received wisdom that, for most organisms, development is uni-directional, a progressive and irreversible restriction of potential and accumulation of organic changes, an ordered process of growth from an egg to a blastocyst (made of two cell types) to all the specialized cell types of the body. Reprogramming technology challenges the idea that a specialized cell's fate and state of restricted potential are fixed and results in a kind of unmooring of the organism's life course from historical time, a rewinding and replaying of development. Techniques like this are increasingly opening up time as a scientific and lay concept, rewriting ideas of biological growth and finitude. Dr. Martin, like other stem cell scientists, uses a developmental biology language to describe reprogramming as making a specialized cell "go back into a stem cell". This language of making specialized cells "go back in time" conflates a cell with an organism; it is the developing organism that begins its life with pluripotent cells. It is reminiscent of the nineteenth-century theory of "recapitulation" in which a developing organism was understood to move through the successive stages of its species' evolutionary development. It is a language that jumps from one developmental scale to another.

Visiting the lab

The first stem cell researcher I ever met was sitting beside me on day one of the Stem Cell Network's inaugural Understanding Stem Cell Controversies course held in Calgary in 2011. Elizabeth was a young Ph.D. student in the University of Toronto's Institute of Biomaterials and Biomedical Engineering and its Program in Genome Biology and Bioinformatics. She was using informatics methods to analyze genomic data in order to study hES cell differentiation as a member of Janet Rossant's lab based at the Hospital for Sick Children, one of Toronto's academic teaching hospitals. Elizabeth offered to show me around the lab. It was 2013 when I emailed her to take her up on her offer. I was worried that she might have finished her degree and moved on or that she might not remember me. She was still doing her Ph.D. research although almost finished and considering career options. As I learned, it takes longer to master working with stem cells and so PhDs in stem cell biology typically take six or seven years, longer than in other science disciplines. She remembered me and we arranged to meet at the Rossant lab.

The Rossant lab is at the Toronto Hospital for Sick Children where Dr. Rossant is Chief of Research and Senior Scientist in the Developmental and Stem Cell Biology Program. I had emailed Dr. Rossant hoping to interview her in 2011 at the start of my fieldwork and it was she who had replied with the strategy common to academic knowledge production across disciplines of acquainting myself with the work of, and differentiating myself from, those already in the field. (She wrote: "Your research proposal is interesting and relevant to the current scene in Canada. There are other players exploring the areas that you are interested in, most notably the groups of Tim

Caulfield and Bartha Knoppers, so it would be useful to contact them so that you can define a niche area for research that has not been covered already.") Like almost all of the Principle Investigators of this study, Dr. Rossant combines teaching with her own research. She is a professor in the University's Department of Molecular Genetics and Department of Obstetrics and Gynaecology. Her institutional base, the Toronto Hospital for Sick Children, is a teaching hospital affiliated with the University of Toronto and as such offers training opportunities for students, post-docs and medical residents.

In 2013, part of the Rossant lab was physically located in the MaRS Centre in the Discovery District, an area roughly two square kilometers running downtown from the University of Toronto and the adjacent seat of provincial government, the Legislative Assembly of Ontario at Queen's Park. Within this relatively small area is a high concentration of university science buildings and research institutes and six big research and training hospitals which are part of the University Health Network or otherwise affiliated with the University of Toronto. In the 1990s the decision was made to capitalize on the geographical proximity of these institutions to each other and to the city's business section to attract researchers to the area and stimulate investment in the city's biomedical sector. The emphasis was on the convergence of business and technology, particularly biotechnology, and MaRS has become the standard-bearer of this ethos.

I took the subway, emerging at Queen's Park station across from the new University of Toronto pharmacy building just completed in 2013, tall cement columns siding a huge, five-story glass atrium. Beside it, the university's Donnelly Centre for cellular and biomolecular research, another structure of glass and light, its east wall windows mixed with multi-coloured windows in stripes reminiscent of the images

produced from laboratory staining techniques or lengths of genetic code, its atrium filled on one side with tall green bamboo trees, was carefully designed to encourage interaction among researchers. Down the street, the MaRS Centre which opened in 2005 is an amalgam of old and new - a large yellow brick building, a former wing of Toronto General Hospital dating from 1913 to which have been added an atrium and two towers of laboratories and offices. The Centre is a public-private partnership and a self-described "innovation hub" for the development and commercialization of publicly-funded research and technologies. Outside the entrance stands a disc bearing the MaRS name in a distinctive font like a cross between an institute name and a company logo.

Elizabeth met me outside the lab and accompanied me in. To work in a biomedical lab is to be subject to a variety of regulations. National guidelines for the treatment of animals in the lab require institutional Animal Care Committees to review protocols. Occupational health and safety rules specific to the biomedical laboratory work environment cover such practices as the handling of pathogens and disposal of biomedical waste. I was reminded of how regulated is the laboratory as I noticed a round red and black warning sign on the door marking the lab as a biohazard containment level 2 designation (level 2 covers work with cell lines as cells are potential carriers of infectious contaminants, particularly viruses.) As we looked at the long benches, lab equipment, laptops and hoods (for ventilation of potentially hazardous biological or chemical materials) in the researchers' work space, she introduced colleagues and told me a little about her scientific career and research. By her own account, she had started university as a dancer in the Fine Arts department until her interest in the mechanics of the body led her to try biology courses and she was hooked. Elizabeth had become an

enthusiastic science communicator and educator, the other creator of the StemCellTalks program to bring stem cell science to high school students. She told me about receiving her hES cells from WiCell at the start of her research. Dr. Rossant, as the lab's PI, ordered the cells and the hospital's technology transfer office signed off on the material transfer agreement from WiCell. The stem cells, she explained to me, are alive but not growing; they are stored in Wisconsin in liquid nitrogen. She remembered with amusement that her cells arrived at the lab in a large, impressive container that looked like a bomb and when opened, housed, underneath all the vapors of nitrogen, a tiny vial containing the cells.

Return to the lab

In the fall of 2015, I discovered online that there was an Embryonic Stem Cell Facility at the Hospital for Sick Children in Toronto, associated with the Rossant lab. The Facility offers materials, testing, training and support on a cost-recovery basis for Sick Kids researchers and external investigators intending to do research on human, mouse or rat ES cells. Since 2005, members of the facility have been deriving mouse ES cell lines, differentiating human ES cell lines into particular cell types, and making modifications to the genes of stem cells. The website touts the expertise of its staff, that its materials meet current research community standards and that its in-house procedures save time and money. It has an extensive website describing a range of services including chromosome counting and expansion and testing of ES cells from other facilities. A few researchers were working at the lab benches during my visit.

So, in the Fall of 2015, I returned to the Rossant lab to meet with Facility and lab scientists. The lab had moved. Its researchers had been spread out over three different sites until 2013, when, not long after Elizabeth and I toured the MaRS location, they all moved into a new research building not far from the main hospital building. Called the Peter Gilgan Centre for Research and Learning, it gathers together all of the hospital's over two thousand scientists. It continues the trend of trying to encourage collaboration among biomedical researchers by building communal spaces into the very architecture of research buildings. The Peter Gilgan Centre was constrained by its lot to be a 21-floor tower of lab and educational spaces but was designed to maximize the possibilities for interaction by linking adjacent floors, two or three at a time opening into atria where researchers can meet, sit, have coffee. It is divided into six research "neighborhoods" around broad research categories, made up of interdisciplinary mixes of researchers. While, like many biomedical research buildings, it has been carefully designed to encourage serendipitous encounters understood to be an important source of productive collaborations, it is constrained by certain architectural necessities that structure movement and practices in laboratories - ventilating chemicals and disposing of waste in regulated ways, eating and drinking in some areas and wearing gloves and lab coats in others.

The security guard checked my name off of the visitors list and buzzed me through the ground floor locking doors which separate visitors from the main tower. Karen met me on the Facility floor and took me inside. She showed me a large tank near the door containing frozen cells. She opened the top, pulled out a rack of cells and we waved our hands in the cold vapours wafting out the top. Locations that store embryonic

stem cells for long periods of time like WiCell or this facility (which is approved to carry certain hES cell lines including Nagy's CA1 and CA2 for in-house use) store them frozen in liquid nitrogen. As we toured the premises we discussed doing research with embryonic stem cells and the administrative work involved in ensuring that the Facility and visiting researchers are in compliance with health and safety regulations and with SCOC and Sick Kid's REB requirements and have the appropriate service agreements, cell import forms and material transfer agreements in place. Then we put on white lab coats and gloves and looked at some hES cells.

The little room hummed with the sounds of machines and air systems: The lab has to be kept at a certain temperature for the cells and reagents. Karen took a plate (a multi-well container) with six wells out of a small fridge set at 37 degrees Celsius, the temperature at which hES cells are stored, the temperature of the healthy human body, a reminder that hES cells have to be kept in just the right conditions. They are life forms existing on condition that their immediate environment is carefully controlled.

The wells contained the ES cells growing on "feeder" cells and were filled with pink and blue liquid - cell media containing a chemical that reacts to the pH level. As the cells use up media and produce waste, it changes the pH and the liquid turns from pink to yellow. The researcher has to come in to the lab every day to give them fresh media. She set up a colony of cells under a microscope, the image reproduced on a computer screen beside it. I looked through the microscope at an irregularly shaped blob of cells that looked grey and jagged around the ends. They looked to me almost like irregular lines of iron filings, little lines broken by the occasional dot or circle. The dots were cells; the little spikes at the edge were cells growing out from the centre of the colony. I mentioned

my memories of university labs past where, not particularly efficient, I was often one of the last to leave and we discussed how some scientists are more adept at the manual skill necessary to lab work than others.

Karen explained that when a researcher receives the cells that have been ordered, she has to thaw and expand the stock which means culturing (growing) them to generate enough cells for experiments. When they start to fill the plate, usually every seven days, the researcher “passages” them and changes the media. “Passaging” involves breaking up the colony into bits of about 20 cells either chemically or by hand and putting the bits in new plates. This maintains their pluripotency and increases cell numbers.

With repeated passages, ES cells tend to differentiate. Karen explained that researchers have to learn to recognize cells that are starting to differentiate and when they break up and “re-plate” the group of cells, they throw those out. She showed me another group of cells with some that looked to me like dark circles or a dumbbell. To her eyes, these cells were clearly differentiating into nerve or other specialized cell types. She told me that it takes researchers new to ES cells months to learn to recognize by sight differentiating cells and that human ES cells can differentiate at any time even after months of careful expansion, a potentially nerve-wracking experience for a student. Students keep a portion of the original frozen stock in reserve for just such eventualities. As one scientist later described it to me, it is as if human ES cells are on a ledge and they can easily be pushed off and start down a differentiation path.

Karen told me that hES cells are harder to grow than other cells (like yeast or HeLa cells, other commonly used cell types) and that working with them is a

commitment. The researchers have to come into the lab every day to tend them and make sure that they are not differentiating. Echoing Dr. Martin's words at the beginning of this chapter, she said that embryonic stem cells have to be cared for like a pet. You have to feed them every day (with fresh media) and remove their waste. Through such practices, stem cell scientists' work lives are shaped by the commitments and rhythms of lab work.

(Not) growing, differentiating, proliferating

Before meeting with Karen in the hES cell facility, I knew that while the most intense ethical controversy over hES cell research has focussed on the destruction of embryos, this issue has receded somewhat in recent years, with expert commentators raising a number of other concerns about pluripotent human cells, concerns surrounding their possible research, reproductive and therapeutic uses and their capitalization. At the 2011 World Stem Cell Summit, I had been impressed by the technical difficulties described by a US scientist who ran a cell manufacturing facility, involved in producing stable cells of therapeutic quality and controlling their behavior when transplanted into patients. He had explained how easily cells change in response to environmental conditions and how difficult this made their manufacture. Adding pluripotency to this challenge would mean scientists would need to discover how to control pluripotent stem cells' differentiation into specialized cell types and prevent their forming tumors. The tumorigenicity of pluripotent stem cells is often cited as a major hurdle to the development of stem cell therapies. When transplanted into animals, ES cells easily form teratomas or turn into cancerous versions of themselves (Blum and Benvenisty, 2008:

133). In her CIHR regenerative medicine course lecture, Janet Rossant expressed the concern over the tumorigenicity of pluripotent stem cells thus: “The good thing about stem cells, I often say, is that they divide indefinitely. The bad thing is that they divide indefinitely.” What I had yet to appreciate was how these challenges manifest themselves in the university lab.

In our interview, Dr. Martin described to me the difficulties his students have in getting their human ES cells to grow in their Petri dishes in the lab. For both elusive adult stem cells and embryonic stem cells, one of the challenges is to grow enough of the cells that you can run your experiments. Describing an experiment in his lab using a mass spectrometer (to determine the chemical structure of molecules) to investigate the connections between adult stem cells and cancer, Dr. Martin explained: we need to “find a way to grow enough of [the stem cells] because we have a limit of detection. If there’s not enough, I don’t care how good the mass spec is you’re not going to see it [the substance secreted by the stem cells].” The Canadian lines, Ca1 and Ca2, are even worse than the common American H1 and H9 lines, he told me - “we’re having a lot more trouble with those.” He continued, “for some reason they’re much harder to grow.” (Mouse ES cells, Dr. Martin told me, although “not as difficult” as human ES cells “are also difficult to grow.” And adult stem cells, a young stem cell scientist told me, are, if anything, even harder to get to grow than pluripotent stem cells. Her postdoc research, she said, had involved trying to get placental cells to reproduce which she never managed to do.)

Since hES cells are very responsive to their environment, students can find it tricky to make them grow without spontaneously differentiating or otherwise changing in

response to some aspect of their culture conditions. Specifying culture conditions is what Dr. Martin's lab members are working on, he told me: finding "all the new laws - you can't keep them too long in this, not too much light, God knows what." When his students' ES cells differentiate of their own accord, their samples are then a mixture of populations of cell types making it pointless to proceed - "now you have a mixture of populations of embryonic stem cells and fibroblasts and some other cells which you don't know and of course there's no point making an analysis on those because you'll get an average."

Drugs (chemicals which have a physiological effect) were the frequent counterpoint to cells. For example, a technology transfer scientist with a background in cancer cell biology described the behavior of cells this way: "Yeah, the darn things just don't stay still and are very susceptible to their environment… a chemical entity, [is the product of] very highly controlled processes so that you know you're producing a very pure compound in a highly reproducible way and, darn cells, they're just hard to make cooperate sometimes." Dr. Vargas, the head of an Ontario cell therapy program and regulatory and clinical translation consultant, similarly explained that "the biology is not as variable with drugs as it is with living cells, so I think there's an unpredictability at a range of responses within the biology of the cells which makes it unique and more challenging."

Dr. Martin pointed out that it takes most students a year and a half to grow enough stem cells to run their experiments but "you have to write your thesis for a master's in two years." It is for this reason that master's degrees in stem cell science typically take two or three years to complete and PhDs six or seven years. Ironically, the

ES cells both resist his lab members' efforts to reproduce them and proliferate into unwanted cell types. While stem cell scientists are expanding their repertoire of techniques for manipulating cells, the recalcitrant "agency" of ES cells is such that they make a number of requirements of the researchers, reciprocally making scientists adjust their time lines. As science studies scholarship suggests, there is no guarantee that experimental materials will engage in the process of producing knowledge about them (Latour 2000, Rheinberger 1998). In this case, the very liveliness of cells which allows for the ever-increasing manipulations of scientists is also what resists them.

Anthropologist Natasha Myers (in a counter-example to the claim that chemical reactions are more reliably predictable than procedures with cells) offers a description of a molecular practice, the "growing" of protein crystals that makes very similar demands on scientists to growing stem cells. Myers focuses on students in academic labs, describing their experiences of working with crystals that are hard to grow and disintegrate easily. Protein modelers "go to extraordinary lengths to keep their proteins 'happy' and to nurture the perfect conditions for their proteins to crystallize" (Myers 2015). As with the stem cells on which Dr. Martin's students run their experiments, Myers describes how "students can't progress to the model building stage unless they can 'grow' crystals that will diffract X-rays well enough that they can gather diffraction data. Graduate students desperately need their proteins to crystallize quickly so that they can solve at least one structure in time to graduate. They have limited funding and limited time to spend in the lab." Lab work and the daily tending of stem cells impose their own rhythms and schedules. As with protein crystals, the indeterminate temporalities of stem cell growth can disrupt academic and bureaucratic timelines. ES cells are also resistant to

the goal of efficiency. Money, time and unusable cells go "down the drain."

"The Whole Science is Changing": Growing knowledge, growing a field

As suggested by Dr. Smith's vivid metaphors for basic research (Chapter One), the image of academic science as progressive, "autonomous," moving according to a pace set by the natural phenomena under study was dominant amongst the scientists of my fieldwork. As Dr. Martin phrased it, emphasizing the role of technical developments, "I may repeat myself but science doesn't go backwards. We move forward, forward, forward. Another technique comes in. It's not linear right? It comes from all directions and then it just grows." The scientists believe in the utility of stem cells and in the directionality of scientific research. Many of them had ready answers to questions about the future of the field, immediately identifying research strands and approaches that they thought would be most likely to result in therapies and in what order. In the face of current failures, as Dr. Martin said, describing stem cell transplant experiments that had caused tumors, "there's no question that at some point some of it will work."

At the same time as depicting a direction to science and faith in the eventual utility of stem cell research, Dr. Martin, like all of the scientists that I interviewed, contextualized stem cell research historically in order to emphasize that stem cell therapies would not become available in the kinds of timeframes they believed that the public expected. Cancer, he told me, has been a funding priority for many years and with very patchy success and it is "the same for the vaccine for HIV. The first success came out last week… [and they] started in the mid-80s. So I think that people have to be very

patient. I hate the hype on some of these things." In this context, stem cell scientists understand their contribution to public communication as an ethical responsibility to manage expectations: "Sometimes I think people try to go too fast I think that's what we have to all understand. As scientists, our society, it takes time, it takes money and it takes time."

The scientists that I interviewed conveyed a sense of a field shifting along multiple axes and often answered my interview questions by comparing the present situation to various moments in the past. At the end of my interview with Dr. Peter Wallace and Dan Monroe, after discussing the scientific and technical appeal of stem cells and the ethical and regulatory anxieties now forming around translation and clinical trials, Dr. Wallace summed up our conversation with: "What I would say is that the landscape is changing. It's an evolving field. It's an evolving technology. It's changing every year and the issues that were relevant even a couple of years ago, are almost irrelevant now as we move to understanding the new challenges."

The idea that stem cell science in Canada has changed significantly in recent years first appeared in my impression that I was, in a sense, too late. Several people told me at the start of my fieldwork that if the regulation of stem cell research was the focus of my research, I had missed the period of most-intense controversy and consultation during the instantiation of the regulatory framework. The difficult work of creating and implementing regulations, of working out the kinks in the system, was finished, the assumption being that the day-to-day work within the regulations was not a particularly interesting subject of study. All that was left was fine-tuning.

Similarly, the literature that I had been reading prior to the start of fieldwork was dominated by issues surrounding ES cell research. As I began talking to scientists, a different view of stem cell science began to take shape, of scientists working on a variety of stem cell types, of research questions and therapeutic modalities which made my impressions of the field seem dated. Dr. McKenzie, the technology transfer officer, told me that cell science had moved far beyond human ES cell research which was a very useful and powerful first step and still a vital reference point "but the next steps aren't going to look like that at all." In his view, stem cell science is transforming into something almost unrecognizable. The experience continued during fieldwork as I repeatedly revised my sense of what researchers considered the most critical conceptual and technical questions. For example, when I mentioned the World Stem Cell Summit lecture on the difficulties of manufacturing cell therapies of reliable quality to a hospital commercialization officer she concurred, but quickly added, "but cell therapy is very ten years ago." It was the much-talked about goal at that time, she told me, but its lustre has faded somewhat since then in relation to other types of therapy.

Dr. Martin's conversation was peppered with references to just published scientific papers and to conference presentations that he had just heard. "The whole science is changing" he told me, describing the latest big publication on iPS-type experiments in which a Toronto team had successfully turned one kind of specialized cell directly into another without having to turn it into a stem cell first.

Again, depicting the intersection of materiality and temporality, he described technologies, techniques, and practices that had become something different between one year's crop of students and the next. Moving from the academic timescale of students

struggling to grow ES cells in time to finish their degree to the historical scale at which technological change is visible, Dr. Martin pointed out that growing human ES cells in culture, like iPS cells, has gone from something that few scientists had the means or practical knowledge to do, to being a requirement for students: “There’s no question, when we started... for our analysis we needed roughly 10 million cells and in 2002 there were probably very few labs in the world that could afford to grow, you know, in a well-defined manner, that is without the differentiation, that many cells. Now everybody can do it.” He continued “Now we have dozens of graduate students, post-docs [growing ES cells] and it's the same everywhere."

Future therapies will also depend on the continuation of stem cell research as a field. The awareness of the stem cell researchers that I spoke with of the current student interest in stem cells co-exists with a concern for the future of stem cell research. Like Janet Rossant’s efforts to spread the news about stem cells, stem cell scientists are concerned about attracting good students to form the next generation of researchers. Dr. Martin said: “We train students and postdocs and they’ll go and then expand… you know that’s one part of research that often is forgotten... At the university, our first role should be training. Of course, we want to be part of discovery but the training is absolutely critical. Without these new people, it’s not going to continue to grow.”

Some stem cell scientists articulated a similar sense that the field is both “very young” and has already gone through rapid change. Dr. Lorenz responded to my suggestion that public ethical anxiety does not tend to distinguish between human ES and other stem cell types with “that’s changing I would say... that’s much less the case now than it was even a little while ago,” to my suggestion that stem cell lines were not

standardized with “that’s changing quickly too,” told me that “the technology to make [induced] pluripotent cells now is widely available and can be done, is being done, probably in almost any research institution of note in the world and certainly North America so it’s not a big deal anymore” and that industry and discovery research “can co-exist” which “is an evolution in my thinking.” This last, personal evolution had resulted in a re-assessment of the value of industry and a shift in career trajectory as he took on the position of Chief Scientific Officer at CCRM.

“The university should have clear roads to engage in industry,” Dr. Lorenz told me: “This isn’t by any means the only or the most important role for the university but it is an aspect of what we do and, especially in this time when we’re received a lot of money from the government, I think one of the ways we can show a return on that investment is in creating jobs and creating products that benefit Canadians... That doesn’t diminish in any way the need for basic discovery research.” He concluded, “it’s funny because if you’d talked to me even two years ago, certainly five years ago, I would have given you a different perspective, I’m sure.” Dr. Lorenz also told me that his changed view was, in part, due to the lack of Canadian biotechnology companies to give newly-minted stem cell scientists who cannot all find jobs in academia, places to do their research. He said: “It was important for me to try to start, for students that wanted to stay in Canada… that they have jobs to go to. You know they can’t all go on to be professors. We need to create jobs in companies so if we can create some technology industry then they have a place to go.” For Dr. Lorenz, shifts in his understanding of his role as a basic stem cell scientist in relation to a sense of civic responsibility and responsibility to his students are entwined with his experience of a changing stem cell field.

As Dr. Martin remarked during our interview: "I think your difficulty will be to put everything in context. What was said two or three years ago when this person wrote the article may be less true now or by the time you submit your thesis……" To Dr. Martin, the accuracy of my own knowledge would depend on its contextualization in recent stem cell history. The perception of a quickly changing field creates a sense of pressure in the present to keep up or risk producing knowledge that has been superseded.

The tempo of innovation

"The technology changes constantly," Dr. Martin said. At the same time, he told me that innovations are not always immediately adopted. For example, he described a colleague's work on stem cells' physical environment: "We've been working with her on the behavior of these cells in so-called hypoxia conditions, so hypoxia means simply low oxygen." "In the body," he explained, "these cells would be [at a] very low oxygen concentration where the concentration in the air is about 20 percent." Dr. Martin and his colleague discovered that all of the stem cells "do better if you grow them in about two percent, three percent oxygen." At that time, he told me, most people grew their cells in 20 percent oxygen, "but now things are changing because the yield's always better; it's much more homogenous; there are fewer other things [present] at one or two percent." Where three years ago, hypoxia was not part of accepted practice, he told me, "basically now it's becoming more or less accepted." He concluded: "So I was at a meeting last year in San Francisco and that was the big thing, you know, and the vendors, of course, were selling incubators with tightly regulated oxygen concentrations at one, two, three, four,

five percent."

Dr. Martin's hypoxia example suggests a tempo to the adoption of innovations that depends on acceptance by peers. "We're gaining a lot of knowledge," he told me, and "some of it is trivial" but "before it becomes accepted by the scientific community [people are unlikely to do it.]" Training and habit play into this process – he told me that each cohort of students has largely been trained in the same techniques and it can take time for them to change their practices; at the same time, change happens relatively rapidly: "It's very hard for me to convince my technician, for example, my graduate students, to try this other technique because they're so familiar with the other one and everybody, especially in the bigger labs… they do it the way it's always been done… It takes a while before some of these things are accepted. So, it takes time, but the methodology and the technology, overall, it really changes very quickly…" To Dr. Martin, there is a temporality of innovation through the accumulation of knowledge, standards and practices as they shift and congeal, punctuated by "game-changing" developments like iPS technology.

"Deliverables"

Analyses of the 2015 national budget identified a decline in science funding since 2009 and an emphasis on commercially usable research (Semeniuk 2015). At the same time, government-funded organizations have five or seven-year funding terms. After they "sunset," as the Stem Cell Network did in 2015, there is no guarantee of continued support. This contributes to the sense among stem cell scientists that public funding has

become ever more competitive and difficult to win. As Dr. Martin told me, “right now (2011) it’s very difficult to get any kind of money.” PIs therefore are always on the look out for money to keep their labs going and filling out grant applications throughout the year. A hospital-based researcher whom I approached about the possibility of an interview in 2013, emailed in response that he was unable to meet me immediately as he was filling out six grant applications at the time.

In this context, academic researchers make strategic use of the possibility that their research will contribute to making stem cell therapies a reality in order to secure funding. Echoing what several stem cell researchers told me, Dr. Martin said: “There’s always, on every grant application you read, Canadian or American, a little bit of an exaggeration… We know damn well there won’t be any commercialization… but that’s the game we have to play, unfortunately.” Speculative claims about future applications of their research produce the funding needed to support present research. Funding, in turn, contributes to the appeal of stem cells and encourages students to enter the field, students who will shape the future of academic and industrial stem cell science. At the same time, stem cell scientists express an ethical posture that is constructed in relation to prior and ongoing support; they believe it is their responsibility to provide a “return” on public investment.

On more than one occasion, a scientist suggested that social scientists like me were less comfortable with business models. Dr. Smith, for example, comparing his academic lab with its need for constant funding to a biotech company, told me that when he applies for grants, he is in a “really different” situation from a social scientist. He is responsible for a team of workers: “so I have eighteen people through that door working

on all sorts of things and it's like a small business and then you have to feed the monster, keep it financed... and in order to be successful you have to publish papers… and hiring good people is the most important part of publishing good papers." At the same time, students and postdocs graduate and move on. The lab make-up and the pace of research fluctuate cyclically by cohort. Dr. Smith has to "manage" the lab as both a business and learning environment: "it's part of the challenge, part of that is one needs to make sure that you have new people coming in before the old people leave… and things go cyclically, a bunch of new people come in at once and it slows things down for a bit and then it takes off again, but good people will move it along."

Several of my interviewees commented on the commitment of time and effort required to secure this funding as well as on the emphasis of government grants and on commercial potential. Dr. Stevens, a cancer stem cell researcher and surgeon-scientist whom I interviewed at an Ontario research institute in the spring of 2013, told me that scientists are applying for grants "always, it's just our life." She explained that this was even more the case for Canadian scientists than for American who are more likely to benefit from endowments - "Their time is protected so they don't have to spend all their time in their office writing grants."

Dr. Martin, as a basic scientist, was critical of the emphasis of government grants on "targeted" or commercially viable academic research: "The problem is, as one of my colleagues says 'you can't exploit what you have not discovered'." Dr. Stevens expressed the same concern, telling me that scientists must demonstrate that their research will result in a "product" that will "benefit society," achievable within the short term: "They want a direct and definable deliverable that will be coming within the next five years –

they don't want to just have science that's open ended, that may generate a discovery 20 or 30 years from now." She considered this to be "a big challenge" for basic scientists, although not for her, since her research projects are "translational:" "For me," she told me, "this is all normal," but for others, she felt it is "a bit artificial to force everyone into a bag where… we're all going to cure cancer or we're all going to make society better." She was also emphatic about the need to fund basic science. She argued for the value of basic research both for "education and for edification," itself "a positive impact on society" and because many practical applications were the product of "serendipity" in research on basic science questions.

Dr. Stevens believed this emphasis on commercialization is a fairly recent phenomenon. She said: "If you look at how scientists functioned twenty, thirty, forty years ago, they didn't have to answer to anybody. They were given a pile of money and they were told 'go study something interesting to you' and there was no deliverable." She continued "but now you'll see that in the grants that we write there's so much language that never occurred to scientists before – milestones, deliverables, endpoints, impact on society." Those scientists whom I interviewed who had industry experience depicted industrial research as moving at a faster rate than academic research and in a more defined fashion. They told me that industrial scientists have specific questions to answer and gaps in knowledge to fill. For Dr. Stevens, grant applications with their industrial language invoke a freer past, eat up time in the present and impose on research premature instrumental goals and foreshortened time horizons.

In the context of patenting, Dr. Smith similarly articulated the contradictions of a belief in the free movement of science and the temporality of commercialization. He

refuses, he told me, to change his practice of publishing or otherwise making results available to other scientists in order to accommodate the different norms and timing of patenting. Speaking of himself and his research collaborators, he said: "We don't hold on to stuff because we're patenting it, we just put it out the door, damn the torpedoes and if the people filing patents get it out in time they're good. They have to hurry."

Conclusion

Sharon Traweek finds that particle physicists working in national laboratories have a sense of time that is institutionally and culturally shaped. She argues that "a physicist learns the insignificance of the past, the fear of having too little time in the present, and anxiety about obsolescence" (Traweek 1988: 17). At the same time, when it comes to the content of their beliefs about the natural world, "although the physicists speak of generations of particles, of lifetimes and decay, they represent the natural world as a stylized dance of only a few forces, endlessly repeating a small set of choreographed interactions" (Traweek 1988: 17). If, as Traweek suggests, these natural forces appear static in physicists' representations, "free of ephemeral time" whose operations in their own lives are sources of anxiety, the "laws" that stem cell researchers are working on concern precisely the biology of ephemeral time, the relationship of time to human development (Traweek 1988: 157). The subject of basic stem cell research is cellular processes through time and at both ends of humans' life course, from the development of the embryo to the processes of decline and disease associated with aging. Stem cell scientists speak of "ephemeral time" somewhat differently from the physicists. They narrate the recent past of their field with an emphasis on the significance of high-profile

achievements. They also experience time pressure in the present created by the challenges of experimenting with stem cells, the delay in obtaining approvals or the impending end of funding for stem cell research-focused government programs. Their anxieties center on losing control of the content or timing of publications and on moving too quickly in the pursuit of therapies – over taking technologies that are "not there yet" into clinical trials or to regulators.

How basic stem cell scientists experience time is a particularly useful lens through which to view the governing of scientific research because it is intimately linked to the worldview of stem cell scientists. Their experiences of time shed light on the effects of the requirement of federal review for hES cell research proposals, and the much-debated question of policy shifts towards commercialization of academic research. In the next chapter, I move further into the university as the key site for scientific knowledge production, examining the role of research review in shaping the ethical sensibilities of researchers.

3. Becoming Ethical: Research review and bioethical rationalities

In the Spring of 2016, the Ontario Institute for Regenerative Medicine, a provincial government-funded organization with ties to the industry-oriented CCRM, hosted "Stem Cells 101" evenings in four Ontario cities to present a glimpse of "the promise and potential" of stem cells to the public. At the Toronto event, held in a small lecture hall in the Hospital for Sick Children's Peter Gilgan Centre, two stem cell scientists introduced some of the therapeutic visions animating current biomedical research and one legal scholar sketched the regulatory environment, each with image-laden PowerPoint presentations, to an audience of about thirty people. The second scientist was Dr. Carney, a bespectacled Irish anaesthesiologist in his forties, interested in the potential use of stem cells to treat critical illnesses such as septic shock and respiratory infections. He began his presentation with a brief history of emergency medicine, showing a 1950s-era photograph of emergency room patients in iron lungs and describing the present-day cost of septic shock. Turning to the subject of stem cells, he wove his move to Canada into a narrative combining the appeal of stem cells and Canada's success in the field, telling us that stem cells had "great potential" for treating critical illness and that he had come to Toronto for its stem cell research community. He quoted Dr. Alan Bernstein, the former head of CIHR who told *The Globe and Mail* in 2012 that "if Canada's game is hockey, its science is stem cells" (Bernstein 2012). Turning to his research interests in acute respiratory distress syndrome, Dr. Carney showed a cartoon depicting a small house beside a huge office tower. A man outside the

house was explaining to his companion, “This is the stem cell lab. The ethics committee is next door.” The image was received with impassive stillness by the members of the audience.

The cartoon suggests that research ethics is a bureaucracy whose infrastructure far outweighs that of the laboratory itself. In emphasizing its bureaucratic expansion, it alludes to a view of research ethics as a time-consuming duty that delays scientists from starting their research and, even amongst the many routinized practices of scientific record-keeping, involves an inordinate amount of paperwork.[1] This impression was vividly materialized to me in the spring of 2013 when I visited a research institute in Ontario for interviews and an REB meeting. One of the interviews was with Dr. Stevens, the cancer stem cell researcher and surgeon-scientist whom I had arranged to meet in her office. As I approached her open door she looked up from her computer and, with a smile, nodded me in and resumed typing busily for several seconds When she had finished, she told me about her research project, an ongoing study in which she and her colleagues derived cancer stem cells from brain tumor tissue surgically removed from patients. She explained that she used separate consent forms for surgery, for collecting tumor tissue and for banking the specimens. Opening her grant applications folder on her computer, she clicked on the icon for her REB file and showed me the multiple folders nested within it representing hundreds of documents - applications, approval

[1] Research ethics experts would like the ethics of research to be incorporated into decision-making about science at all levels. The reduction of research ethics to REB review is strongly challenged by many bioethicists. Canadian ethicist Michael McDonald, for example, critiques the temporal and substantive narrowness of research ethics review. He understands as ethical the many decisions made by the wide range of actors who directly or indirectly influence scientific research. He contends that bioethics should be thought to encompass all aspects of the scientific research “life cycle” from research program priority setting to the dissemination of results.

notifications, updates, renewals and consent forms. A folder for the tumors, a folder for the controls, another for the animal protocol - page after page, year after year. Dr. Stevens did not need national-level approval; the documents represented on the screen were solely those generated by the review committees at her hospital-based institute.

The REB review process and the practices they mandate for researchers are an unremarkable and unquestioned part of doing biomedical research at Canadian institutions. As Dr. Stevens phrased it, "it's now entrenched in all of our institutions… at every level." Ethics approval is not only required before scientists can begin any research involving human participants, their biological materials or data, evidence of REB approval is increasingly required by institutions before they will authorize the transfer of materials or data and by granting agencies before they release funds; even a number of prestigious journals require approval before they will publish articles.

Anthropologists studying bioethics as a regime of abstract, putatively universal principles have analyzed it as a culturally specific form of public morality (Sperling 2004), attended to the way in which its procedures are variously taken up, modified, ignored or critiqued "on the ground" in clinical trials or health projects in specific socio-political contexts (Das 1999; Liu 2011; Ong 2010; Petryna 2005; Silbey 2012; Sleeboom-Faulkner 2010) and analyzed it as a life sciences ethics industry crucial to the international biomedical enterprise and its reshapings of political economy (Petryna, Lakoff and Kleinman 2006, Sunder Rajan 2003). In a related strand of anthropological attention to bureaucratic practices in the academy (Brenneis 2009), anthropologists have studied ethics review of anthropological research as modernist, bureaucratic "knowledge

practices" that centrally involve documentation[2] or as an instantiation of cultural shifts that have developed in recent years around accountability and "audit practices," associated with a neoliberal politics (Strathern 2000). They point out that research ethics review is understood to incorporate the interests of society at large or specific social groups and is an important way of conferring legitimacy to biomedical research (Hayden 2003: 225). As anthropologist Marilyn Strathern has written, referring to the proliferation of interdisciplinary ethics committees and medical review panels that began in the 1990s, ideas of accountability have led to society imagined as "drawn into the scientific enterprise" through attention to wider "social, legal and ethical" concerns (2004a: 71, 89).

However, social scientists have not attended closely to two aspects of ethics review, review of biomedical proposals and biomedical scientists' experiences of their ethics bureaucracy. Charis Thompson has most extensively explored the multiple senses in which stem cell science "has ethics" but she does not attend closely to institutional ethics committees depicting them as enabling controversial research to continue rather than as sites of any genuine ethical work, as emblematic of bioethics practice "of institutionalizing acceptable ways around people's ethical objections" (Thompson 2013: 64).[3] More closely exploring understandings and practices of institutional ethics

[2] See Introduction footnote 1.

[3] Reflecting particularly on her experience sitting on a US institutional stem cell research oversight committee, Thompson writes: "Indeed, bioethics seems almost to render redundant precisely those dimensions of the ethical that require reference to behavior, virtue, training, the acceptability of a means or an end, or a greater good or good unto itself. In the United States, the labor of bioethics is typically distributed among people tapped for their distinct expertise, and to an institutional ethics committee on which they all serve. Likewise, the work of the committee typically involves regulatory compliance rather than ethical deliberation, making sure that regulations enacted at various governmental and/or institutional levels are followed. While some more wide-ranging issues can occasionally be raised in these forums, it is usually a misrecognition of one's role to attempt to do so. Serving on these committees, one has the

committees might shine a light on their entrenched source of legitimacy for biomedical research. Neither the "gate-keeping" (or the related "speed bump") view of research review nor its depiction as circumventing ethical concerns seem quite adequate.

Drawing on my experience of obtaining ethics approval and attending REB meetings and on interviews, particularly one with Dr. Patel, a scientist turned bioethicist who sits both on health research REBs and on SCOC, I consider in this chapter how science, society and ethical practice are entangled in ethics review and how the research ethics regime is viewed by the stem cell researchers and other scientists of my fieldwork. I build on the work of social scientists who have studied the meanings of categories used in deliberative meetings such as peer review and Institutional Review Board (IRB) meetings (Brenneis 2004, Stark 2006) and of anthropologists who have studied understandings and practices surrounding accountability and the construction of publics in science (Hayden 2003, Strathern 2000). I suggest that bioethics ways of thinking make moral questions "do-able" (to borrow from Chris Kelty and Elise McCarthy 2010) through their narrow reframing as harm prevention and use of a risk/benefit binary, which, in REB meetings, often makes reviewers' critiques of research proposals seem like common sense. In "Common Sense as a Cultural System," Clifford Geertz approaches common sense as a "genre of cultural expression" and situates its legitimacy in its apparent self-evidence (Geertz 1983: 84). I find Geertz' essay useful in the context of REB evaluations because he approaches common sense as a species of thought that entwines moral and practical conceptions with conceptions of the true or the real; and

impression that the ethical work has already been done when the regulations were negotiated, or even that the ethics itself has somehow been bypassed." (Thompson 2013: 63).

because it situates the authority of common sense, as he argues, in the way in which it appears to be "the mere matter-of-fact apprehension of reality" rather than a culturally shaped "interpretation of the immediacies of experience" (76). While sources of authority among REB members may vary and affect the perceived validity of their critiques (Laura Stark charts how such factors as subject expertise, personal experience and position on the board influence the way comments are received), many of the uncontested claims that I observed put forward seemed to compel consent with their obviousness about how nature or reality works.

Ethical practices contribute to shaping the milieu in which stem cell scientists do their research as do broader notions of accountability to patients and to society. Dr. Carney's presentation at the Stem Cells 101 event, his rhetorical attention to the Canadian-ness of stem cell science and to the bureaucratic elaborateness of research ethics committees echoes an association of Canadian science, Canadian values and regulatory ethics procedure that emerged in my fieldwork. In interview after interview, stem cell scientists spoke of Canadian regulatory ethics (the REB, SCOC or Health Canada) vis-a-vis the relation of science to society, speaking of Canadian research oversight practices as appropriate for Canada and making scientists accountable to the Canadian public. At the same time, society had a semantic fuzziness; scientists use ideas of the relation of science to society to comment on their experiences of changing norms of biomedical practice and of international research.

Obtaining ethics approval

Obtaining ethics approval at Princeton involved submitting an application to the university's IRB and completing university-mandated online training in research with human subjects. My IRB application was approved in July 2011 (and renewed annually thereafter). As well as the standard procedures for anonymizing information and keeping it confidential and secure, the terms of the approval included oral informed consent from potential interview subjects. There was also an understanding that if my research were to become a study of one particular lab, I would obtain approval from its PI. With Princeton's approval in hand, I began fieldwork at Stem Cell Network events and interviewing scientists, emailing them information about myself and my research (and the anonymizing measures that I was taking) and asking if they would be willing to be interviewed.

After several months, I began approaching research ethics officers. Each one turned my requests for an interview into exchanges over institutional policy and REB procedure. A quick succession of such interactions made it obvious that I would have to investigate whether I needed local approvals and what were the local conventions for ethnographic research. By far the most bruising of these interactions was with an ethics officer in February 2012 in Alberta where I had arranged to interview scientists. After the interviews and knowing I would not have the chance to return, I approached the university's research ethics office staff, explained who I was and what my fieldwork was about and asked if there was someone I could speak with about the review process for biomedical research before returning to Toronto. Approachable and friendly, they suggested some individuals to contact including Dr. Post in medical bioethics who was

on the health sciences REB and would be back in the office in roughly an hour; if I returned then, she might be willing to speak with me. On my return, one of the staff went in to ask permission on my behalf, then ushered me in. Shortly after I introduced myself and my project, Dr. Post asked me to consider the ethics of my own research and it soon became clear that she was referring to this meeting as itself a breach of research ethics. I was attempting to speak with her as part of my fieldwork without first approaching her with an email (as I had the scientists), and, at a minimum, with a letter of introduction and a written consent form. Where was my documentation, she asked? I explained that I had obtained my home university's IRB approval and that what I considered thoughtful and appropriate modifications to allow verbal informed consent had been made. In response, she gave me a copy of the TCPS, 2nd Edition and urged me to read it, particularly the sections on qualitative research newly added to the second edition in a chapter of its own[4]. Later that afternoon, I emailed her to apologize and promised to start using the documents that she had mentioned. She emailed back, characterizing the incident as a learning experience and wishing me luck, adding: "I hope you enjoy the TCPS and are able to apply some sound Canadian standards shortly!"

Shortly after this incident, back in Toronto, I emailed a University of Southern Ontario ethics officer to reschedule a meeting that we had planned in October 2011. I had met her after my interviews on campus, as she was closing the office for the evening, and told her about my research. Following up by email the next day from Toronto, I had made

[4] A research ethics panel, created by Canada's three federal funding agencies, with responsibility for the TCPS2, has explicitly addressed ethnographic methodology in that document. In my reading, it subsumes various species of dialogue under the form of interview and requires documentation that confirms consent was given (even in the absence of a signed form). Until this point, I had been thinking of more informal exchanges as a distinct category from structured or semi-structured interviews.

an appointment to interview her at her office in several weeks' time, but, in the end, we had had to cancel it because of a death in her family. She replied to my new message: "Thank you for your email. I was under the understanding the day we chatted that you were a new Southern Ontario University student doing your research here. If you wish to carry out research with [our] student/faculty or staff, you will need to have ethics approval from our REB." She continued: "If I were to give you ethics approval I would unfortunately be unable to chat with you about the study because it would be a conflict" and concluded: "If you wish to send your letter of information along to me, I could see if it would be something that one of the other officers would be able to sit down with you and discuss, with ethics approval from [this university] of course. Please advise."

Remembering that, with regard to research at other institutions, Princeton's IRB application had specified that "participants may be recruited elsewhere only with written permission of an appropriate official," I had also emailed senior research administrative staff at three of the Toronto hospitals in which stem cell researchers had labs to find out if the hospitals required me to obtain REB approval. I had explained the goals of my research, identified the individuals I was hoping to interview, attached some newly generated documentation attesting to my identity and describing the project and asked their advice on how to proceed, offering to apply for hospital REB approval if needed. All three gave their consent to my continuing without REB approval, two of them forwarding my documents directly to the individuals whom I wanted to approach.[5] Ten

[5] The substance of the three responses was as follows: The first, "...I do not think you need to contact the (hospital) REB to obtain permission to conduct the study, since it is not a (hospital) study, but members of the (hospital) staff are the study subjects..."; the next, "I will pass your request on to the relevant people and if they are interested in doing this they will contact you"; and the last, "I've copied Mr. T. D. who directs our (technology transfer) program and also has administrative oversight of the clinical research contracts. If he's willing to help, I've no problem."

days after obtaining what I understood was permission to proceed from the last hospital, I emailed the head of the REB, mentioning that I had permission from a director of research at the hospital, to ask if she knew of anyone on the board who would be willing to be interviewed. Her response began: "Thank you for your email. To clarify, is your intent to submit this research study to the (hospital) REB for review? It would seem from your attached description that you will be conducting research at our site…" It continued with "please see our website for details on our submission policies" and ended: "In terms of interviewing REB members, please note that interactions between the REB and investigators are confidential…"

According to the TCPS2, which provides the backbone of a Canadian national policy with regard to ethics review, each institution is in charge of working out the details of how to apply the policy. As I learned, they can interpret it quite differently. An ethics officer at the University of Toronto, the prime institutional affiliation of many stem cell researchers (26% of the country's regenerative medicine scientists, according to a 2012 Industry Canada report (Industry Canada 2012: 2)), told me that if I were planning to physically "conduct interviews or recruit participants" at the University I would need REB approval. In contrast, a McMaster University research ethics officer told me that "our policy is if you are recruiting directly yourself, without consuming resources here, i.e., asking other people to help you recruit, convene work groups to discuss recruiting, etc., you don't require our ethics clearance."[6] Not only do these policies vary from

[6] Subsequent to my experience, the research ethics panel, responding to public requests for interpretations of the TCPS2, explicitly addressed the question of whether researchers with their own institution's approval and gathering data from participants who are members of other institutions are required to obtain REB approval from those institutions. In a statement published on their website they write that if the researcher would not be using the resources of the institutions for recruitment, "for example, if names and emails of faculty or department heads are publicly available on websites or through some disciplinary association and

institution to institution, concerns over the potential for conflict of interest and the impartiality of REB review have resulted in offices of research ethics and REBs that are independent of the institution's larger research administration. Their semi-autonomy from their host institution means that their exact relation to lines of authority and jurisdiction within the larger research governance structure is not entirely clear. Other parties, like the senior staff that I contacted, are not always aware of their institution's ethics office policies.

In the Spring of 2012, I suspended my fieldwork and began filling out REB applications. I soon discovered that both university and hospital REB applications could not be completed without a local researcher or "sponsor" to take responsibility for the conduct of the research (to be listed in the application as the study's PI with my Princeton supervisor as "co-investigator"). In some cases, his/her department head also had to "sign off" on the application. At universities, I could enlist the help of an anthropologist to act as sponsor. In the case of Southern Ontario University, for example, the head of the anthropology department cast around on my behalf for any faculty member who might be willing to act as sponsor. (That this is not a routine occurrence is suggested by an exchange in which I characterized my situation as "unusual" and he concurred with "this is indeed an unusual request...") Initially, no one volunteered. The timing was not fortuitous as it was May and the Canadian academic year was over. After a month of hearing nothing, I emailed the department head again who returned to the challenge. In the end, a young faculty member volunteered to act as sponsor and help me submit the

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the researcher uses this information to recruit them as participants, then REB review at the researcher's institution would suffice" ("Multi-Jurisdictional Research" n.d.).

application. (In exchange, the head suggested I present my research to the department's students as a “quid pro quo.”)

At hospitals, it was much harder to find a researcher who could in good conscience sign off on my protocol. The hospital researchers whose work seemed closest to my field of research were bioethicists. I contacted the resident bioethicists for two hospitals asking if they could act as my sponsor. “Conflict of interest” concerns again emerged, the first bioethicist taking the time to comment on my research protocol but stating that he could not support my project for this reason, writing “I would be in a conflict of interest if I sponsored research that both studies my REB colleagues and includes me in several of its potential participant groups.” The second agreed to discuss the possibility on the phone. Studying the workings of REBs was an excellent idea, he suggested; there had been little done on the subject. Of course, he continued, this meant that they were not used to being themselves the subjects of research. He was doubtful that he could act as a sponsor for my research and did not respond to a subsequent email.[7]

In the end, the University of Southern Ontario, classifying my project by subject matter, required me to submit a Health Sciences application and to commit to using two Letters of Information, one for interviews and a separate one for participant-observation and a script to use for email recruitment. These documents were based on templates provided by the research ethics office. I received approval from the University of Southern Ontario Health Science REB, after revisions, in September 2012 after six

[7] It was not till the end of the second year of fieldwork, June 2013, that I obtained an interview with a university research ethics person and she was the only one to volunteer the information that REBs allow visitors at their meetings. She recommended that I approach another university-based bioethicist and together they were the only two ethicists who agreed to be interviewed during the period of my fieldwork.

months of interactions with the ethics office on the subject of my research's review. Since many of the individuals that I wanted to interview at hospitals were also affiliated with the U of T whose REB approval I eventually obtained through affiliation with the Centre for Ethnography, I did not pursue hospital REB approval. (This did not prevent my observing hospital REB meetings which are mandated to provide for members of the public to attend.[8])

The majority of biomedical research projects are reviewed with the highest level of scrutiny and stem cell scientists are accustomed to the complex co-ordination needed to conduct "multi-site" research projects and to the requirement of ethics approval at every institution involved. I, however, began fieldwork with social science critiques of ethics review procedures and of "mission creep" (as more and more modes of enquiry come under the purview of institutional review) fresh in mind. I had anticipated that a mutual understanding of what I should know, what I could record and what I could write about would be worked out dialogically in each interaction (or, to Princeton's IRB, in the process of "oral informed consent"). The encounter with Dr. Post made clear to me that I was thinking of the ethics of research to reside in issues of analysis and representation, whereas for her, it was located in procedure and centrally concerned with informed consent and documentation (Heimer and Petty 2010). As social scientists have pointed out, one of the defining features of research ethics procedures is the generation of documents that function symbolically as evidence of compliance and, practically, as tools making researchers' practices available to increasingly prevalent audit practices (Riles

[8] In this, I was met with a more positive reaction than Canadian sociologist Will Van Den Hoonaard who hoped to observe fifteen board meetings for a book on the REB but was given permission by only five (2011).

2007). Dr. Stevens' performance in opening the files was a display of the completion of the requisite documents and of the considerable investment of time and effort that such documentation requires. Medical anthropologist Cheryl Mattingly has attested to the fact that IRBs using a medical model have over the last twenty years become increasingly influential in universities and hospitals and "scrutinize proposals and, especially, consent forms, with a level of attention unheard of when I began in the mid-1980s" (Mattingly 2005: 454). (Her own hospital research consent form, she notes, has gone from a one-and-a-half-page form that she used for all participants in 1986 to five single-spaced pages of legalistic text that comes in eight different versions depending on the category of participant as of 2005 (Mattingly 2005: 454).)

Studying the REB

My efforts to include research ethics meetings in this project grew out of my interest in biomedical understandings of the ethics of research, in how biomedical research proposals are evaluated and in how they might be shaped by REB review. That this became the most challenging part of my fieldwork highlights ideological and structural dimensions of the review system and the way in which they have the potential to obstruct research into regulatory review itself.

The policies and conventions of research ethics offices do not easily apply to themselves. Applying for REB approval required finding a sponsor from the researchers within the institution to be "jointly responsible for the conduct of the research". Practically, this requirement proved so awkward that I ended up abandoning my attempt

to gain REB permission at the hospitals. It would have protected patients if those had been the subjects which I was proposing to study. However, when potential study subjects are themselves members of the institution, it becomes more difficult to fulfill this requirement due, if not to sponsors' reluctance for themselves or their colleagues to be studied, then to perceptions of conflict of interest. As the outgoing head of the department at the University of Toronto remarked in response to my sponsorship dilemma, "I hadn't realized our hospitals were quite so controlling..." Conflict of interest, in particular, has been made a particularly significant topic in bioethics and regulatory literature because of concerns over the intrusion of commercial interests into scientific research. (Lemmens and Waring 2005). However, it may also make it more difficult for studies that challenge power structures.[9]

After applying to the Health Sciences board at the University of Southern Ontario, conflict of interest concerns were again raised, this time effectively making it impossible for me to study the university's ethics review process for any biomedical research because my protocol was reviewed by members of the board that reviewed biomedical research. Conflict of interest was then given as the reason why I could not speak to anyone on that board. The tangles that resulted from my attempts to include research ethics officers in my research suggests that there is an opacity to ethics review.

More fundamentally, my experiences with bioethicists and REB members highlight the unequal power dynamic inherent in the category of "study subject". With

[9] The TCPS2 acknowledges this in a section on "critical inquiry" (separate from the section on ethnographic research) which states that a researcher engaging in a study "critical" of an organization does not need to obtain its approval, suggesting that the study must be predetermined as "critical" (CIHR, NSERC and SSHRC 2010: 35-36).

their roots in the horrors of past human rights abuses conducted in the name of medical science, human research subjects' protections and their main tool, institutional research review committees, take the unequal power of researcher and study subject who must therefore be protected from exploitation or abuse as a key assumption. Preventing a researcher from approaching a potential subject unmediated by a review board, this premise, paradoxically, undermines the subject's autonomy in attempting to preserve it by assigning responsibility for its protection to others, a version of the opposition of autonomy and paternalism generated at the core of liberal theory. In my case, my study subjects were experts engaged in research or working in other capacities at high levels in university or hospital research governance structures. This led to some contradictory reactions.

For example, my encounter with Dr. Post and subsequent work on REB applications taught me to think like an REB and mentally recast Dr. Post as a "study subject." The key questions then are whether her consent was "fully and freely informed" and to what degree of "harm" my actions had exposed her. If, at the time, I had been using a recruitment email script, letter of information and written consent form, the harm that could have been pre-empted was her social discomfiture which ironically was largely created by her expectations surrounding these practices themselves.[10] At the same time,

[10] After this experience, I became preoccupied with being perceived as putting undue pressure on individuals to participate in my research. Dr. Post was an expert in research ethics and the rights of study subjects (such as their right to say "no" if they do not want to be part of a research project), but perhaps I had inadvertently created a social situation in which she felt pressured. That I was physically present in the outer office, that the secretary was, in a sense, petitioning on my behalf and that she had to make a decision on the spot could all have made it more difficult for her to say no. As fieldwork progressed, I began also to wonder about the "ethics" of other "recruitment" issues such as, for example, whether or not it was acceptable to capitalize on a face-to-face meeting by following up with an interview request or to mention to a prospective research participant that someone else had encouraged me to speak with him/her (in case this created a fear of disappointing a colleague).

my approach to REB chairs which resembled a colleague or student approaching an academic rather than a researcher approaching a potential subject was received positively. I reverted in my emails to REB chairs to my earlier approach of explaining who I was and what my research was about and asking permission to attend a meeting. It did not occur to me to use the "invitation" to be a research subject recruitment script. The Chair's permission seemed sufficient as though the REB did not itself need the mediation or protection of an REB review.

My intuitions in this regard seemed mirrored by my reception - The Chairs took on the mediating role, representing the interests of the board members and obtaining their agreement before allowing me to attend. Even although I did not have REB approval from any of the hospitals, the Chairs that I emailed about observing meetings agreed without raising the issue. Only once, at a hospital REB meeting, did my lack of approval come up in conversation. The Chair stated that I did not have the hospital's approval to attend the meeting: "I know. I checked." I explained that I had tried but run aground and he asked what had happened. I launched into an account of emailing a senior administrator who did not seem to think that REB approval was necessary (which was wrong, he asserted) and then trying unsuccessfully to find a bioethicist at the hospital to co-sponsor my project. He wanted to know whom I was talking about and started throwing out names. This was the same Chair who had been concerned enough about the confidentiality of his board members to ask me for a one-page document on the subject. He either did not view the exchanges that I was describing as part of my research or else considered himself as belonging to the category of REB reviewer rather than that of those among whom identities are supposed to remain concealed.

That my interviewees were not accustomed to thinking of themselves as study subjects was most vividly illustrated by one hospital-based stem cell scientist. Fresh from working through local REB applications, I began the interview by confirming his consent. I repeated the information that I had emailed him about myself, my research and my commitment to disguising identities and, telling him briefly about the difficulties of finding a local sponsor, made it clear that if we proceeded, I would be interviewing him with IRB approval from Princeton but without the permission of his hospital's REB. He waved a hand airily and remarked with some bemusement, "I can talk to whoever I like." I felt a little foolish. I understood his reaction (and slight impatience) as a sign that he resented being put in the position of "study subject" in need of protection (and, by extension, resented my concern over lacking approval) and as an implicit critique of the review model for its assumption that, as social scientists have pointed out, researcher and subject are necessarily unequal with incommensurable kinds of agency (Lederman 2006: 488).

The mainstay of human subjects' protections is the idea of informed consent premised on the assumption that access to unbiased information allows for an "autonomous" decision to be made to be included in a study. A decision made without coercion, pressure, influence or self-delusion allows for "free and informed" consent. "Respect for autonomy" is therefore operationalized by removing from communications with potential subjects any references that are personal and therefore understood as potentially biasing. My own recruitment email modeled on the boilerplate template from the University of Southern Ontario website – "Invitation to participate in research" and included the line (to be used verbatim): "If you would like more information on this study

or would like to receive a letter of information about this study please contact the researcher at the contact information given below". The language of the recruitment script was spare and impersonal and clearly designed to avoid pressuring individuals in any way to participate as even the use of the word "invitation" rather than "request" or "enquiry" suggests. The REB therefore pares text down to a bare minimum, deciding for both the researcher and the potential subjects what information potential subjects should initially be given and there is room in the script for only a brief description of the project; the recipients of the email have actively to open attached documents to find out more or contact the researcher if they have questions, but, of course, they do not know what it is they do not know and which might affect their decision. REB protocols are built on a presumption that research can be abstracted from a social context, that the researcher can be separated from his or her research. It is precisely the idea that they are inseparable that is one of the core epistemological commitments of anthropology.

Descriptions of research abstracted from all social context distill the description into information. Information appears as factual and independent of the person relaying it. Suggested by the term itself, informed consent makes information central to a potential research subject's decision to participate, of a piece with understandings of transparency as the disclosure of information. And it makes the flow of information one way, from researcher to participant. For example, one of the Health Canada officers at the beginning of our telephone interview offered to sign and send back the consent form that I had emailed her if I really needed it but seemed to think that I was miscategorising our interaction, saying of the form, "It kind of sounded like we were subjects of your research versus providing information." A research subject is the source of "data," not a neutral

purveyor of information.

“Bad Science is Unethical Science”: research review as common sense

The bioethics logic of protection’s operational power emerged in REB meetings as I listened to the board members’ summaries, evaluations and discussions of research proposals. The logic of protection, an “ethical ideology” of guarding against harm, is operationalized in REB evaluations via risk/benefit analysis (Swiffen 2007: 219). As I observed it in action, this was an effective mechanism for evaluating research proposals from various highly specialized fields and for justifying the evaluation of the quality of their design and methodology as human subjects’ protection.

I observed full board meetings of REBs in the health sciences covering such areas as biomedicine, public health, social work, nursing and pharmacology, and including boards for a community-based hospital, an academic research-intense hospital, university faculties of medicine and related departments and integrated hospital and university-hospital systems. The university and hospital REB meetings that I attended looked very similar to one another. They were comprised of six to ten members, including a community representative seemingly chosen because he/she was a “stakeholder,” not in the health sciences. (The community member of one hospital REB, for example, had spent considerable time in treatment there as a child.) They met once, a few twice, a month. REBs are composed of a minimum of five members, including two experts in the general subject area covered by the REB, one expert in ethics and one community member to provide the “lay” or patient perspective. Other than stipulating that this person

have no official affiliation with the institution, the TCPS 2 leaves the criteria for community member open. For biomedical research, a legal expert is also required. In an analysis of the public consultation which the Canadian Royal Commission on Reproductive Technologies conducted with the goal of representing Canadian society, Marilyn Strathern has pointed out that despite the emergence of ELSI (ethical, legal and social implications of science) rubrics, ethics review committees do not include experts in society (Strathern 2005: 474). Society appears as something that can be conferred with directly through public consultation or that can represent itself through community involvement in the REB; it does not need the mediation of an expert (Strathern 2005: 474).

The REBs met in a boardroom, sitting around a table, flipping through documents, approving minutes, reporting on protocols and working through the meeting agenda. They followed the same general procedure. As one Chair explained it to me, the review process begins with a quick scan of the application to determine which board members' expertise would make them the best qualified to review it. Then a primary and a secondary reviewer are assigned. If there is no one in the same field as the research proposal under review, the REBs assign the members with the most relevant expertise. In the meetings that I observed, a few members (the primary reviewers) each presented their assigned research proposal to the group, summarizing the main ideas, goals and methods of the research and then proceeding to a critique before opening the floor to wider comment and discussion. The “community members” took their turn as primary reviewer. Sometimes the reviewer had very few criticisms to make. At other times, he/she had a long list of comments and questions, many of which would eventually be relayed to the

researchers.[11]

I began attending REB meetings expecting to find board members frequently referring to rules, policies and precedents, or else becoming embroiled in ethical conundrums. Instead, I found a bioethics logic relying on a premise that all research brings risks which the researcher has to acknowledge and mitigate. It is a practical limitation of a health sciences ethics review board that its general subject experts cannot have the expertise to cover every specific subject area for which the board is responsible. As a result, also, of concerns over conflict of interest, biomedical REB members must necessarily review a number of research proposals in areas in which they do not have specialized knowledge. In meeting after meeting, the identification and assessment of potential harms prompted critiques of choices of procedure and measures, many of which struck me as commonsensical. Reviewers were looking for sound reasoning and evidence that the decisions that had been taken were logical and consistent. They attended closely to language. Clearly reasoned, well-supported, well-written and carefully presented research proposals were valued most highly.[12] A study that was poorly designed, loosely

[11] While each institution's REB followed the same basic procedures, the atmosphere varied somewhat between groups. In all meetings, the Chair was clearly the leader, but his/her personality, experience and personal style could give a different tone to the discussions. For example, in one meeting, the Chair was very experienced with establishing and running REBs. Perhaps partly in response to my presence as both an outsider and a student, the meeting was more educational in tone and at times felt like a university seminar, compared to the others which moved briskly through the agenda in a business-like fashion. At the end, the Chair gave me the opportunity to address the group with any thoughts or questions that I might have. In fact, this particular meeting was, I was told, fairly unusual, in that it began with two PIs answering the board's questions about their protocol in person. The board members seemed to find it helpful to be able to ask for clarifications, express their concerns and receive an immediate response in the back-and-forth of dialogue; not only did it provide the board with the answers that they needed and highlight an application's strengths and weaknesses ("the PIs can either dig themselves out of a hole or dig themselves into one," commented one board member), it was, the Chair argued, a useful learning experience for the PIs on seeing and thinking about ethical issues.

[12] Reviewers take sloppiness as a proxy for the researcher's ability and sense of responsibility – as Laura Stark phrases it, as the basis for a moral judgement of the researcher's "scholastic virtues" (Stark 2006: 176).

reasoned or insufficiently supported by the available evidence was challenged on ethical grounds since the less likely a research proposal was to produce meaningful results, the less ethically justifiable it was deemed to subject subjects to risk.[13]

Reviewers were particularly attuned to drawing out unstated assumptions that researchers appeared to be making. At times, they imagined scenarios that might be consequent to the proposed research activities that might harm the participants and which the researchers gave no indication of having considered. At other times, they were concerned that the unstated assumptions were based on an unrealistic, inaccurate, or illogical appraisal of the phenomena under study, one that would bias the results. Then they asked whether the researchers would really measure what they thought they were going to be measuring or whether something else would affect the behavior they were studying; would confounding variables undermine the legitimacy of the conclusions?

In response to gaps in logic or evidence, a frequent question was therefore "what is the rationale for doing this?" Reviewers expected the reasons for proposing specific measures, procedures or numbers (such as dosages) to be clear so that they could assess whether or not they were scientifically and ethically justified. What was deemed a well thought out proposal used the same evidence to make a scientifically sound argument and an ethically sound argument that the merits of the research outweigh the risks. I

[13] REB members brought personal experiences to bear on the research under review. For example, in a review of a speech pathology research project on "turn-taking," a board member referred to his experiences with his autistic son to underline the significance of this line of research. On another occasion, the board was discussing the degree of discomfort that might be involved for participants in a study on walking for amputees and an older board member, referring to his own health challenges, solidified the board's opinion by saying "as someone who has had to teach himself to walk again twice, I can tell you inclines are difficult…" Anecdotal evidence of this kind appeared to hold its own amidst the pieces of corroborated scientific evidence, suggesting that experience carries considerable epistemic (and rhetorical) weight.

witnessed several discussions on the justification for certain decisions in relation to the "standard of care". Without information on the current medical standard of care, they said, they could not assess the risk/benefit balance of proposed research interventions. If, then, a medically accepted treatment for a condition already exists and the researchers are proposing modifying or replacing it with something else that may turn out to be less effective, the potential knowledge created would have to be sufficiently valuable to outweigh the potential risk to the participants.

For example, one REB debated the relation of proposed research interventions to prevailing standards in response to a research proposal on blood-forming stem cells. The researchers were proposing to give blood transfusions at 70 and 90 units of measurement when the clinical standard is 80 units of measurement. The REB members who discussed this project made several points: 1) The available evidence, even if it is slim, suggests that 80 is the optimal level which is why it is the value used by the vast majority of clinics. 2) The researchers were proposing to compare only two values. 3) The study risked being irrelevant to clinical practice since neither of those values was the current standard. Two key questions emerged in discussion: How strong was the evidence to suggest that the values chosen would have any effect other than a more harmful one compared to the current standard? They wanted this information to assess the level of risk participants would be running. Then, given those risks, would the knowledge produced by the study be useful and relevant enough to medical practitioners to warrant subjecting participants to them?

At such times, reviewers' critiques extended from illogicalities and

inconsistencies to more direct assessment of basic research design and methodology.[14] The REB members would, at times, self-consciously separate "the ethics" from "the science" in their comments, but it was understood that scientific evaluation was a part of ethical evaluation. Indeed, on several occasions I heard a version of the opinion that "good science is ethical science." I repeated this phrase to the REB members on the occasion when the chair allowed me to address them and one of them suggested that instead "bad science is unethical science." Another then said that the decisions researchers make when putting together a research project are normative while a colleague added, "There is no such thing as value-free science."[15]

If the idea that ethical evaluation necessarily involves evaluation of the science is a tenet of research ethics, it appears to lead to a lack of clarity of roles. For example, during a hospital REB meeting, after a discussion of some of the methodological weaknesses of a student researcher's proposal, a board member commented that methodological issues seemed to him to be taking up an increasing amount of their time. Where, he asked, did the board's mandate end in this regard? Was addressing methodological issues not the job of the supervisor? Would the supervisor feel that the board was stepping on his toes if they kept questioning the scientific rationale for certain

[14] In this they are likely different from academic communities without medical schools where a tradition of departmental autonomy may mean that REB committees are more likely to leave evaluations of research design itself to the judgment of faculty, as Rena Lederman found at Princeton (Lederman 2006: 486). All of these REBs were at institutions with medical schools or engaged in biomedical research. I suspect that the amount of biomedical research conducted at the institution is a more salient distinction among ethics committees than that between Canada and the US.

[15] In a historical and ethnographic study of IRBs, sociologist Laura Stark illustrates a further way in which ethical evaluation is inextricable from scientific merit (Stark 2006). Using the history of deception within psychology, she illustrates how certain research practices which were initially controversial became standard practice once they were certified as ethically acceptable. In this way, ethical judgements are embodied in scientific practices themselves.

decisions? This was the second time they had seen this particular proposal and were wondering if it had passed muster within its home department. How far could they insert themselves into the supervisor-student relationship? After critiquing what she considered a particularly unsatisfactory proposal, one reviewer asserted that researchers should at least be able to demonstrate to the REB that they have a basic understanding of research.

To Dr. Grant, the Chair of the community hospital meeting, REB review could be compared favourably to peer review. He told me that he had also served on peer review committees and implied that the REB review process produced a more thorough evaluation of proposed research projects. Peer review committee members, he claimed, often do not even discuss thirty of the fifty projects submitted to them because they are weeded out, leaving only the "big name" scientists' proposals for consideration and the committee largely takes it on trust that these scientists know how to run an ethical study. His implication was that REBs are more democratic as they subject all researchers to scrutiny regardless of their status or reputation and that peer review committees should also be attentive to both the scientific quality and ethicality of proposals.

Risk has, of course, been the object of considerable sociological attention approached as a key element of modernity in the form of the "risk society" (Beck 1992), as a biopolitical strategy (which raises the question: Who is assuming the risk in emerging biopolitical and bioeconomic regimes?) (Cooper 2008; Cooper and Waldby 2014; Sunder Rajan 2005; Weir 2006), and as a core technology of regulatory institutions (Brown 2014; Hutter and Power 2005; Kemshall 2014; Power 2007). This last focus has produced research that is particularly germane here, such as the work of Bridget Hutter who has explored the rise of risk approaches in the context of deregulation initiatives,

particularly those that appeared in Britain and the US in the 1980s and 1990s (Hutter 2005). Hutter summarizes those elements of the appeal of risk analyses that, she argues, particularly resonated at this time: "Such a climate arguably created and sustained an environment which favoured the adoption of approaches which incorporated costs benefit analysis, were apparently 'objective' and apparently transparent. Risk based approaches appear to satisfy these criteria with the added bonus of coming from the business sector. Risk based tools came to be seen as efficient instruments for making policy choices and aiding in decision-making" (Hutter 2005: 304). While appearing objective, risk management tools necessarily rely on identification of future harms, or more accurately, losses, which are identified as such from a particular point of view and could be understood differently. Also, and this is a point Hutter among others has made, these kinds of analyses leave unanswered the question of what is an acceptable level of risk or an acceptable cost (Hutter 2005: 310). As Weber asserted that science can provide the most rational means to an end but not decide what those ends should be (Weber 1946: 151), so risk matrices and calculations, as tools, say nothing about which units to apply them to or how to use the information they produce. Identifying risks and making decisions about the acceptability of risks is the work of the REB. As the board deployed risk in their discussions, it had the appearance of an objective and scientific concept, yet it also seemed to be frequently identified intuitively and to be interchangeable with harm.

In their probing of assumptions, part of what the REBs were doing is reminiscent of Strathern's characterization of Euro-American knowledge making in general, and anthropology in its social constructionist mode, specifically, as endeavors that make the implicit explicit in a process of "literalisation" (Strathern 1992: 5). As Geertz' common

sense is made of cultural "presuppositions," "literalisation" involves making taken-for-granted assumptions about nature or reality explicit. Just as a large part of the epistemic and rhetorical persuasiveness of common sense is due to its appearance as simple, true statements about the world ("the unspoken premise from which common sense draws its authority – [is] that it presents reality neat" (Geertz 1983: 76)), the perception of Euro-American knowledge making, Strathern writes, is that, "Clear away the assumptions, and you will get to the truth" (Strathern 1992: 7).

Part of the power and appeal of the "literalisation" of social constructionism for anthropologists is that it shows the contingency of current arrangements, that things could be otherwise. REB common sense with its ideological commitments performs an unearthing analogous to the one that anthropology's constructionist analysis performs on culture or ideology. In the case of the REB, the most common effect may well be to further entrench the axiomatic status of taken-for-granted ideas and values. However, in what follows I suggest that it is also clear from my discussion of the REB with Dr. Vargas (the stem cell scientist introduced in Chapter One who had assisted several Canadian and foreign researchers take stem cell projects through regulatory requirements) that different scientific disciplines can make such different assumptions about the world that REB critiques can lead away from "the real" in the eyes of the researcher.

I had been told to speak to Dr. Vargas about REB review of stem cell research projects as she was particularly experienced in this area. Indeed, in our interview, her expertise emerged as one of the key things that, in her opinion, structured her experience of review. REB members, she explained, are "doctors or PhDs in whatever their area is,

so they'll ask you questions that occur to them without necessarily understanding it from an expert level." She said: "they have a lot of questions which are sometimes difficult to address because I haven't even thought of those kinds of questions or that those questions could exist so I think it's an education process for them." Wondering whether such questions had a reciprocal influence on her, I asked her if feedback she had received from REB members ever made her reconsider her scientific questions. To this, she responded: "Well I definitely think they make you think about, not your scientific questions, but your scientific rationale and the justification that you have to provide for it." She continued: "I do think it provokes you because they're not content experts in your field but they may be content experts in immunology or something else and you haven't really thought of it from that side… It's definitely thought-provoking. It gets you to think of things from a different angle."[16]

In response to provocative REB requests, she told me, she and her team sometimes have to conduct experiments to generate further data to add support to their proposal and sometimes they can only provide hypothetical evidence. She described a recent incident where "they asked us a very specific question and there's no good way to answer that." She said: "We'd done some experiments but the experiment to prove that doesn't actually exist. But we thought about it and we did some thought experiments." She continued: "often I find these are thought experiments that you have to design to best answer it and use physical data that you have to supplement the thought experiments to kind of say 'well this is the reason it's feasible'…" They provided as much physical data

[16] Interestingly, Laura Stark found that critique of the quality of the science tended to come from experts belonging to disciplines other than that of the investigator (2006: 180).

as they could and the rest existed in imagination. For Dr. Vargas, interdisciplinary REBs, tasked with the ethical evaluation of her stem cell research projects, raise technical questions that can be answered only with counterfactuals.

Dr. Patel: "Science done well."

Bioethicist Dr. Patel offered a bioethics explanation of why ethical evaluation involves scientific evaluation in research review. I met Dr. Patel, an affable, thirty-something faculty member in bioethics in his university office. A molecular biologist by training, he had done doctoral research in cancer biology before moving into bioethics for a Master's and a Postdoc with the American Medical Association where he worked on dual-use research (not long after September 11th and the anthrax attacks). He had started taking ethics courses as an undergraduate "just for fun". He told me: "As a geneticist in training I was rather shocked that we were being told we had twelve compulsory genetics courses and none of them had an ethics component so you're training people to manipulate DNA… but you're not teaching them to think about the impact of these things on society and on patients." After his Postdoc, Dr. Patel had worked at the Ontario Genomics Institute helping it enact a new Genome Canada (the country's national genomics funder) program called GE³LS (short for genomics-related ethical, economic, environmental, legal and social issues), through which Genome Canada requires biomedical research projects be integrated with ELSI projects.[17] At the time of our

[17] My conversation with Dr. Patel suggests that Genome Canada's GE³LS program has had mixed success in its goal of encouraging integration of scientific and ELSI components into joint research projects. The attempt by Gaymon Bennett and Paul Rabinow to rethink constitutive concepts and the nature of

interview, he had been working in a university Global Health program helping develop it into a research ethics consulting organization and working with the Gates Foundation. He had also served on several REBs and was the longest-serving member of SCOC.

For Dr. Patel ethical requirements for research necessarily go beyond human subjects' protections strictly defined and include research design and methodology as a basic tenet of research ethics because "if you're running a trial that has, through its design, no hope of answering the research question then you're subjecting patients to risk for no good reason." In that situation, he continued, "you can't justify subjecting them to any level of risk so there's a necessary amount of validity that needs to be in place for a trial to be considered ethical." For example, if the results will not be statistically meaningful, because "you're not powered well enough… meaning you haven't got a large enough subject pool to answer the research question then you're subjecting people again to risk for no possible benefit even knowledge benefit."

The view Dr. Patel articulates dominates in biomedical ethics writing. It is found, for example, in the International Ethical Guidelines for Biomedical Research Involving Human Subjects published by a WHO-affiliated NGO which states: "Scientific review and ethical review cannot be separated: scientifically unsound research involving humans is ipso facto unethical in that it may expose them to risk or inconvenience to no purpose…" (Council for International Organizations of Medical Sciences 2002: 25). In Dr. Patel's opinion, while REBs consider the science, asking to hear statistical justifications, for example, they generally do not press hard enough on scientific validity.

collaboration together with synthetic biologists illustrates the challenges of irreconcilable epistemological differences (Rabinow and Bennett 2012).

He told me, “if it has passed peer review, it’s unlikely an REB is going to stop it.” Dr. Patel, then, would like more questions of scientific merit to be subject to the risk/benefit calculus that dominates research review. That Dr. Patel’s examples of questionable scientific validity focused on statistics is of a piece with a kind of evidence-based approach to ethics, one that tries to make processes of evaluation maximally objective, processes that are shaped, as social scientists have illustrated (Stark 2006), by the history and structure of the REB and the dynamics of member interactions. A second key tenet of research ethics for Dr. Patel is social benefit of the research. In the same way that good science is necessary but not sufficient for ethical science, for Dr. Patel, the production of valid knowledge is necessary but not sufficient to make a research project ethical; it needs to produce some kind of “social value”. I had suggested a role for “knowledge for knowledge’s sake” and he responded by drawing on a general example from his global health work - a clinical trial of an intervention in a population that could never actually benefit from it. He said: “there’s got to be something more to it, especially if you’re going, say, into a developing country setting where you’ve got people who are already profoundly disadvantaged and you’re asking them to incur risk. If there’s no value to them, if it’s strictly some esoteric knowledge creation, I’m not sure that that would meet the threshold of an adequate level of value to justify the trial.” This is an area in which he thinks REBs again fall short. He stated: “Without the potential for social value, you shouldn’t be doing the trial. It’s a well-established element of ethical research but REBs are not very well positioned to adjudicate social value.” Dr. Patel reflects a recent turn in research ethics scholarship to the importance of social value as the ultimate justification for biomedical research. Despite a history of reflection and debate in philosophy and the

social sciences on the concepts of society and value, relatively little critical attention has been given to social value in bioethics literature (Habets, Delden and Bredenoord 2014).[18] To the extent that health sciences REBs consider the social value of the research they are reviewing, (which is designed using inclusion/exclusion criteria determined by the investigator), "social" seems to refer to little more than the instrumental value of the anticipated knowledge.

In my interview of Dr. Patel, I rather inartfully suggested that bioethics could be considered to be in the service of biomedicine and he replied "I don't think it's in the service of science, though I would say if done right ethics can be enabling of better science, of science done well." To Dr. Patel, research ethics documents have necessarily to be interpreted which means that difficult ethical decisions require people to apply "the spirit" of ethical guidelines. At the same time, he told me that scholars are working on developing a risk-benefit framework to "give people a tool for better decision-making around the risk/benefit assessments." After introducing such open and abstract concepts as scientific validity and social value, Dr. Patel expresses an aspiration to instrumentalize such notions which suggests that the validity of bioethics decisions relies on a formalized reduction of thorny political and moral questions.

A prominent strand of social theory depicts the state's legitimacy in the face of irreconcilable moral positions as an effect of recasting them as technical problems with solutions offered by value-free science. In his analysis of the reception of hES cell

[18] Ethicists Habets, Delden and Bredenoord point out the ambiguity surrounding the concept of "social value" in the research ethics literature which has been more concerned with taxonomies of value than with interrogation of the concept of society (Habets, Delden and Bredenoord 2014).

science in Germany, Stefan Sperling, for example, argues that the bureaucratic routine that ethics committees eventually established turned open-ended ethical and policy questions into questions of scientific merit with technical or scientific answers (Sperling 2008: 373). Dr. Patel's portrayal of bioethics tenets supports this depiction of ethically-contentious debate neutralized by objective, rational bioethics decision-making tools. However, I would argue that while there is a reduction or selective translation of ethical concerns as they are moved from the public and other realms to the arena of ethics committees, the scientific or technical framing does not supplant ethical concerns. Indeed, to the REB members of my fieldwork, ethical concerns are always already present, inherent in the practice of any science that takes humans as subjects of research and directed towards the improvement of people's health. If stem cell policies turn ethical issues into technical ones, REB analysis turns questions of scientific merit and methodology back into ethical issues.

Science in society, society in science

Speaking of the debates leading to the AHR Act for stem cell research, the stem cell scientists of my fieldwork were critical of lawmakers that they considered ill-informed about the science. With regard to ethical regulation in general, they were suspicious of opinion, of normative philosophy, of decisions made for political reasons and of religious or pseudo-religious views which they contrasted with the facts, the science and the evidence. However, perhaps partly motivated by the knowledge that I was a social scientist, they spoke of ethics regulations in relation to society and as a

necessary mediator. In my interview with Dr. Stevens, I commented on the difficulty I had been having finding ethics officers who would agree to be interviewed and she responded by depicting the REB at her hospital as representative of Canadian society: "I know our REB is made up of a broad spectrum of people from all across the university and the hospital - I know most of them - and so I'm aware that they're reviewing my research process constantly. And it's very interesting because the REB, it's almost like they're falling back to some degree on a compilation of personal ethics because everyone at the table has a different role in society and they all perform different functions and they all get together and they offer a group sort of ethics survey… so they do represent society I think." Other stem cell scientists spoke more generally of science, distinct from the public or society and related them to one another with deliberative bodies like the REB or peer review committees enforcing "appropriate" Canadian standards. Ethicist Dr. Post offered the most forceful example of an understanding of research ethics review in Canada as rigorous and reflective of Canadian values, but many scientists pointed out, like Dr. Stevens, that "it's the public purse" through government or donor grants that support their research making scientists accountable to society. The view is of a piece with regulatory instruments such as the TCPS2 and SCOC. In the TCPS2 new knowledge "benefits society in general" (CIHR, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada 2010: 5). The document equates society and the individual - society can be subject to the risks as well as the benefits of research. Largely congruent, society and the public come apart when responsibility falls to "society" to ensure the ethical conduct of research: "We must do all that we can as a society to ensure that research is conducted in an ethical manner so

as to build public confidence and trust" (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada 2010: 6). In the work of SCOC, Canadian society appears composed of groups of differentially affected stakeholders. SCOC is made up of members with different expertise, including "representatives from the general public" who are understood to "represent the views and values of Canadians potentially affected by the new technologies" (Terms of Reference 2014).

The incorporation of Canadian views also animated the process through which Parliament came to have knowledge about Canadian society's views of reproductive technologies and research via the Royal Commission's report which it entitled "Proceed With Care" in 1993 (Baylis and Herder 2009). The Commission posited that collective values could be represented (as they could be ascertained during periods of consultation) through the views of individuals. Scholars have pointed out that "society" as it appears in bioethics is an abstraction often deployed in pre-emptive research governance strategies (Strathern 2004). In this light, Canada's policy framework for stem cell research followed consultation of the public through soliciting the views of individuals from different social groups understood to make up society as a whole (Baylis and Herder 2009). As Dr. Marks (in the Introduction) was suspicious of a few "subsets" of the population directing national policy response, the Commission tried to ascertain the views of the body politic through a comprehensive incorporation of various groups.

In interview after interview, stem cell scientists emphasized, approvingly, how much more rigorous certain research practices have now become such as those surrounding the use of animals, in response to societal concern. Dr. Stevens, for example,

narrated a past of relatively little oversight and an informal research ethics of "pragmatic opportunism" that allowed scientists to make the most out of bodily waste: "So you go to the operating room and you take out a tumor and traditionally it was always sent to the pathologist and the pathologist has been the keeper of the tissue. And so in the past before REBs were developed - I'm talking 60, 75 years ago – the pathologist would make the diagnosis based on the tissue and then they had a whole bunch of tissue left." Pathologists, she told me, have traditionally "made a lot of the biggest research advancements because they had all this excess tissue which became theirs." She concluded, "then came all the restrictions and so on and then everyone realized just because we get that tissue and study it doesn't mean it's ours."

Dr. Stevens provided the most vivid example of ethics review as the imposition of "red tape" that can be "mind-bogglingly confounding," but, as a surgeon-scientist, she also viewed herself as having "a foot in both worlds." She told me: "As a researcher, if you don't have an assistant who is doing this work for you, this is a significant amount of your time, and for every grant I apply for this all has to be in order." At the same time, "I see the people those rules are meant to be protecting – they're my patients," she told me. She assimilated the imposed ethics structures around "having to ask" before collecting tumor specimens for banking and research to surgical consent. Her own patients have all donated tumor samples to her ongoing stem cell research project. "People see a huge benefit in potential good coming from their child's misfortune," she told me. They are donating to science and perhaps helping bring about a cure to benefit society.

For some, ethics innovations are the province of scientists and other experts. Dr. Kim, for example, talked of ethics as regulation and as informed by scientific

developments. Where contextualizing in relation to past medical practice led Dr. Stevens to suggest that the current research environment is less permissive than in the past, some like Dr. Kim presented today's environment as more permissive. To Dr. Kim, working in basic research, scientists are today ahead ethically as they are scientifically. He said "if you think of what we are doing in medical research which is totally ethical and ok and how that kind of thing would have been judged 50 years ago, you see that there has been enormous change." Practices which are "normal now" would have been surrounded "by big ethical restrictions." If "our ethical and regulatory structure" does not keep up with the speed of the science, he told me, "then it's going to create a break certainly." To Dr. Kim, societal values and regulatory structures are changing with regard to stem cell research to be more in line with scientists' practices, if not quickly enough.

In my discussion with Dr. Smith, he offered a similar view of social norms changing over time to be more in line with scientific consensus views, a depiction of technology as integrated into the social fabric. I had mentioned the public uproar at the news of Dolly and he countered: "Yes, but you know, things change quickly too. So, with in vitro fertilization, when the first test-tube baby was born it was hugely controversial and many jurisdictions thought about making it illegal. Now, I don't know, 20-something years later, it's a part of a woman's spectrum of reproductive rights, you know what I mean? It's not something you easily take away from people as a medical procedure." Rather than the speed of the science, Dr. Smith speaks of the speed with which technologies become part of people's lives, identities and values.

Global Others

Canadian legal and policy scholars who have been working on stem cell policy since the advent of the human ES cell field, many of them associated with the Stem Cell Network, began their research into stem cell policy by tracking the emerging international policy landscape, systematizing the various national and intra-jurisdictional policies on hES cell research around the world and situating Canada's policy in international perspective. The leading institutional location for the scholars engaging in this work was the Centre for Genomics and Policy at McGill University. The comparative framing of this early research was echoed in my fieldwork where the sense that "human subjects' protection" in Canada is acted out through an entrenched and elaborate ethics bureaucracy rhetorically distinguished Canada's stem cell research environment from that of other countries. In presentations, interviews and conversations, scientists presented Canada's ethics framework in general and SCOC in particular as a marker of Canadian research vis-à-vis other jurisdictions. From invocations of stem cell tourism and bogus stem cell cosmetics to references to the questionable provenance of other countries' cell lines, Canada's system was contrasted with various Others.

During the course of my fieldwork, one of the most prominent stories about stem cells in the Canadian press was about former hockey star Gordie Howe's two trips to Mexico for unproven stroke treatments. He received an injection of stem cells in his spine in late 2014 and again in 2015 (Ubelacker 2015). In a newspaper response, Dr. Janet Rossant, stem cell scientist and policy adviser, and James Price, President and CEO of the Canadian Stem Cell Foundation, write that the broader scientific community cannot evaluate the treatments offered by such clinics because, being unregulated, they have not

released their data to outside scrutiny. They offer an alternative vision, one of "made-in-Canada treatments" that would be "rigorously reviewed" and, "once proven," would be available to all Canadians through the public health care system. (Price and Rossant 2015).

"Stem cell tourism" was a recurring topic at Stem Cell Network events presenting suspect clinics as a problem for other countries understood to have poor regulatory bite. At the Stem Cell Network's second course on socio-regulatory issues held in Montreal in 2013, there was yet another session on stem cell tourism. At the end of the presentations on the threat to unsuspecting patients of bogus foreign clinics, one of the legal scholars suggested to the assembled group that we should not become so caught up with the topic that we forget that there are also threats to the integrity of "our" own stem cell research, particularly collaborative research and the sharing of materials. If she was hoping to disrupt the framing of ethically suspect behaviour as something happening elsewhere with the potential to tarnish legitimate research here, she was unsuccessful. No-one spoke. At the conclusion of the course on regulatory and ethical issues, a scientist and ethicist was tasked with summing up the themes of the course. Looking down at the notes he had taken, he read out his own brief summaries of the topics covered. He referenced the stem cell tourism discussion with the question "what differentiates us from the snake oil salesmen?" As silence ensued, he quickly looked up and added, "There is no mystery to it..." A fundamental divide between legitimate and illegitimate science was affirmed in the moment, although, to me, it seemed as if that brief, perilous silence opened up the norms of legitimate science to question.

To Dr. Smith, the lack of unifying federal regulation in the US means that "from a

regulatory point of view, it's the Wild West." In the US, he told me, "if you have your own money you can do whatever the hell you want if the institution allows it whereas in Canada you're always put under this national program." Dr. Smith also highlights the prominence of the biotech industry in the US as an Other to publicly-funded research: "In terms of ethics, you know, anything goes if you're in a company. It's very different."

For Karen, the Peter Gilgan Centre hES cell lab manager in Chapter Two, regulatory differences had led to her being unable to complete part of her research in a collaborative project. She told me that she was part of a research project on the epigenetics of stem cells jointly funded by CIHR and the Japan Science and Technology Agency (one of three teams awarded funding in 2013 through this partnership), but had been forced to cede part of her research to her Japanese colleagues because the cell line they were using was not approved by SCOC. While pre-approval of common cell lines has accelerated the process considerably from the early days of the committee, an application to use an unapproved line would have taken too long to move through the SCOC approval process. She said waiting for the committee to acquire and assess the documentation was out of the question.

In interviews, I would often ask stem cell researchers if they had found jurisdictional differences affecting research collaborations and was told no. Only Karen had been hindered from research collaboration. However, scientists concerned with research management raised hypothetical problems involving the transfer of products, anticipating potential dilemmas posed by problematic regulatory regimes. Canadian bioethicist Zubin Master and US bioethicist David Resnik argue that MTAs are mechanisms through which scientists and management staff can exercise "social

responsibility," keeping materials out of the hands of unethical scientists (Master and Resnik 2011). Dr. McKenzie, the technology transfer officer who worked with Dr. Nagy on the MTA for his ground-breaking human ES cell lines, told me that the MTA needs to be consistent with Canada's regulations, the terms of the patient consent form and the regulations of the jurisdiction to which it would be sent. Creating an agreement for the United States was easy, he told me, as "there are quite well-defined and rigorous rules around embryonic stem cell research" but "what do we do if we get a request from China or some other jurisdiction where we don't really know what level of control or rules there are?" I quickly asked "so what happens in that kind of scenario?" and he responded "so, fortunately, we haven't had such a request yet."

Similarly, Dr. Patel wondered how Health Canada would handle an application for a clinical trial of a therapy made from human ES cells created in a lab for the purposes of creating a therapy (Only surplus IVF embryos can be used in Canada). Could they approve a drug that Canadian scientists could not test in their own labs? Or if a therapy using such cells was a success, he speculated, "you would have outcry if patient groups were not allowed to have access to that drug and at the same time you'd have a real conflict on your hands because Canada's moral code prohibits Canadian scientists from doing that so it's essentially saying 'well we're not going to let you do that here but if you do it elsewhere we'll still take advantage of your looser regulations to our eventual benefit; that's problematic.'"

Anthropologist Margaret Sleeboom-Faulkner who studies stem cell regulation in Asia has analyzed the boundary work of Chinese stem cell scientists as they discursively delineate their work from Others on both scientific and ethical grounds as valid and

legitimate (Sleeboom-Faulkner 2010). Sleeboom-Faulkner argues that even more important for Chinese scientists than concerns over patient safety or the legitimacy of their research was the imperative to be part of the international stem cell community and the collaborations, funding sources and publications it offers. Canadian stem cell scientists appear to be more confident of their place internationally - "we're punching above our weight" a researcher told me - but concerned to differentiate themselves as part of an ethical system that is carefully enforced in all areas of research.

Conclusion

Interdisciplinary ethics committees and stem cell scientists work with the same risk/benefit logic and fundamentals of scientific method. A key component of a proposal's assessment as good science is the researcher's skill at presenting their research in a way which evokes a form of argumentation that relies on logical analysis and well-reasoned justification of a position as the grounds for action. Stem cell science is still a contentious field in some quarters and stem cell scientists find the REB a welcome process; they express a certain comfort in their institution's requirements and the demonstration of approvals. They also use the institutional procedures and paperwork surrounding their research to comment on their experience of larger social shifts such as changing conceptions of the doctor-patient relationship and of the human body, changes that create new expectations of biomedical researchers, new procedures and forms of accountability (and paperwork). The next chapter looks further into the acquisition and movement of human materials, a particular focus of regulatory ethics, to illuminate two

different modes, one that is reflexive and adaptive and one that is more rigid and procedural. Examining the work in procurement of Stem Cell Network law and policy experts reveals the absorptive capacity of bioethics which legitimates the science and vice versa.

4. Becoming custodians: cells, models and policy innovations

The summer before officially beginning fieldwork, I visited Toronto's Mt. Sinai Hospital for a public education event on stem cell science. I looked down a microscope at beating heart stem cells then joined a tour of a stem cell lab, led by one of its graduate students. Having just learned about the new Donnelly Centre at the University of Toronto designed to encourage its inhabitants to mix and mingle across disciplinary or laboratory boundaries, and with scientific collaborations and cross-pollination of ideas in mind, I asked him about the physical layout of the space and the proximity of different researchers to one another. In response, he told me that researchers from different labs with different PIs may be sharing the same space and if they ran out of a reagent there is nothing stopping them from borrowing some from their neighbour at the next bench. I had been expecting him to talk about intellectual borrowings and I was struck by the fact that his response was specifically about the movement of materials and the possibility of their restriction. This led me to enquire into where the human cells used in Canadian stem cell research labs come from, what kinds of restrictions might there be on sharing stem cells, and what window on the regulatory and bioethical context of stem cell research does an enquiry into the acquisition and movement of materials open? As I learned about the practicalities of acquiring hES and iPS cells, I realized that the politics of procurement that emerged in the early days of stem cell research when the focus was on embryos have been made more complex by the development of reprogramming techniques; in the realm of procurement also, the emergence of iPS cell technology has brought new uncertainties.

The creation of hES cells has been the central issue of stem cell regulation with countries that allow hES cell research focusing on determining acceptable conditions under which embryos may be destroyed (Caulfield et al. 2009) and scholarly study of hES research has similarly focused on countries' regulatory responses to the ethical controversy surrounding the procurement of human embryos, as embedded in specific socio-political contexts or in global economies. For example, in the period of greatest public controversy in Canada over the moral status of the embryo, Canadian bioethicists brought attention to the health of women donors of eggs and embryos and the realities that the technology for acquiring them created for the women involved.[1]

Similarly, sociologists and anthropologists concerned with the commodification of body parts and a political economy surrounding the production of raw materials for research have directed attention to the role of women in supplying the embryos, eggs, fetal tissue and umbilical cord tissue and the potential for exploitation (Dickenson 2013; Cooper 2008; Scheper-Hughes 2011). Dominated by Marxian approaches, these scholars analyze women and their bodily substances and productivity as part of circuits of monetized and "altruistic" exchanges that have global reach and that are reinforcing and transforming hierarchies of inequality. (Waldby and Mitchell 2006; Cooper and Waldby 2014). For stem cell research in developed nations these materials largely enter the bioeconomy without direct payment. (Cooper and Waldby 2014). Other scholars like Sarah Franklin or Mette Svendsen have studied ethnographically the complex co-ordination needed to turn embryos that are deemed without reproductive value in the IVF

[1] For example, Francoise Baylis kept attention on the fact that a need for fresh as opposed to frozen eggs usually involved the donor going through extra sessions of IVF than would otherwise have been necessary with its not insignificant physical and emotional health risks (McLeod and Baylis 2007).

clinic into valuable research materials (Franklin 2014) and the decision-making of families asked to donate embryos (Svendsen 2011).[2]

Focusing on the procurement of embryos and its relation to the fertility clinic opens an important ethnographic window on the nationally-inflected representations and transformations that allow an embryo to move from a reproductive to a research context, processes that are obscured by the focus on the embryo as a potential life abstracted from kin relations which structured much of the policy and public debate around stem cell knowledge production. The raw materials of scientific research are vital to its existence and the rush of enthusiasm globally over the therapeutic potential of stem cells made it crucial to highlight and theorize the hidden labor of those supplying the raw materials to the bioeconomy.

However, iPS cells make gendered analyses of the stem cell economy more difficult because they rewrite biology in such a radical way. For example, Melinda Cooper and Catherine Waldby analyze the work done by female reproductive biology as the source of value in stem cell science in Marxian terms as women's alienation from the products of their reproductive labor. They characterize women's role in the emerging "stem cell industries" as reproductive labor which is obscured in the celebratory language invoking the regenerative potential of stem cells (Cooper and Waldby 2010). In a reworking of Marxian concepts of labor and value, they analyze stem cell science as a move from what they call reproductive to regenerative labor symbolized in the self-

[2] Svendsen analyzes the moment of transition from foreclosed future child to possible research resource as a re-conceptualization of the embryo taking it out of a web of kin relations and into a relationship with an abstract society to help produce therapies for unknown future patients – as a moment that happens in "the bin" (Svendsen 2011).

reproducing stem cell. They argue that iPS cells illustrate that "bodily potentiality is itself being reconfigured at the interface of new labour relations and the biological sciences" (Cooper and Waldby 2010: 17). This threatens their argument about the central material role of women's reproductive biology in the stem cell industries since with reprogramming technology, "regenerative labour" is unrelated to the reproductive capacity and the sex of the body. (They write, "While reproductive medicine demands a literal labour of reproduction from the female body, regenerative medicine is interested in *the body's* capacity for embryonic self-regeneration..." [my italics]) (Cooper and Waldby 2010: 17). It is precisely the distinction between reproductive productivity and other forms of bodily production that stem cell biology challenges as the understanding of the fixity and mutability of differentiated cells changes.

Other social scientists have examined the procurement of human embryos in relation to the bioethical regime installed to control it, particularly in Asian countries where stem cell science met with varying levels of public concern (Liu 2011; Sleeboom-Faulkner 2011; Zhang 2011). Sociologist Charis Thompson uses a Foucauldian approach to her study of stem cell science in California, arguing that hES cell research was "normalized" and achieved the level of public support that it did in the state despite pockets of resistance because of a bioscape - "constitutive technical, political and ethical trajectories of ideas, bureaucracy, and equipment" (Thompson 2013: 56) - that she calls "procurial" to highlight the importance of practices of procurement of embryos (as well as the pro-cures framing of many stem cell science advocates and, increasingly, the practices of curating biological samples in biobanks) (Thompson 2013). In Thompson's approach to procurement, the instantiation of a bioethics bureaucracy and its framing of

certain hES cells as “acceptable” were work-arounds in reaction to anti-abortion sentiment. She argues that the temporality of the bureaucracy was crucial to the successful establishment of stem cell science in the state and to whose ethical concerns and interests were recognized. The “upstream” placement of bioethical management of procurement is also at the centre of a normative argument that she makes that ethical attention prior to scientific research and development allows it to be made integral to the science rather than easily externalized and viewed as marginal to it (Thompson 2013: 29). In this, her approach echoes arguments being made within policy circles with notions of anticipatory governance, the need to influence the course of science through a simultaneous and prior consideration of scientific and ethical goals (Guston 2014). To Thompson, good stem cell science requires a deeper such intertwining of science and ethics (Thompson 2013: 29).

In this chapter, I build on Thompson’s attention to the entwining of technical and ethical concerns surrounding procurement but also draw attention to two aspects of bioethical attention to procurement that are less considered by Thompson, its orientation to uncertainty instead of risk and the reflexivity of its analyses. In this chapter, therefore, I move from prior review to notions of anticipatory governance of scientific research using, by way of example, the work of an international organization, the International Stem Cell Forum (ISCF). I suggest that its work is a form of governing configured to the uncertainties of scientific research and one that approaches the ethical and the technical in a more reflexive mode than the REB. I consider some of the ways in which scientists’ understandings of the human biological materials of their research change when those materials are from patients (such as tumors containing cancer stem cells or patient cells

turned into iPS cells), rather than established cell lines. How scientists think of the stem cells in their research reflects complex recent histories of controversy over the ethics of research with human samples; histories which have led to bureaucratic bioethical solutions that are currently entrenched in informed consent conventions. Returning to the work of the ISCF and drawing on recent anthropological work on uncertainty as distinct from risk, I look at how, indeed, ISCF policy experts are rethinking the ethics of procuring patient samples in response to current stem cell research and in a way that challenges bioethical conceptions of informed consent and its protectionist logic. By attending to the ISCF's strategic co-ordination of scientific and ethical/policy expertise, I shine some light on how another form of ethical reflection becomes incorporated into stem cell science. At stake in the research use of human cells are the perennial issues of who is included in the project of biomedicine and how risks and presumed eventual benefits are distributed.

The ISCF

The first example of an effort to jointly address technical and ethical concerns that I was offered in my fieldwork came in the 2012 interview with Dan Monroe mentioned in Chapter Two. He told me about an international effort to standardize stem cell lines in which Canadian scientists had played a major role. That endeavor was organized by the International Stem Cell Forum (ISCF). Created in 2003 from the nine major funding agencies from the various countries most heavily involved in stem cell science at the time – including the US, the UK, Canada, Australia, Israel and Sweden - countries with similar scientific and regulatory approaches and resources, the ISCF was one of several

international organizations that emerged in the early years of hES cell research, anchoring an emerging international stem cell research community. The Forum has been working in four areas – cell lines standardization, ethics, intellectual property rights and stem cell banking. Canadian researchers were heavily involved in the ISCF with Janet Rossant on the Steering Committee and Andras Nagy and other Canadian stem cell scientists co-ordinating standardization studies.

Canada's CIHR was in charge of establishing the Ethics Working Party (EWP). It is housed in the Faculty of Law at the University of Montreal with legal scholar Bartha Knoppers as its Chair. Dr. Knoppers, Director of the McGill University Centre of Genomics and Policy, has for a long time lent her expertise to help shape Canadian policy on medicine and science (she was one of the authors of the Royal Commission Report on new reproductive technologies) and has been a member of several international organizations of biomedical policy and bioethics such as the International Ethics Committee of the Human Genome Organization (HUGO) and UNESCO's International Bioethics Committee. Canadian legal scholar, Laura Isaacs, an internationally-recognized expert in stem cell policy, is another key member of the EWP. Isaacs is active in policy research and an authority on stem cell research policy, particularly on issues surrounding procurement. Originally from Peru, she was at the McGill University Centre of Genomics and Policy for several years before leaving in 2015 for a position at a US medical school with appointments to programs in genetics, bioethics and stem cells. Isaacs has said that assuring the ethical procurement of stem cells was the most important topic in EWP discussions.

The first meeting in 2003 was chaired by the UK's Medical Research Council Chief Executive officer. Over the next two years, membership grew to 16 agencies. Their stated goal was to encourage international collaboration and funding for stem cell research and they emphasized the sharing of materials, information and data. They adopted common principles that underpin international organizations for the promotion of stem cell research – an opposition to human reproductive cloning and using all variety of stem cells as well as embryonic. Two further principles guided their initial efforts - to minimize the creation of new hES cell lines and to encourage the harmonization of ethical and intellectual property practices. The ISCF promotes "global good practice" with the ultimate justification of medical progress (About the ISCF 2015).

The scientists conducted experiments to develop a consensus around criteria for the derivation, characterization and maintenance of stem cell lines with the hope that these standards would be used globally. In the first project, several laboratories throughout the world analyzed 59 hES cell lines and media, comparing the cell lines for characteristics in common, then, in the second, they tested the effect on the cells of the various media they are kept in.[3] The scientists used the same reagents and protocols and the results were published in 2005 with the idea that the wider scientific community would be able to reproduce and build on the work. They state that scientists are so convinced by the importance of hES cell research to benefit the public that they have a

[3] The results of the first study showed that the hES cell lines did share an identifiable set of common characteristics. As the study researchers wrote: "all the independent hES cell lines studied exhibited a common expression pattern for a specific set of marker antigens and genes, despite their different genetic backgrounds and their derivation in different laboratories using different techniques. Although more subtle differences between the lines… cannot be excluded, this study provides no evidence for markedly distinct subsets of hES cell lines" (Adewumi et al. 2007: 804).

"collective responsibility" that this potential "is thoroughly explored in a timely fashion" (Adewumi et al. 2007: 797).

Since scientists do not really understand why pluripotent stem cells behave in the ways that they do, the third project was to begin to address the scientific and technical issues around pluripotency by trying to establish common protocols for comparing the pluripotent capacity of different hES and iPS cell lines.[4] These early studies were on stem cells used in basic research. In more recent years the ISCF has begun working towards standards that will eventually be needed for "quality control" in the production of therapies. In the early years of hES cell research, labs were using different protocols for the creation and maintenance of cell lines. Combined with the tendency for lines to accumulate mutations over time, and the year in which the ISCF was created, Dr. Smith was telling Parliament that "everyone is getting different results."

A key scientific issue for stem cell researchers is how to define pluripotency. The conceptual definition of pluripotency is relatively uncontroversial but the biological definition is unclear; hence the project to determine whether various human ES cell lines shared certain biomarkers (measurable characteristics). Since a pluripotent cell can by definition form all the cell types of the body, the actual survival through development and birth of a live creature from a pluripotent cell is logically the ultimate demonstration of pluripotency. While it can be done in animals, the AHR Act prohibits scientists from putting hES cells into a human or animal embryo, so instead the main test used to demonstrate pluripotency in hES cells is producing a teratoma out of the hES cells. As

[4] It is unclear to what degree iPS cells and hES cells are the same thing as it is unclear to what degree pluripotency in humans and mice is the same thing.

further evidence of pluripotency, I was told, researchers have got used to using cells from multiple lines in their experiments. If they get the same results in at least two lines, then it is considered satisfactory evidence. The lack of a quantified test for pluripotency in human cells and the lack of standardized human pluripotent cells is an ethical, epistemic and practical issue. In short, the definition of pluripotency in humans is largely conceptual rather than elaborated through experimental findings; scientists do not really know whether their pluripotent cells actually meet the definition of pluripotency and they do not really know whether all human pluripotent cells have the same capacities. The Initiative was an attempt to address this, a coalescing around standards arrived at inductively as a proxy for experimental demonstration, a response to the ethical limits to understanding what a pluripotent human cell is as opposed to the better-studied mouse one.

The fact that hES cells are genetically unstable and prone to mutations, particularly the ones that have been growing in culture for a long time, led the scientific team to focus initially on criteria for identifying embryonic stem cells by establishing whether differences among cell lines reflect the different genetic makeup of the cells, differences among protocols or genetic changes over time in culture. Researchers need to know that the cell lines they order will still show the characteristics described in the literature.

The ISCF's characterization studies illustrate the anthropological idea that social and natural orders are stabilized together. They are also an example of a strategic bringing together of the ethical and technical. When I told a legal scholar that I was interested in this entwining of ethical and technical goals, she responded, "addressing

issues proactively from a principled approach and practically from a scientific one is called anticipatory governance." Anticipatory governance is a term with current salience particularly in science policy where it is used to refer to a number of normative ideas such as public participation, foresight, and integration. Notions of "anticipatory governance" have bubbled up recently in relation to emerging sciences such as nanotechnology.[5]

The ISCF responded to the ethical sensitivity around the destruction of human embryos by focusing on the consolidation of ethical standards for stem cell research and on the co-ordination of research around a few standard embryonic stem cell lines. Along with their limitless potential to renew themselves in their undifferentiated state, hES cells are also referred to by scientists as "limited" because they rely on embryos which like eggs are in relatively short supply (unlike the body cells like skin cells used to make iPS cells) and because they could only ever represent a small fraction of the population's genes and therefore be compatible for very few transplants. That iPS cell techniques appear to offer a way out of the shortage of hES cells dovetails with the ethical sensitivity around the use of reproductive materials. There is a convergence of ethics and science in "good practice" where ethical principles meet procedural values like consistency, accessibility and transparency to allow, for example, cross-checking of data between labs, pragmatic values such as efficiency in collaboration to reduce unnecessary work (and

[5] McGill legal scholar, Yann Joly, writes of anticipatory governance that it is a combination of foresight and "a move away from a top-down government approach to an approach where management by people, private actors and institutions becomes possible without detailed and compartmentalized regulation from the top." It is a strategy in which "effective action must be based on more than good analytical capacities and relevant empirical knowledge; it also emerges out of a distributed collection of social and epistemological capacities, including collective self-criticism, imagination, and the disposition to learn from trial and error" (Joly 2010: 271).

unnecessary destruction of more human embryos) and epistemic values embodied in systematic comparison.

The process of making data comparable and thereby scientifically useful involves encouraging the adoption of procedures that are certified ethically as well as making practical or technical sense. In an early publication describing their plans for the characterization projects, the scientific steering committee of the ISCF argue that their findings will help guide ethics review decisions on the necessity for new hES cell lines – if all 59 lines are "roughly similar," then "the argument for deriving additional cell lines using existing technologies cannot be strong, provided that the lines can be made routinely available worldwide" (Andrews et al. 2005: 797). This converges with the EWP which sees itself as simultaneously working towards scientific and ethical integrity of research as inextricable from each other. It is working towards a "transparent and well-regulated ethical framework in every country" as both a good in itself and a practical step – "harmonization" of regulatory and policy frameworks covering the procurement of embryos, the distribution of cell lines and their research, they believe, will facilitate international collaboration.

As Dan Monroe phrased it in our interview: "They said 'you know what? We recognize that there is, globally, public concern that we should work with stem cells in a very responsible manner. So, let's pool our funding to do some collaborative work across all of these countries in defining what are the characteristics of embryonic stem cells.'" That the majority of stem cell scientists work on the same few cell lines, Dan argued, "was almost a conscious push by all of the funding agencies to say 'let's not go off in a million directions here and have the public be concerned about us creating hundreds of

new stem cell lines.'" They created a list of questions and tested multiple cell lines in an attempt "to produce some standards that everybody could work off." He pointed out that by coordinating the work of different labs, they were trying to move stem cell research forward in a way that individual labs would not have been able to do. To Dan, this early co-ordination of the emerging hES cell field was unique, impressive, and effectively forestalled further controversy: By encouraging researchers to "develop a consensus around what to work with," it helped "mitigate" the issues "that might have been anticipated eight, nine years ago." In his opinion, this early concerted response was uniquely collaborative and it was this co-ordination that should really be described as "exceptional." He said, "this field has developed scientifically at a very rapid pace in many, many different directions just the same as any other field of science might" but the initial controversy surrounding the use of embryos "forced people at the funding agencies and at the scientific level to get their act together really early on to force some standardization, to force some really proactive thinking about the legal, ethical and regulatory issues to smooth the path."

The ISCF response to hES cell research which so impressed Dan is exemplary of a kind of international civil society response to sensitive biomedical developments that is bringing a heightened awareness of ethical concerns into science governance.

Cellular models

A well-known anecdote about geneticist Walter Gilbert, a supporter of the Human Genome Project, describes him as prophesying that one day every individual would own

a CD of his or her individual genome and be able to say "Here is a human being. It's me." (Quoted in M'charek 2005) The anecdote suggests that for Gilbert the complete sequencing of the human genome held out the promise of revealing something essential about what it is to be human. It could be understood to raise the paradox of something that is both general and particular as in general knowledge and a specific biology or the generic human and a unique individual; or it could be read as a statement of the ways in which scientific understandings are made part of our identity and subjectivity. Here, I propose reading his claim as a question of representation. What is the relation of stem cells used in basic research stem cell labs to the people from whom they came? By filling in some of this picture, I aim to give a taste of how the emergence of iPS cells has re-opened classic questions of inclusion and privacy.

More than a decade after Andras Nagy created the first Canadian hES cell lines, none of the scientists in my study are making hES cells, creating cell lines directly from human embryos.[6] It is also striking that I heard almost no mention of gender during my fieldwork. Canadian scientists using hES cells in their research are using available cell lines, maintained in various banks. The primary repository in North America is the non-profit WiCell housed at the University of Wisconsin-Madison. WiCell grew out of the hES cell lines derived in 1998 by James Thomson, the developmental scientist credited with being the first person to successfully create hES cells. After court challenges to patents on the cell lines held by the university's technology transfer office - patents which had attracted criticism for being overly broad - WiCell modified its policy in 2008 to

[6] The CIHR national registry currently contains four successfully created Canadian lines. There are currently Nagy's lines derived from fresh embryos and two lines created by Derrick Rancourt derived from frozen embryos. Since 2004 very few researchers have applied to SCOC to try and derive new hES cell lines and none since 2012 (Caulfield et al. 2015: 4).

allow researchers to transfer cells amongst themselves more easily by dropping licensing fees for academic researchers. Over the years, WiCell's offerings of stem cells has grown from the original 21 hES cell lines approved by President Bush to over twelve hundred embryonic and iPS cell lines today, available to order online from their Stem Cell Catalog.

In contrast to the regulatory approach to human embryos as entities with moral and cultural significance, several researchers made a point of referring to hES cells as reagents, no different from other cellular research tools. Indeed, for scientists doing stem cell research, working with hES cells has largely become indistinguishable from research with other types of human biological materials. For example, Elizabeth, the graduate student finishing her Ph.D. research in informatics and hES cells described in Chapter One, told me that hES cells were treated no differently from other kinds of cells; hES cells are "a little trickier than skin cells [to grow] otherwise they are treated in the same way." As she showed me around the Janet Rossant lab where she worked, in the lab's new premises in the Peter Gilgan Centre in Toronto's Hospital for Sick Children, I had asked her whether there were any special procedures for handling hES cells in the lab. The only type of situation in which ethical considerations specific to the use of hES cells might determine how scientists handle the cells in the lab, she suggested, is in the US; if a researcher with NIH funding is using cell lines that are not approved for federally-funded research, then the researcher might need two sets of equipment to keep them separate. Otherwise, she said, scientists can order hES cells online; they can borrow some from a

researcher at the next bench; they can throw them out in the lab's regular trash where they become medical waste.[7]

hES cells can be compared to cells from patient samples with regard to their movement and disposal. A conversation with Dr. Carter, a young postdoc, made the difference clear to me. Dr. Carter had not long moved to Canada from Britain and was using both hES cells and reprogramming patient tissue samples. In comparison to the one-time process involved in ordering hES cells, she told me, patient tissue samples have to be carefully recorded. One cannot just give some to a colleague. Any time that a sample is divided the portions have to be tracked. In that way, if the patient decides to withdraw his or her sample from research, it can be done. However, in her own research, she told me, that has never happened. "I don't keep track because a patient will withdraw. I keep track to show that I have." hES cell lines may be more controversial research materials but, from the perspective of the researcher at the bench, they are tools that can be freely shared without audit.

Dr. Carter also told me that she thinks differently about human ES cells and iPS cells. She uses the ES cells as a control. They represent the normal human. Cells are not like blood samples that can be pooled according to type; they bear the unique genome of the person from which they came. So hES cell lines could be referred back to the individual from whom they came. However, she conceptualizes only the cells taken from

[7] The debate over the moral status of human embryos has been punctuated by images of human embryos "discarded". I remember the public furore that erupted in the UK in the late 1990s when it was discovered that an IVF clinic had "flushed" unused embryos. In the lab, the fact that hES cells are so prone to unwanted differentiation or to developing chromosomal abnormalities means that, as a practical matter, a lot of hES cells end up being thrown out. Researchers throw hES cells from cell lines into the garbage placing them in a class of objects that are neither valuable nor harmful nor scientifically productive.

someone with a disease in relation to the unique biology of the individual from which they came.

One part of the answer, then, to the question of what is being modeled by the stem cells as scientists think of them involves the concerted early international efforts to stabilize practices and meanings surrounding hES cells. By working to understand the differences among lines and to standardize practices, the ISCF helped make the most commonly used cell lines into dependable research tools and stabilized their meaning as representing the universal healthy human. Researchers use them against which to measure the potential of all of the human cell types that succeed embryonic stem cells (all cells subsequently developed are understood as increasingly restricted relative to embryonic stem cells) and of other cells with stem cell-like properties including iPS cells. Another way in which many of my interviewees expressed this was that (human) embryonic stem cells are the "gold standard" of normal biological processes. In contrast, Dr. Carter told me that she thinks of the iPS cells made from patient tissue in terms of the individual who donated the sample. The cells from the patient are the marked category and the iPS cell lines made from them model disease.

Another part of the answer involves the shift towards understanding materials from the human body as belonging to the person from whom they came. Patient donors of samples have some degree of control over the research use of the samples, understood as something they own. Henrietta Lacks who died in 1951 and whose cancer cells were used for research without her knowledge or consent, eventually becoming a ubiquitous and profitable research tool, the HeLa cell. Her story captured the public imagination and, as depicted in the book, "The Immortal Life of Henrietta Lacks," fed into an American

narrative of racism, poverty and a profit-driven biomedical industry (Skloot 2010). It prompted bioethical attention to the donation of biological material or genetic information as an instance of research participation. In the years since HeLa became a locus of ethical and legal concern, various regulations and conventions have grown around the acquisition, storage and disposal of human material (with the UK passing a Human Tissue Act addressing these practices in 2004). For example, patient samples are today identified by researchers by code; no research material made from a human body would be named after the person from which it came, in the way that HeLa was. That the relationship of ownership implied by a name is severed facilitates the allocation of financial value "downstream" from procurement.

My interview with surgeon-scientist Dr. Stevens (Chapter Three) best illustrates researchers' experiences of a new understanding on the part of patients vis-à-vis the medical-research establishment of their body as property in which they potentially have rights. For Dr. Stevens, the shift towards viewing human biological materials as property seemed particularly salient because she was working with waste materials discarded during surgery, materials without value. Now researchers have to ask before they retain biological materials for their research as respect for the autonomy of the patient and because it is possible that there may be future profits. Now, as she expressed it, researchers "realize" that people have "rights to their property, their own tissue, their body, their cell."

Ethics scholar Michael McDonald articulates these conceptualizations in his work on research ethics. As founding director of the University of British Columbia's Centre for Applied Ethics, McDonald has written extensively on the use of human subjects in

health research, has advised the government on the issue and played a major role in the generation of the original TCPS (Tri-Council Policy Statement for the Ethical Conduct of Research Involving Humans). The primary author of a Stem Cell Ethics Website for Canadian scientists, he is still involved in multiple research projects on health research governance and stem cell science although retired from teaching in 2010. Tall and slim with white hair and beard, he expresses himself with a soft-spoken authority. In the Stem Cell Ethics Website, McDonald instructs researchers to consider themselves as custodians of samples, temporarily responsible for them. While in the past scientists considered donated samples to become their personal property, he writes that for researchers, "it is essential to understand that ethically and legally, there is no personal property in human tissue" (McDonald et al. 2010).

That hES cells represent the universal human is a problem to some precisely because of who has been represented in the materials of ES cell research. For example, scientist turned bioethicist, Dr. Patel, has argued that the lack of genetic diversity could make Canada's law allowing only surplus embryos to be used for derivation discriminatory in its effect. As he said to me, "suppose the only stem cell therapies were ones that were created from embryos leftover from IVF and then look at the socioeconomic diversity of Canada and look at the much different socioeconomic diversity of those seeking IVF and then consider tissue compatibility problems…" If, he continued, "a lot of the people that would stand to benefit from stem cell therapies are from parts of society that for economic or cultural reasons don't use IVF [they] may have less opportunity to ensure a genetic match to the available therapies." Considerations of this sort have contributed to the development of increasing numbers of biobanks. The

lack of "genetic diversity" in stem cell samples was one of the concerns which led stem cell scientists to push for the creation of a public cord blood stem cell bank. Press stories have highlighted that a diverse city like Toronto needs greater diversity in its cord blood bank (Weeks 2012). Working with the Canadian biomedical establishment's unquestioned assumption that stem cell science will and should be funded to produce therapies, experts like Dr. Patel promote values such as equality of access to health care and ("cultural" and genetic) diversity as an ethical dimension to the procurement and use of embryos rather than addressing the more controversial issue of their moral status. In such arguments, it is scientists' responsibility to serve the therapeutic needs of the country's diverse citizenry.

"Who's working on your disease? You want to know, right?"

Researchers clearly desire and acquire stem cell reagents as consumers. STEMCELL Technologies, a Vancouver-based company, for example, offers numerous products that support stem cell research, such as cell culture media. They also offer cells from a number of stem cell lines mostly from sources like cord blood and bone marrow. That this is a business with marketing strategies designed to appeal to researchers is clear - On the main page of the embryonic and iPS cell section of their website there is an advertisement for one of their new cell culture systems that reads "Maximize Your Pluripotential." A prominent strand of research on biotechnology suggests that bio-economic processes are inseparable from forms of power and subjectivity implicated in individual consumer desires (Sunder Rajan 2011: 207; Taussig, Rapp and Heath 2005). While a focus on subjectification in relation to the biomedical industry underscores that

power relations are reinscribed by biotechnology, it frames scientists as producers and the public as consumers of biotechnology. Advertisements for companies that stock laboratories, gracing conference booths and programs, are a common sight and suggest that scientists are themselves motivated by consumer desires and aspirations.

Patient samples and iPS cells, in contrast, can index complex relationships. Dr. Franks, the young stem cell scientist injured in a car crash introduced in Chapter One, whose relationship with Anne, a patient advocate, stood out against the anonymizing research ethics practices and the totalizing discourse of suffering patients that dominated my fieldwork, spoke, as Dr. Carter did, of iPS cells as representing both a disease and an individual's disease. Dr. Franks wanted to work on Anne's cells (which she also wanted) but, due to the research ethics restrictions related to the use of human samples was not allowed to do so: "We couldn't in [the lab] work on Anne's disease. Like we could work on the disease itself but we couldn't work on her cells. There's a line you have to draw. So even though we were being funded through the Foundation we couldn't work on her cells." As a member of the organization at which he is currently employed, he can make iPS cells out of the patient cell samples that researchers give him which means he can finally make iPS cells out of particular individuals' cells (as long as he anonymizes them before he hands them back to the researchers). He seemed to express a certain satisfaction about being able to assist research on the cells of actual patients: "it kind of gives me another opportunity to be a part of the game without actually being in the game."

Dr. Franks illustrates how iPS cells made out of a patient sample can embody the doctor/researcher-patient relation (research ethics concerns of undue influence on the patient or scientific bias, notwithstanding). His narrative revealed a form of "biosociality"

in which identities and relationships are created around individual manifestations of a disease as well as around disease categories (Rabinow 1992). His relationship to Anne is more reciprocal than the researcher/patient model of research ethics. As a patient, he felt that there was a need to know the individual scientists working on one's condition. As he said of Anne's disease, from her perspective: "it's a very rare disorder that if you have it… who's working on your disease? You want to know, right?"

The desire of Dr. Franks to recognize or reinstate social relationships and individual identity in a way that the decontextualizing and anonymizing practices of ethics review work against seemed echoed in the actions of scientists when they overlooked the REB's prescription of confidentiality in their discussions with me. Many members of the Canadian stem cell community know one another and they frequently interrupted my attempts to maintain the anonymity of others during interviews by trying to guess whom I was talking about or by asking me directly.

Anticipation, consent and the limits of risk

In the fall of 2015, I attended the first Symposium on Research Management of the University Health Network. I was sitting at a table with research ethics officers who told me that their attendance at this meeting was mandatory as it had replaced their annual ethics office meeting. A member of the ISCF EWP, Dr. Isaacs, was there with a requisite PowerPoint presentation which was called "Re-evaluating Current Approaches to Informed Consent for Stem Cell Research." It presented the recommendations of the ISCF's EWP in response to the rise of biobanking. Post-genomic biomedicine is

increasingly filled with individuals' genetic information and with human biological samples and there have been increasing talk on the part of scientists about the usefulness of comparative studies. In stem cell science, researchers' desire to reprogram patient samples, to bank and use iPS cell lines or to make and use iPS cell lines out of existing collections of tissue samples is raising a range of possible research uses that were unimagined at the time consent was originally given. Stem cell scientists would like to transfer samples among themselves more easily and use them for a variety of studies (Caulfield and Knoppers 2010).

At the Research Management Symposium, Dr. Isaacs began her presentation by explaining that ensuring the ethical provenance of stem cells remained a "pre-requisite for scientific integrity," then guided the audience through emerging norms of informed consent for iPS cell lines and biobanked samples. A main focus of her presentation was a hot-button policy issue in this area - does a researcher need to "re-consent" in order to make an iPS cell line out of an already banked sample? The question, as Isaacs phrased it, is if a reasonable person cannot have anticipated a particular research use but that use is indeed for generalizable scientific knowledge, can the researcher proceed without obtaining new consent?

As with the kerfuffle over Nagy's MTA, appropriate interpretation of informed consent documentation has emerged as a crucial point in the bureaucratic control of the movement of iPS cell lines and banked materials. Informed consent forms are the material objects at the confluence of institutional bureaucracies and policies, research regulations, bioethics logics and patients, researchers, samples and cells. Informed consent documents, from an anthropological perspective, are the bureaucratic product of

technocratic knowledge and of multiple histories. For the experts of my fieldwork, the instrumental nature of these documents makes them an unremarkable part of institutional life but the principle of informed consent as a sine qua non of ethical research is subject to continued debate. In the literature on the ethics and policy of banking biological samples, debate over informed consent centers on the question of whether "broad consent" for unknown future research can still be justified as informed. Bioethics convention as embodied in informed consent forms is to respect the donor's wishes with regard to the research use of their sample as an instantiation of their autonomy and to re-consent for every new use.

A Canadian cancer research institute sample consent form for banking patient samples provides an example of the way in which a "broad consent" form currently handles the unknowns of future research and clearly illustrates the challenge to informed consent. It refers to the collection and storage of samples simply "for future use." It then prompts researchers to provide a more detailed description of anticipated research uses of the samples and data, providing a sample answer with bullet points itemizing each research objective. This section concludes with "it is not possible to predict all of the ways in which biobanks might be used in the future, so it is not possible to tell you exactly how your sample will be used." The form offers somewhat contradictory messages - an instruction to researchers to "provide as much detail as possible" about future research uses and, immediately following, a statement that completely accurate prediction is an impossibility. It is a juxtaposition of precision and detail vis-à-vis samples and procedures for collecting, storing and securing them, in the usual informational mode of bureaucratic knowledge practices, and an acknowledgement of not

knowing, of not being able to know. Similarly, a section on risks prompts researchers to describe risks such as linkage, discrimination and privacy intrusions and then includes a final statement that "due to the rapid pace of technological advances," potential future uses are unknown and "therefore the potential future risks are also unknown." These statements are of a piece with the rest of the consent document, a relay of information that reads like a legal disclaimer.

Isaacs argued that there is risk inherent in all research but at the same time it is impossible to avoid all risks. They cannot definitively say that donors' privacy, for example, will be safe. A key cartoon in her presentation depicts a research ethics committee of men and women in suits sitting around a board-room table with the edge of a skyscraper visible through the window behind them with the head of the committee saying "We've considered every potential risk except the risk of avoiding all risks." The cartoon suggests that an excessive focus on risks downplays the possible good that could come out of the research. It does not conflate uncertain outcomes with harmful ones and in this illustrates a notion of uncertainty that cannot be reduced to risk (Samimian-Darash and Rabinow 2015). It is also an illustration of a kind of reflexivity associated with anticipatory governance of controversial emerging sciences, a form of self observation and analysis that privileges responsiveness to scientific and social developments.

Policy experts like Isaacs are struggling with how best to adapt or re-think informed consent practices. The informed consent document is the site of researcher and donor's interests which are presumed in research ethics logics to be at odds. Isaacs presented informed consent as the balance of protecting donors while allowing research to proceed in the most efficient manner ("maximizing the utility" of the samples).

Requiring a researcher to go back to the donor at every step of research beyond what the donor originally agreed to, she said, was a "very bureaucratic" solution. Instead, she suggested that an optimal consent process should be "robust enough to cover various uses." Her solution to the problem of how to make informed consent robust in such situations involved framing it as a process of ongoing communication over time rather than a singular moment. Her model of informed consent presents consent as a form of governance. Indeed, governance of biobanked human samples has become a favored policy proposal amongst law and policy scholars understood as a more flexible way to manage the unpredictable path of research and needs of researchers. Knoppers and Caulfield, for example, have also suggested in the case of biobanks that one option is to have the donor consent in broad terms to future research and then create a biobank committee as an "appropriate governance" mechanism to decide on a case-by-case basis whether or not proposals violate the original terms of the informed consent form (Caulfield and Knoppers 2010).

Dr. Isaacs argued in favor of a flexible, context-sensitive reading of informed consent documents and one that did not elevate the values and prior decisions solidified in research ethics procedures over those of participants. Attributing greater agency to donors, some of whom she told us felt that the system is patronizing, she narrated a story of an American woman who, frustrated with the research ethics approach to privacy, had defied its protective measures and published her genomic data online, an exercise of agency that speaks, again, to the desire of individuals to be included in research.

Isaacs' challenge to entrenched research norms involving informed consent met with some resistance from the Symposium audience. The suggestion that patients might

want their samples used for research (which was also the argument made against too restrictive a reading of the Nagy consent form) even if their privacy was potentially compromised prompted a member of the audience to stand up and say that he had only two words - Henrietta Lacks. The invocation of her name suggested how powerful a symbol of "patients' rights" she has become. If informed consent in its traditional risk management mode is no longer the optimal procedure according to Isaacs, this runs counter to the standardization and risk metrics of research ethics.

Meanwhile, genetic research has already raised scientific reasons for identifying donors. With iPS cell research also, despite the efforts of research ethics practices to de-personalize and anonymize, scientists argue that they will need to re-link iPS cells to their originators. Personalizing in the context of disease models is about biological particularity, the problem for ethics being that while this is mostly genetic it is not entirely genetic and knowledge of their lives as social beings, of their life history or "life style" may be scientifically relevant. For personalized medical treatments to be possible, the procedures of anonymization considered ethical "best practice" will need to be rethought. While many of the issues surrounding informed consent for the acquisition of patient samples are shared by other fields like genomics, the vision of individualized disease models and treatments to which iPS cells are contributing is poised to shift research ethics practices central to the legal-bioethical framing of biological materials. The EWP's response to the direction of research and its understanding of scientific integrity as depending on a weighing of the interests of scientists and patients suggests that the work of ensuring the continued legitimacy of the field is contributing to a shift in the politics of procurement.

Bureaucratic anticipation

The work of anticipating issues to come and helping shape the field that people like Isaacs are doing is not without its enjoyment. One strand of recent anthropological attention to documents as the emblematic artifact of bureaucracy explores people's experiences with them and the constitutive effects on their subjectivity (Riles 2006). With this in mind, I describe Dr. Patel's comments on his work with SCOC which spends much of its time checking documents, particularly consent forms. In contrast to the Weberian image of bureaucratic work as dehumanizing, Dr. Patel told me how much he enjoys the committee's work both when it involves investigating consent documentation and imagining possible bureaucratic tangles. SCOC's mandate is to confirm the ethical provenance of hES cells (and acceptable use of pluripotent stem cells). This means that, for the committee, as he told me, "any time embryonic stem cells are used we need to make sure that the cells that are being used were created in a manner that conforms to Canada's guidelines." He continued: "Once in a while - it's rare but it's really fun - we'll get someone who wants to use a cell line that's not yet approved for use in Canada." He went on to describe the process of verifying that such a cell line conforms: "Oh it's great, that's why you're there, man! It's great! No, it's good fun. Because you know what the guidelines are so you know, 'Well, we got to find out this. Well, if it says you need a consent from both parties, well, where's the documentation? Do [this]. Do [that]." He added: "That stuff's great because then you get to do some thinking. Thinking about questions like is there potential for conflict down the road if there is a stem cell therapy that comes in and applies for use in a trial as a drug or biological therapy, but was created in a manner that doesn't conform to our guidelines? What then? Whose job is it to say

yes or no that's appropriate or not? Because that's not clear…" Dr. Patel enjoys both the procedural and archival work of looking for and verifying documentation and also the anticipation of potential governance problems themselves.

Conclusion

As with REB review, the anticipatory work of the ISCF illustrates a mutual legitimation of bioethics and biomedicine. However, despite efforts by bioethicists to suggest that research ethics involves the consideration of the ethicality of decisions throughout the "lifecycle" of a research project, prior review is still largely a one-time practice. Anticipatory governance models of bioethics management, in contrast, involve looking ahead and monitoring science as it happens. While still situating its capacity of legitimation in the certification of virtue, it also situates it in its apparent "real-time" responsiveness to scientific and social developments. Whether and how stem cell research will become more inclusive of Canadian "diversity" will depend, in part, on the creativity of such governance experiments and their reflexive, instrumental analyses. In the next chapter, I explore the mode of moral decision-making involved in research translation, highlighting the characteristics it shares with market logics and a certain Canadian particularity.

5. Becoming Entrepreneurial: Strategizing, collaborating and recognizing value

At the 2013 Till and McCulloch annual meeting, I was handed a complimentary, autographed copy of a book written by journalist Joe Sornberger with funding from the Canadian Stem Cell Foundation about the eponymous Canadian discoverers of human stem cells, James Till and Ernest McCulloch. It was called *Dreams & Due Diligence: Till and McCulloch's Stem Cell Discovery and Legacy*. A conventional narrative of individual genius, it presents the scientists as opposite and complementary personalities, McCulloch, the Toronto-raised son of middle-class parents of Scottish descent, is the creative dreamer and Till, the Alberta farm boy, is precise, thorough and analytical. Being relegated to a peripheral lab, as Sornberger tells the story, gives them the freedom to explore which, along with the synergy of their contrasting styles, results in the discovery of stem cells.

The motif of dreams and due diligence contrasts notions of creativity, intuition and visionary insight with notions of care, labor, prudence, and reasonableness and their business and legal connotations. It is a motif that plays on biomedicine's necessary embeddedness in systems of production of health care. As publicly-funded stem cell scientists work towards actualizing applications of their science, their research articulates with other sectors and organizations, particularly the biotechnology and pharmaceutical industries. Various actors in their institution become involved, chiefly technology transfer officers, a key part of whose job is to commercialize discoveries and facilitate industry partnerships.

The concept of due diligence is also apposite, more specifically, because anthropologist Bill Maurer in an analysis of global financial markets has argued that due diligence is a new form of managing financial risk, a bureaucratic practice of virtue that inserts people in "a community of regard" (Maurer 2005). His study is one of a number of anthropological analyses of the moral and non-calculable of markets (e.g., Carrier and Luetchford 2012; Rudnyckyj 2010). With such work in mind, in this chapter, I explore how technology transfer officers mediate market, legal and regulatory regimes to the extent that they do and I juxtapose regulatory decisions with technology transfer decisions about how to turn research into public goods. I argue that in some ways those working in technology transfer are critical mediators; for example, they bring research into other regulatory domains such as Health Canada oversight of clinical trials and legal domains of intellectual property. In other ways, they are, by their own accounts, struggling to make academy inventions appealing to industry. They describe their efforts to persuade industry to invest in the long process of translation in terms of bottlenecks, gaps and barriers, in contrast to institutional and government rhetoric about how collaborations between academia and industry are driving discovery and innovation. The ways that they discuss their work indicates that there is a sense of a Canadian cultural uniqueness that manifests itself in their caution and cooperation, and, as I will suggest, accounts for the relatively uncontentious status of stem cell translational activities. Comparing the modes of reasoning of Health Canada and REBs to those used by technology transfer officers leads me to argue that they are united by their use of a cost/benefit form of analysis and by the ambiguity of terms like social benefit, risk and value. Drawing out such similarities in modes of evaluation among actors from very

different locations offers glimpses of people working within the constraints of institutional or governmental mandates and regulatory technologies while negotiating and reshaping the realities of health care-in-the-making.

Technology transfer: Between the academy and the market

The emphasis on commercial integration with academic science arguably began in the US with the passage of the Bayh-Dole Act in 1980 and in Canada with the creation of a Canadian National Biotechnology Strategy in 1983.[1] The years since have seen an increase in the number of technology transfer offices at institutions and in the number of specialized careers in science commercialization. Commercialization activities have been going on for decades in certain research organizations, but it is only in recent years that every research institution has come to house an office of technology transfer or industrial liaison. That there has been an increasing emphasis (particularly in government funding programs) on tech transfer is reflected in the emergence of professional organizations devoted to those who work in the field; the main association for technology transfer in Canada, the Alliance for the Commercialization of Canadian Technologies, was created in 2005.

Technology transfer officers in Canada are working in the context of universal health care and are aware that such issues as differential provincial reimbursement for

[1] The Bayh-Dole Act allowed universities, businesses or non-profits to own the intellectual property generated by government-funded research rather than assigning it to the government. In Canada, IP ownership policies are set by each institution and range from complete researcher to complete institutional ownership.

what will likely be expensive stem cell therapies are looming. However, more immediately, the development of therapies is largely a financial challenge. Their institution only has so much money it can invest in basic research inventions. Those working in commercialization all told me that, compared to the US, investor financing for biotech start-ups is virtually non-existent in Canada. Speculative investment in "early-stage" research could, if it issued in that rare thing, a "blockbuster" drug, result in a very high return on investment, but a lot of capital is needed and the risk is high. Nor are they working in a similar landscape of "receptor" companies which can add enough value to an invention to attract investment. They are struggling to encourage the interest of larger companies with sufficient funds and infrastructure for further development and clinical trials.

As technology transfer officers described it to me, the goal of their job is to move knowledge out of the lab to the benefit of society, which includes moving it into the hands of people who may be able to turn it to the benefit of patients. They see their job as having both a broad scope – facilitating the dissemination of knowledge in order to allow others to access it by such means as publication or collaboration with public or private scientists, or the transfer of information, materials or personnel to other sites – and a narrower focus on the development of medical products often by way of commercialization (translational medicine). In large institutions, there are commercialization managers and contract staff who handle the day-to-day "bread and butter" agreements that allow research to proceed such as research contracts and MTAs. This means that technology transfer staff are doing legal work, drawing up contracts, assessing whether or not something is patentable, whether or not the researcher has the

"freedom to operate" and can pursue turning his or her invention into a product without infringing on others' intellectual property.

As the name suggests, the role of technology transfer was created by design to act as an intermediary between scientists in their labs and the public realm. Technology transfer officers are particularly oriented to industry. Many of the staff are scientists with experience working for a company. Several of the technology transfer officers whom I interviewed appeared at times as if they were ambassadors from another realm, that of industrial science. For example, one technology transfer officer presented basic research and product development science as two contrasting categories of science. I had just been listening to Dr. Smith (Chapter One) describe basic science as following the contours of the land, when I went down a floor and met with Dr. Jones, the head of the Institute's technology transfer office. An approachable young woman with a French accent, she explained that she was herself a former researcher in Dr. Smith's lab before working in industry. Dr. Jones described applied research, in particular industrial R&D, as having a very different pace and rhythm from basic research. Applied science, she told me, is about standard values and procedures. In order to conduct clinical trials and ultimately produce a therapeutic product, company scientists have to meet specific regulatory standards surrounding validation and testing, manufacturing and delivery. They are goal-driven and directed. They have to find ways to speed up the research and development process. In a context of forecasts, predictions and reports to investors, she told me, the challenge for biomedical companies is to reconcile business plans with the unforeseeable results of the scientific process. I repeated to her Dr. Smith's view that "the unexpected is where the opportunities lie," and she remarked that biomedical companies need positive

answers to their research questions; with shareholders, regulatory standards and expensive clinical trials, any other result is potentially disastrous.

In fact, the points that Dr. Jones made, as she contrasted her former PI's remarks about research with a depiction of industrial science, fitted into a narrative about academic scientists' relative freedom and lack of awareness of the R&D process that emerged during my fieldwork. Technology transfer professionals emphasized to me that product development is a long, iterative and time-consuming process with many potential points of derailment. For their part, stem cell scientists whom I asked about working with industry were cautious if not dismissive of the idea and concerned with the "strings attached" to industry funding.[2] Both technology transfer officers and stem cell scientists agreed that the juncture between academia and industry around the stage of clinical trials is a particularly difficult one to cross. Indeed, it is widely referred to as "the valley of death" because few discoveries make it that far and then the vast majority of clinical trials fail.[3]

Dr. Duncan is a senior commercialization manager of a technology transfer office for a large research university whom I interviewed in 2012. In his office, he answered my somewhat exploratory questions about his work with lengthy, patient responses delivered in a slightly world-weary tone, from time to time interjecting "It's a thankless job;" "it's a ridiculous job." With a combination of elite qualifications including a Ph.D. in analytical chemistry and an MBA, Dr. Duncan sketched a picture of a relatively new career type at

[2] The "strings" are perceived restrictions on publishing or presenting scientific findings.
[3] In response to the high attrition rate of potential therapies, some Canadian commentators have critiqued the "pipeline" model of translation, offering "networked" models instead, with the notions of collaboration that this suggests.

the intersection of several expert knowledges and spoke languages of science, law and business which seemed to meld seamlessly into one another.

At Dr. Duncan's university, researchers with discoveries that might have potential commercial value file an invention disclosure. Dr. Duncan then assesses the inventions, beginning a commercialization process which he characterized as a collection of activities necessary to the proper translation of inventions and involving the evaluation of the science, its market potential and any relevant intellectual property. He tossed out a string of questions that he asks a researcher considering commercialization which they need to consider, beginning with the science: "What is the technology? How much data do you have to support your invention? Is it really early stage or do you want to make a product out of this invention? How far does it have to go?... The experiments that you've chosen to define your invention, are they the right experiments? Do they really actually show what you think that they're showing?" Then he continued, "Has this been done before? Are there any patenting issues we need to worry about? ... Is there a market for this? Is there someone interested? Who's doing work on this? Is it competitive?..." Dr. Duncan's description of his job depicted his work as very dependent on his command of multiple realms of expertise including the scientific and market knowledge needed to identify discoveries with potential value, an awareness of IP issues and a knowledge of the clinical trial application process and on his ability to cultivate the right relationships to connect academic scientists with the right industry players. As he himself informed me, "our role, if you're good, or if you've been doing it for a while covers an extremely broad spectrum of competency." From negotiating IP terms or items in a licensing contract to helping researchers put together preclinical data packages for the FDA,

technology transfer directors like Dr. Duncan are working at the intersection of multiple, inextricable domains.

With regard to stem cell therapies, many of these domains are marked by uncertainty. While REBs are finding it increasingly necessary to consider problematic industry links and conflicts of interest, their decision-making with regard to stem cell research is, now that the regulations are in place, largely straightforward, constrained as it is by the national regulatory apparatus that has been established for stem cells. In contrast, technology transfer professionals are working in the absence of a history of stem cell therapy development and technical standards.

As Dr. Duncan described it, the evaluative process for commercialization is essentially a form of peer review similar to that which I observed during REB meetings. The scientific expertise of technology transfer professionals is appreciated; when I commented to Dr. Duncan that commercialization experts in technology transfer offices like him have a unique skill set and that researchers would benefit from their expertise, he responded, “they love people who know science.” He relies on his science knowledge in the evaluation of the discoveries that might have commercial potential. It allows him to “ask the right questions”. But he also relies on it in helping researchers think through and present their arguments in writing, primarily in grant applications and patent manuscripts. For example, as he explained, a discovery or invention for which a commercial path exists can be developed a little bit more within the university or licensed out to someone who might be able to make a product out of it. If they decide to develop it within the university they have to raise funding and he and the researcher will work together at grant proposals, thinking about whether they have chosen the right experiments to make a

winning argument. As with the REB review process, researchers must craft a proposal and marshal their evidence and their research is critiqued by institutional actors.

Similarly, the patent application is often based on one of the researcher's papers but the researcher, the technology transfer officer and a patent lawyer may work together to decide on the claims they are making and how to structure the argument. In patent applications in Canada as in the U.S. the researcher must describe their discovery or invention in words. They may include drawings but the core of the application is a specification of exactly what the researcher is applying to protect, why it satisfies the criteria for patenting and what would be the limits of patent protection. The Canadian Intellectual Property Office defines the goal of the description as allowing a practitioner in the same field to recreate the discovery or invention from the description alone. Through working collaboratively at the process of verbalizing and strengthening the evidence needed to persuade others of the merits of the research, technology transfer officers are making contributions to the research that are substantive as well as methodological or rhetorical. Scientists and technology transfer professionals must be able to write articulately as they are constantly presenting research for the judgment of others in such places as REB protocols, grant applications, peer-reviewed journal submissions, or intellectual property applications. As one hospital-based researcher, acknowledging the constant evaluation and critique her work was subject to commented, “it's rarely a bad thing to have your work scrutinized by a lot of people”. In these contexts, researchers must articulate and communicate their science verbally. Technology transfer officers must be in command of the documentary and evidentiary practices required by each regulatory domain.

Patenting: Navigating "muddy waters"

Technology transfer professionals' commercialization work largely involves patenting and licensing. Attending to the experiential reality of scientists who work with this legal technology offers a glimpse of the landscape in which technology transfer officers make decisions about commercialization "paths." Those with commercial experience in the stem cell field described the stem cell patent landscape as "a mess" with numerous patents and for a number of reasons, including the status of stem cell science as a "hot" field with considerable therapeutic potential. They also attributed the state of the patent landscape to the science itself - the biology of cells is very complex.

For example, Dr. Marks, the company scientist whom I interviewed in Calgary in 2011 suggested that the complex systems appreciated by academic researchers translate into complex and overlapping patents that, as Dr. Jones phrased it, "are very muddy waters to navigate." Dr. Marks told me that "there are enormous amounts of patenting that have been done in the stem cell area." Giving an example from the biology of the brain, he argued: "Every biological system is integrated. You have proteins. You have cells. You have the interaction of cells. The basic unit of the brain is a blood vessel and a Schwann cell or a combination of cells combined with other support cells and you can argue from any of those directions that an effect on one thing will have a beneficial effect on the others." This means that for patenting "you could write eight separate patents, saying the effect of a drug affects one of those elements of an integrated system and so provides therapeutic benefit." The result is that "you naturally get this sort of scattered glass kind of effect where patents lie on top of each another to some extent and claims are granted." He concluded: "It's onerous to understand what has value and what doesn't for

that reason. You're trying to patent a highly complicated biological entity." Over the course of my fieldwork, I would mention Dr. Marks' "scattered glass" metaphor to technology transfer officers when our discussions turned to the patenting of stem cell discoveries and each time they would promptly respond that it was an excellent and very apt image.

At the same time, there is a lot of controversy and uncertainty around patenting in the life sciences. While there is a different history of patent protection in Canada than that of the US, technology transfer officers are attuned to US court decisions, in part because the US is such a big market. Patent law is an evolving field and the results of individual court cases are unpredictable. My mentions of high-profile court decisions on patenting to technology transfer professionals were usually met with a certain resigned wait-and-see attitude. Technology transfer officers told me that they try and stay up to date with these developments since they can have a wide-reaching impact on the biomedical industry and therefore on their own patenting decisions but that there are always cases working their way through the courts and in almost every single therapeutic area.[4] They seemed used to the uncertainty as cases make their way through the US court system over years. When decisions are made, "things that people may have thought patentable two weeks ago may not be today…"

Patenting decisions, then, are challenging to make because they require technical knowledge - a degree of familiarity with the science, up-to-date awareness of shifts in

[4] For example, court decisions on gene patents as in the diagnostic kit at issue in the Myriad case will, I was told, have an effect on companies' strategies with regard to personalized medicine which depends on the production of test results according to which therapies should be tailored.

what is patentable, and a sense, gleaned from experience, of which discoveries may be valuable because they are not encumbered by others' patents. At the same time, patenting decisions are, in many ways, constrained by financial realities. Discoveries that will require patent protection will likely be too expensive a proposition for a spin-off company, government sponsorship or philanthropy to fund alone; they will need the involvement of industry. Indeed, everyone with commercialization experience emphasized to me how expensive patenting and enforcing patents is. Dr. Mark again offered a vivid depiction of why patenting has the reputation of being so costly. It is an explanation that highlights two aspects of his experience, the global stage on which technology transfer officers seem to be accustomed to making commercialization decisions and the rather proliferative capacity of legal claims: "You don't just apply to one country. You apply to every country in the world, or a select group of countries, so while it may cost you 10,000 dollars in Canada, you have thirty other countries. You're already at 300,000 dollars." He continued: "What also happens is, if your patent is too general or lists too many complexities, they make you break down that patent into the subordinate complexities and patents and so you can see that it turns into this arborized tree of applications very quickly." When one patent already costs $300,000, then "dividing that patent down further is so onerous that you need serious granting money to be able to do it."

Because patenting is so expensive, technology transfer officers emphasized to me that philanthropic or government support is not enough; they will need industry investment if a discovery is to be patented and taken to clinical trials. Dr. McKenzie, the technology transfer officer who helped Andras Nagy deposit his hES cell lines with the

NIH, told me in our interview that this was a reality that those who work in biomedicine appreciate: “It’s a difference of biomedical research versus some other areas of research - sociological, anthropological - where there tends to be - and I’ll use this term but I don’t mean it negatively - more of a left wing concept of the way the world should work.” For Dr. McKenzie, academic researchers may not have their work shaped by corporate timelines as Dr. Jones described, but, if they are physically conducting their research in a hospital, they see medical companies’ products in use. Hospitals, then, are sites where market and legal forces and patient suffering collide and researchers are witness: “Just being in a hospital environment where you see patients and their families on a daily basis you want to see that your research doesn’t just generate interesting ideas but makes an impact on the delivery of healthcare.” Compared to “a university where it’s easier to dissociate and it’s an interesting puzzle to solve,” he told me, “there is much more of an outcome focus in an academic hospital setting.” He said: “particularly in a hospital setting we know that somebody’s got to invest millions of dollars to turn something, an interesting research finding, into a product that will actually be used in the world. So, as I say, I don’t mean that negatively, but I know that’s the reality in a university setting. We see it [at the university here] all the time.”

Technology transfer officers are therefore particularly attuned to changes in industrial practices with regard to licensing patents, changes driven by complex technological, market and legal forces. Dr. McKenzie, for example, spoke of shifts in what industry is interested in licensing and this has changed considerably over the last twenty years. In contrast to the “gene hunter” days of the 1990s, he recounted, before the sequencing of the human genome, people were able to get broad patents with limited

data. Patents were issued on sequenced genes that had an unclear association with a disease and companies were keen to license them: “You know at one point if you had a novel gene that was tied to some disease process and you had an early stage molecule that seemed to be affecting it, you’d have a bidding war, multiple companies wanting to acquire that. Nowadays nobody’s going to acquire those sorts of rights from you. That’s fallen by the wayside so we don’t do that anymore.” Today, he continued, the validity of many of these gene patents is in question and gene sequences tend to be put into libraries instead. Industries are now looking for substances that have an effect on a disease process and for robust data on that effect. Dr. McKenzie and the scientists that he works with are more likely to protect a compound for which they have “ideally, both some in vitro and in vivo data that it is modulating in some way a disease process.” Similarly, research tools and methods have become less interesting to industry than finished therapeutic or diagnostic products. It is unlikely that research institutions will decide to spend the money obtaining and enforcing these kinds of patents. As he explained, “in my world of academic tech transfer, we do those things that industry is willing and interested in having us do for them.”

At the same time, he spoke approvingly of “a growing trend in the biomedical world that is very different from what it was 10 or 15 years ago towards what’s called open innovation.” This referred, he told me, to an “increasing recognition that putting tight controls around research tools and research enablers is in fact a barrier to research not an enabler as it was intended to be.” Patents appear in the literature as a tool to “incentivize” innovation. “It’s still an evolving field and the pharmaceutical industry at senior levels talks a good story about open innovation. The reality on a day to day basis is

a little bit different and I think that ethos hasn't fully permeated the industry but it is certainly a growing trend." The lab scientists that I interviewed were divided on the necessity of patents but that Dr. McKenzie spoke of open innovation in this way suggests that he would like to see more sharing of research tools and more data in the public domain, and that he views patents as strategic moves to enable research and, ultimately, the development of therapies.

Comparisons: Technology transfer, Health Canada, REB

Health Canada officers and technology transfer officers understand ethics to be the province of governmental mandate. An interview I conducted in the form of a teleconference with three Health Canada officials from the Biologics and Genetic Therapies Directorate in October 2011 made this particularly clear. There are many facets to Health Canada's mandate to protect the health and safety of the public, including controlling the safety and quality of therapeutic products and overseeing clinical trials. The first job arguably belongs most clearly to the realm of consumer protection (which could be understood in terms of a moral imperative). The latter is an extension of consumer protection concerns but also involves human participants. This led to some confusion on my part during our interview because their oversight of clinical trials appeared to involve approving or halting clinical research on the grounds of the safety of the participants. To my interviewees, however, their control of clinical trials is not "ethical." It is instead a reflection of their mandate - keeping the Canadian public safe.

They explained that Health Canada and the regulations for clinical studies (under

Canada's Food and Drugs Act) address the safety of products. The AHR Act controls the creation of hES cell lines and the types of research performed with them; as my primary interlocutor explained, the bureaucracy created by the AHR Act "look into some of the other things that are ethical or bordering on legal issues, where you're getting stem cells from." Then clinical trials and the introduction of products falls under Health Canada and the regulations under the Food and Drugs Act that deal with the safety and efficacy of products. "Ethical" oversight is "procedural" and temporally located prior to research. Describing the many kinds of preclinical information Health Canada requires that researchers submit with a clinical trial application, they explained: "Usually with drugs, it's [about] the chemical manufacturing, but with biologics, and in particular stem cells, there will be a lot of information about how the donors will be screened… and all focusing on safety rather than ethics or on other procedural things." Researchers submitting clinical trial applications to Health Canada have to demonstrate that they obtained the appropriate research ethics approvals which are a completely separate process from their own deliberations.

In other words, the three Health Canada officials in this interview understood ethics in a particular way. While their own evaluations of clinical trial applications also clearly involve moral decisions about the acceptability of proposed research, they talked about their decisions as entirely "based on" safety considerations. For example, my interviewees pointed out that there were a significant number of therapies that were last ditch attempts for seriously ill individuals being brought to Health Canada for clinical trials. In these cases, the patient population may have a 90% or 95% mortality rate and the researchers are hoping to augment a minimal therapeutic benefit or to provide even a

slight benefit for the patients when all else has failed. They spoke of the huge technical challenges to proving some efficacy in this situation and they spoke of the risk/benefit analysis that they might use to allow a clinical trial for a particularly unproven therapy to go ahead: “Our reviewers do take into consideration the safety, quality and efficacy on a benefit/risk basis... [I]f you have such a high risk of dying whether you get the treatment or not… the benefit/risk profile will maybe suggest approving a clinical trial that wouldn’t be used if there were other treatments available.”

These kinds of risk/benefit analyses and assessments of scientific data are simultaneously technical and moral problems. My interviewees’ description of the way in which Health Canada evaluates clinical trial applications and drug submissions suggested that Health Canada officials approach them in a similar manner to the REBs; while they are particularly concerned to ensure regulatory compliance, they also appear to be assessing the strength of the researchers’ evidence for the projected degree of harm to which trial participants might be subjected and deciding whether that degree of harm is acceptable. My interviewees’ discussion of these evaluations was framed in terms of risk which lends itself to quantification more than does harm which dominates REB (and the TCPS 2) discussion. That the two must be engaging in similar deliberations is suggested by the references Health Canada makes to its role in regulating clinical trials to be found on its website where they write that they can halt a drug trial if the sponsor of the clinical trial has not met regulatory requirements or “where there are reasonable grounds to believe that the use of the drug for the purposes of the clinical trial endangers health, is contrary to the best interests of the clinical trial subject or if the objectives of the clinical trial will not be achieved” (Health Canada 2014). While this reads like a statement of

research ethics, Health Canada officials see their evaluations of clinical trial applications in terms of safety data and risk/benefit ratios (with risk and benefit, like safety, understood in physiological terms). Safety, efficacy and quality refer to the realm of the technical, standardized and regulatory, not the "ethical".

The technology transfer officers would similarly separate their work from any ethical considerations which they assume have all been addressed already. However, their work, as they described it, involves decisions with consequences for access to therapies. Technology transfer officers told me that the high cost of patenting means that publicly-funded institutions have to be strategic in their decisions over what to patent. For example, my interview with Dr. Jones suggested that commercialization decisions are economic calculations in the service of humanitarian goals. She was emphatic that, in general, for an invention to reach patients, "someone will have to make money out of it, guaranteed." In situations where there is no money to be made, her decisions about whether and how to commercialize an invention seemed easier. She offered an illustration of a hypothetical case in which there is no profit to be made, a hypothetical therapy for progeria, a disease of accelerated aging. She told me, "there are about 90 people in the world that are affected by it and should you find a cure for it and should it be patentable, you're not going to patent it because there are 90 people in the world that are going to benefit from it so you want to make it available for free." She continued, "You don't want to put barriers to accessing something like that" and added, "besides, no company is ever going to think that they're going to make money out of a 90-people population."

In this way, Dr. Jones depicted patenting decisions as "a balancing act" involving

the assessment of an invention by the technical criteria of patentability but also involving thinking about whether a patent would be a help or a hindrance to the process of producing a therapy. It could provide an incentive to a company to continue with research and development since they will ultimately make money off licensing the patent but at the cost of restricting general access to the knowledge so that other researchers will not be able to build on it. The chance of making money off of licensing patents is so slim and patenting is so expensive that the calculation that Dr. Jones described making is that the patent has to at least "have a chance to break even" so that the institution does not lose on the proposition. Patenting decisions appear as strategic moves in the process of translation that can either inhibit or enable patient access to therapies.

Both technology transfer professionals and REBs are thinking about the utility of research, speaking of "public benefit" and calculating how to get research to work for patient populations. These parallels appeared most clearly in an interview with Dr. Lee, a microbiologist turned business development expert associated with a stem cell research institute, at an Ontario university in 2013; the conversation turned to the REB in the context of a discussion of how stem cell scientists chose their research topics. I had expressed curiosity about whether academic scientists were ever dissuaded from going down a particular research path because the technical hurdles just seemed too high (to make cell therapies safe, for example). Describing academic science as "solutions looking for problems" in that "sometimes you have something, you just don't know what it's useful for and it may be useful for nothing," he made the popular argument that basic research should not be neglected at the expense of research with clear application as the future therapeutic value of basic research is unknowable. I told him about my discussion

with bioethicist, Dr. Patel, about whether research that is a purely knowledge generating exercise with no potential value to the research subjects involved is justified and Dr. Lee saw parallels with his own assessments of value - “So it’s funny that you say that… even from that side [there is an emphasis on application].” In other words, while arguing for the need for basic science, a large part of Dr. Lee’s job in business development was to help researchers “identify potential value” and he saw this duty reflected in my description of REB attention to questions of the potential value of proposed research to patients. Technology transfer professionals tend to speak of value in a way that plays on the multiple meanings of the term - value as financial, as utility and as worth. For both commercialization experts like Dr. Lee and for REBs, knowledge has to be applicable and in a way the justifies financial or human risks.

In sum, both REB assessments of biomedical research proposals and technology transfer assessments of discoveries or inventions share a similar style of thinking. REBs explicitly preclude market considerations when making their decisions where technology transfer professionals must by necessity assess and work within a market context. Both groups see themselves as working to the ultimate benefit of patients. The TCPS 2 and REBs are very aware of real or perceived conflicts of interest, including the possibility of companies influencing REB decision-making and REBs are perceived as a bulwark for the protection of individuals against market forces. At the same time, both realms use the same cost/benefit logic that runs through financial and human participants' protection assessments. Both are institutional sites that involve moral decisions (whether or not this is made explicit) though they are differently situated components of the regulatory and market nexus in which contemporary biomedicine is played out.

At a 2014 summer school entitled “Biotechnology, Biosocialities and the Governance of Life Sciences” in São Paulo, Brazil, philosopher Susanne Lettow stressed the crucial role that regulatory ethics plays in the normative and legal infrastructure that underpins the bioeconomy. In order to become economic objects, information and samples must be properly obtained through proper consent procedures that are well documented. As Lettow noted, informed consent facilitates the constitution of biological agents as goods that have a juridical status and can move within monetized circuits of exchange. By attributing (moral) value to objects through the certification of ethical procurement, bioethics constitutes them as economic objects. As I have tried to suggest, by exploring the practices of professionals in technology transfer in relation to research ethics and product regulation we begin to shed light on how members of academic bureaucracies shape and are shaped by prevailing norms and how they effect early transformations of value that may be as consequential as those produced through the work of large biotechnology companies.

The CCRM and John Hu

Social scientists have argued that one of the most distinctive characteristics of publicly-funded biomedicine as it is practiced today is the extent to which industry and market forces are implicated in research (Atkinson-Grosjean 2006; Fleising and Mather 2005; Metcalfe 2010). Some have suggested that commercial interests have entered into the practice of science to an unprecedented degree or, as Sunder Rajan puts it in relation to the life sciences, that "the grammars of the life sciences and of capital are co-

constituted." (Sunder Rajan 2006: 283) The conversation is taking place amongst social scientists of “academic capitalism” (Metcalfe 2010; Slaughter and Leslie 1999; Slaughter and Rhoades 2004), those studying biomedicine as a global enterprise complexly linked to global capitalism (Fischer 2016; Franklin 2005; Ong 2016; Petryna, Lakoff and Kleinman 2006; Sunder Rajan 2003, 2005, 2006, 2011), scholars concerned with the implications of the biotechnology industry's strategy of making property out of nature (Hayden 2003; Lock 2001; Prudham 2007), and those illustrating how new forms of biomedical subjectivity are emerging in relation to entrenched inequalities (Petryna 2009; Petryna et al. 2006; Sunder Rajan 2011; Waldby and Mitchell 2006). These scholars are writing about US biomedicine, or in relation to it, which reveals its shaping by specific American histories and ethos.

While a number of the Canadian scientists whom I interviewed share social scientists’ concern over the increasing role of industry funding in academia and the practices that come with it, and a few of my interviewees were concerned also about the commodification and commercialization of human materials, their daily work centers on a lack of industry interest in financially risky early-stage research rather than its intrusion into academic science. CCRM was designed precisely to address the “barriers” to stem cell commercialization.

The networks of the Canadian government’s restructured science funding system, one type for scientific research centres (NCE networks) and another type for commercialization organizations (CECR centres), have intersected at stem cell science which the government has significantly funded in a bid to position Canada at the forefront of the field. The Stem Cell Network was an NCE network and in 2011 it was

joined by a new CECR centre devoted to regenerative medicine, the Toronto-based CCRM. CCRM is a non-profit organization responsible for the commercialization of research in stem cells and related technologies at a large number of Canadian publicly-funded institutions. Before CCRM, academic stem cell scientists in the Toronto area whose research had commercial potential worked with another CECR centre, MaRS Innovation, created in 2008. Both CCRM and MaRS are organizations designed to help turn academic research discoveries into health care products. They are both designed with the idea of "de-risking" early stage inventions by providing some of the investment and crucially by co-ordinating the inventions of multiple research institutes.

Housed in the MaRS Centre, MaRS Innovation is a not-for-profit commercialization office with the goal of finding a path to the market for very "early-stage" research from publicly-funded academic labs. It has partnered with fifteen institutions including Toronto's universities and most of its research hospitals plus the residents of the MaRS Centre itself. MaRS Innovation office is not the easiest place for a member of the public to find. I stumbled upon their office by accident one day in February 2013. Seeing me peering tentatively through the locked glass door, a young woman invited me in for a chat about the work of the office. I had not been aware of the existence of MaRS Innovation until then. "We're a bit of a well-kept secret," she joked. MaRS Innovation works with invention disclosures from their multiple member institutions and encourages private sector partnerships and licensing of intellectual property. CCRM took over all commercialization activities related to regenerative medicine from MaRS Innovation. While it shares some of the characteristics of MaRS, then, CCRM focuses on the regenerative medicine field with the idea that the challenges

to commercialization in the field are distinct enough to benefit from a sharing of expertise, IP and infrastructure.

Stem cell science is a particularly difficult sell to investors. Stem cell and regenerative medicine technologies more generally are seen as a potentially very lucrative business with global health markets but investors have historically been wary of it with business commentaries frequently citing the high-risk nature of the science and "regulatory uncertainties." In fact, other than blood, marrow and skin transplants, there are still few clinical applications currently in use. In North America stem cell companies have been finding it difficult to raise private funding. In the U.S., there is little venture capital funding to be had for stem cell commercialization and in Canada it is almost non-existent. In this context, CCRM is attempting to "align" academic stem cell researchers with industry needs, to bring academic researchers and companies together to fill the translational gap. While scholars have noted that academy-industry collaborations are increasingly frequent (Rabinow 1999, Rabinow and Dan-Cohen 2005, Shapin 2008, Sunder Rajan 2006), the emergence of organizations like CCRM suggests that academic science and industry are not coming together as often or as productively as some have hoped. CCRM is one model of a translational institution attempting to connect academic researchers to industry partners and private investors, and, more generally, to bring together various kinds of expertise, facilities and funding in productive ways. It is engaged in bringing into being a new configuration of biology, technology, finance, and regulatory practice.

I emailed Dr. John Hu, an executive at CCRM, for an interview and he readily agreed to speak with me. CCRM is housed in the Banting Institute, a University of

Toronto building across the street from the MaRS Discovery District Centre and named after Frederick Banting who with Charles Best is famed for the discovery of insulin for the treatment of diabetes. The building is part of the University's Banting and Best Centre for Innovation and Entrepreneurship. The old university building has been converted into office and lab space. At the end of a hallway, it is more of a low-key presence than the large MaRS building with its eye-catching blue discus by the front doors. I first met Dr. Hu in a small room that seemed like a cross between a university meeting room and a company board room. Dynamic and articulate, he struck me as a man accustomed to giving pep talks to employees and making large claims about the potential embodied in the Canadian stem cell community and the investors the organization would like to attract.

Hu is a biomedical engineer who created a spin-off company from the University of Toronto in the field of tissue engineering. The goal, as he explained it to me, was to take early stage inventions from the academic environment and enhance them to a point where larger companies would be interested in them. Similarly, his strategy for CCRM is to advance inventions coming out of academic research labs to a stage where they have sufficient value that companies will license them. CCRM therefore works on the earliest stages of translation. It attempts to connect the leading Canadian research institutions working in the field of stem cells and regenerative medicine with a “consortium” of companies in the regenerative medicine industry. Canadian biotech companies are far fewer than in the US, tend to be smaller and to focus on manufacturing of products such as tools and reagents. CCRM uses academic infrastructure but the work is not done by academic scientists. It has chosen to consolidate its resources in a few areas, mostly in the

category of “enabling” technologies surrounding cell manufacturing and biomaterials that will ultimately be needed if therapies are to reach the stage of clinical trials. Other CCRM scientists work on reprogramming technology and create iPS cells on a fee-for-service basis.

As we discussed the relation of academic scientific research to industry, Dr. Hu impressed on me the amount of work that a company must do in order to bring an early stage idea or invention to the point of a product. Academic researchers do not always appreciate all the steps involved, he asserted: “coming up with an idea and doing a little bit of research on it at the bench in a university and inventing something is the easiest part of the process. It's one step. It's an important one, but the amount of money and the amount of time to take an idea and make it into a product is about ten times the resource requirements and input that actually just coming up with the idea is.” Acknowledging that some researchers play an important role in moving an invention forward, he continued, “but coming up with a product and validating it in animals and validating it in humans and getting it to market and selling it takes millions of dollars and an incredible amount of time and so the frustration is that some postdoc and a prof come up with a new idea. They do a few experiments on it and they say it's the most valuable thing in the world. Well yes, probably, but it's far, far, far from the end game.” To Hu, a researcher's new idea may be a valuable contribution to knowledge; it may be an intellectually, emotionally or aesthetically satisfying creation; it may suggest exciting therapeutic applications but as a basic research discovery with therapeutic potential it is at the beginning of a very long and iterative process of further research and development if it wants to reach the clinic. This is a common theme in the literature on the pharmaceutical

industry (Paul 2010). It is also fairly common to read that stem cell therapies in all likelihood will take even longer (Giebel 2005).

The relative lack of venture capital compared to the situation in the U.S is one of the oft-cited reasons for the low rate of commercialization in Canada. Several of my interlocutors told me emphatically that Canada does not have a good record of commercialization. It has scientific ideas and expertise but few commercial successes. Recent analyses of US biotechnology have emphasized the role of speculative capital. Kaushik Sunder Rajan is, arguably, the scholar who has offered the most elaborated argument that technoscience and speculative capitalism have become inextricably enmeshed (Sunder Rajan 2003, 2005, 2006, 2011). He argues that innovation and speculation both involve visions of the future. There is, he argues, a specific temporality associated with speculative capitalism. The future is called on to account for the present, thereby creating the conditions of possibility for the present and the generation of value – large amounts of capital exchanged for the promissory note of biotechnology. Speculative investment is encouraged by the hype that it is in companies' self-interest to create which therefore plays an important role in the financing of biotech visions of the future. This state of affairs is most dominant in the US but, as his exploration of the Indian biotech industry suggests, structures the aspirations of scientists, policy-makers and entrepreneurs around the world (2007). His book *Biocapital* could be read as an attempt to critique economistic understandings of value – approaching neoliberalism as an ideology that both reinforces historical global inequalities and creates new ones — while remaining sensitive to the role of individual desire and the imaginaries that commodities create. Ethnographically exploring instances in which Indian actors from entrepreneurs to state

politicians attempt to replicate the American free market system, he argues that "the real power differential between the two locales lies in the ways that global imaginaries get structured" (285), such that "American global techno-capitalist hegemony" is dependent on the way in which "the imaginaries of the American free market become such global objects of desire... " (286). This kind of speculative biotech capital is very scarce in Canada.

Hu is consciously attempting to find other ways to align academic and industry interests and to identify strategies for funding translational research other than venture capital. He describes CCRM as the fruit of a uniquely Canadian approach to science funding — Canada's creation of the network programs (centres of excellence and centres of excellence for the commercialization of research) was, in his eyes, an effective strategy that other countries with limited resources and capital would do well to adopt. One of the benefits of this "Canadian model" is its fostering of collaboration. American business culture strikes him as ruthlessly competitive in comparison - With a laugh he told me: "collaboration in the US is merger and acquisition!" (but, he quickly added, eventually "they'll figure it out and do it better than us.") Hu's commentary on the CCRM experiment evokes an ambivalent relationship vis-a-vis the idea of American biotech between, on the one hand, the availability and scale of private funds and the competitive nature of commercial relations and, on the other, collegial relations and collaboration.

Hu has what he calls a "B.R.A.G." a Bold, Radical, Audacious Goal that, if reached, would mean no-one could gainsay CCRM's success and that is to attract half a billion dollars to Toronto for regenerative medicine. He is counting on being able to attract risk capital, large-scale investment in regenerative medicine. Hu is clearly a

businessman and his “BRAG” involves attracting investors and selling a vision of the benefits of regenerative medicine and of the particular strengths of the Canadian research community and collaborative culture. The restructuring of Canada's science funding that happened in the 1990s installed a more “neoliberal” orientation in its bringing together of public research and industry. Certainly, Hu’s talk of strategic management of the Canadian science “ecosystem” – the combined academic and commercial expertise and resources in research and development - to eventual economic and social benefit and of better integrating academic science output with industry “pull” epitomizes the discourse of entrepreneurial science in the furtherance of the nation’s global competitiveness. Hu’s vision of the future involves the success of the model and the strength of the entire regenerative medicine research community.

While not directly dependent on the market, the fate of CCRM is similarly unpredictable; it is itself an experiment and as such its outcome is unknown. The stakes are high. Its lifespan has clear constraints; Hu does not have to sell his vision successfully to investors to fund CCRM's very existence, but as a government center, he is stringing together funding terms of finite length. Without investor funding, he told me, “everything we do right now here will just get orphaned two, three, four years from now.” Hu and CCRM are under pressure to prove that their new institutional model for translation is viable and valuable. His hope is that the companies in the consortium will provide money to help advance the technologies that they are interested in, thereby sharing the financial risk. CCRM aims to be a commercialization model that brings academia and industry into a more productive relationship through centralizing academic regenerative medicine inventions and translational and development expertise and coordinating industry

funding. It is possible that his efforts to bring regenerative medicine to patients and to profits will be cut short and the link to the future will be ruptured.

Echoing Dr. Jones' attempts not to obstruct the movement of knowledge and technologies out of labs, Dr. Hu depicted the translation process as full of bottlenecks caused by technical issues, intellectual property, regulation and business models. With a sigh, he concluded: "Actually, it would be much easier just to create a coffee company and sell a product to people who are addicted. Life science and stem cells is just layer upon layer of failure points." Despite an acute awareness of the limits of his knowledge and power to change economic realities, Dr. Hu works tirelessly to sell regenerative medicine and the expertise and creativity of Canadian scientists. While stem cell research has a similar network funding structure in the UK and Australia, the existence of both the Stem Cell Network and CCRM arguably makes Canada a unique translational environment as does the much-noted collaborative environment that exists for stem cell research in the Toronto area. In a similar fashion to stem cell researchers viewing the regulatory framework as appropriately Canadian, Dr. Hu sees himself as contributing to a distinctively Canadian form of biomedical innovation.

Conclusion

In anthropology, technology transfer offices are an under-studied component of biomedicine. Yet, in the course of my research, I found that they play an important mediating role for regulatory and legal regimes and for governmental commercialization agendas. They are a site of institutional structuring of biomedicine through the

application of market and legal regulatory mechanisms to academic research. Because they exist at the confluence of many of the forces shaping biomedical research today and are sites of interdisciplinary (and multi-sectoral) collaboration, technology transfer offices are important sites for the discussion of emerging ethical issues in stem cell science. Technology transfer directors do not decide funding priorities or steer research programs, but they are taking the research products that those programs produce and making decisions about how they could be put to best use while necessarily working within and around market logics. They are strategizing how to keep discoveries moving, hopefully, ultimately "into the clinic" while balancing this against the need to generate revenues or at least maintain the level of funding necessary to support the goals of their research institutes. The decisions they make about the transfer of materials, the publication of results and whether effectively to turn knowledge into property or put it in the public domain can foreclose or help shape subsequent knowledge production and the development of therapies.

Those working to commercialize stem cell research are both part of a global biomedical economy and embedded in national, local and institutional settings. They are oriented towards large markets like the US but are working within a distinctively Canadian market and legal and political culture. They expressed complex and ambivalent views of US biomedicine in our interviews. They were impressed by the wealth of resources available in the US at all stages of biomedical research from university legacies to angel investors and by the country's global dominance in biotechnology. Dr. Lee told me that he and his family had lived in Boston before returning home to Canada and said: "In my 10-minute walk to work there were more companies than in all of Canada. I'm

not kidding."

At the same time, they felt that they had benefitted from human stem cell research emerging in Canada as a less polarized and partisan political issue than in the US. Still, they are being cautious in their decisions over what to try and commercialize. Several of them opined that the then conservative government would likely quash any attempt to bring a hES cell therapy to Health Canada for clinical trials. Instead of hES cell therapies, they were therefore focusing instead on commercializing adult stem cell discoveries, on drugs to stimulate endogenous stem cell repair and on manufacturing practices that might appeal to industry. Nor have any of them tried to patent hES cell discoveries either. The generally low public profile of biotechnology ventures in Canada relative to the US, Canadian commercialization actors' somewhat conservative decisions over what to pursue and a self-consciousness on their part of the perils of over-promising (as in previous US biotech bubbles) have contributed to the largely uncontentious reputation that stem cell science currently has in Canada. Their risk averse decisions with regard to patenting hES cell discoveries, for example, have kept concerns over commodifying human beings to a minimum. Stem cell science appears much like other emerging sciences that are grappling with myriad unknowns.

Conclusion

"Canada's science"

The experts in science, ethics, law, policy and business who people this dissertation are working to bring into being their visions of what good science, effective treatments, a robust Canadian biotechnology sector and an equitable health care system should look like. Stem cell science in Canada is a popular field, still dependent on human embryos, overlapping into areas of concern such as the commodification of human life and the humanization of animals and moving towards even more contentious technologies like gene editing (a type of genetic engineering) to model human disease in vitro more accurately using iPS cells. I have argued in this dissertation that it has been more successful in attracting scientists and less publicly divisive than might have been expected because of a self-imposed restraint on the part of stem cell scientists that tempers their excitement (Chapter One), because, despite temporalities specific to the field, it shares many of the characteristics of other "fast-paced" research (Chapter Two), because it is legitimated by REB review (Chapter Three), because of deliberate efforts to create a governance mode of co-ordinated anticipation and response (Chapter Four) and because people working in commercialization meld technical expertise with an understanding of the political and cultural climate specific to Canada (Chapter Five).

Canadian stem cell scientists are concerned with perceived challenges to their autonomy such as industry control over what findings they can publish or parliamentarians determining what types of experiments they can conduct. Their relation to the state is one of multi-directional vectors of influence as many of them act as

government advisers, their research is under a national regulatory regime and they still largely depend on government funding. Dan Monroe, who came from the world of economics and business to become President of the Stem Cell Network in 2001 when the federal health funding agency, CIHR, was developing its guidelines for pluripotent stem cell research, pointed out that for several years only a few Canadian researchers were engaged in these practices so members of CIHR could come to the Stem Cell Network's annual Till and McCulloch meetings and talk to literally all the scientists affected. After stepping down as President of the Stem Cell Network in 2013, Dan himself moved to a new position at CIHR. It was announced at the 2013 Till and McCulloch meetings, half-jokingly, that he would now be the stem cell scientists' "inside man" at the agency.

At the same time, there are myriad, more indirect linkages between state regulation and stem cell science mediated by various discourses and an expert apparatus of institutional bureaucracy. Quasi-legal procedures enable stem cells to be created or imported to labs which are themselves structured by various governmental regulatory regimes and where the cells are used variously to represent the human, specific disease categories and individual genomes. In technology transfer offices, staff take discoveries from this research and make complex valuation decisions shaped by markets and legal regimes.

Stem cell scientists speak a language of ethics as pragmatic, commonsensical, factual and tied to the efficient use of resources such as animals, funding and time. Among knowledge practices which seemed so familiar to me, this conception of ethics that closed off broader reflection caught me off guard in my fieldwork and I found echoes of it across institutional domains, particularly in its instrumentality. As I learned about

the ISCF's standardization projects and listened to Dr. Isaacs recapitulate the thinking of its EWP on informed consent for biobank donations at the Research Management Symposium, I felt that these scientific governance experiments with reflexivity and response also seemed both too similar and too different. Although the informed consent practices that Dr. Isaacs was promoting challenged the entrenched ethics procedures of the REB, they appeared just as effectively to short-circuit rather than open up questions of participation. The informed consent best practices that she presented were the product of an expert consensus oriented to international norms and referencing American clashes over patients' control of their genetic information. The ISCF's anticipatory governance effort to pre-empt conflict in member countries like Canada seemed also to be pre-empting debate.

Lingering questions concern patenting. Despite attempts to harmonize different jurisdictions' intellectual property laws such as the World Trade Organization's Trade-related Intellectual Property Rights agreement of 1995, there are some significant national differences with regard to life science patenting. Life science "inventions" granted patents in the US such as the well-known OncoMouse, a mouse genetically manipulated to develop cancer, have been unsuccessful in Canada. The US patent covered the genome of the mouse as well as the process by which it was created. While the US and the UK granted such patents, the Supreme Court of Canada ruled that a "higher life form" is not a manufacture or composition of matter. The distinction between nature and a technological construction was accepted as unproblematic by the US court. In 2013, US courts ruled certain gene patents invalid such as the high-profile ruling against Myriad Genetics and its BRCA1 and 2 (breast cancer gene) patents,

developments which trouble the narrative of the US embrace of intellectual property rights summed up in the oft-quoted assertion that in the US “anything under the sun that is made by man” is patentable.

As well as technical and normative questions over patentability and intriguing questions about national differences in patenting decisions, patents raise questions of labor and whose contributions count. The patent application requires identifying one or a few inventors out of a team that would otherwise be recognized for their work and focuses on the conceptual rather than the bodily, technical or institutional labor. Citing an article by Greg Myers that compares invention claims made in patent documents with discovery claims made in scientific articles, legal scholar Graham Dutfield identifies one of the key differences to be the extent to which the author appeals to other texts. A patent effaces the work of others in order to stake a claim to individual, novel invention. It tends to sever legally the network of ties to related artefacts (Dutfield 2009: 45). To acknowledge them would strengthen the author's case in a scientific article but, in patent documents, it weakens it by opening the door to potential legal challenges involving, for example, queries about the genuine novelty or "non-obviousness" of the invention or about the existence of prior or co-inventors. This is an interesting complication to the classic actor-network theory analysis of the solidification of a scientific fact through the enrollment of the expertise of increasing numbers of scientists (Latour 1987). The attention that anthropologists have recently given to documentary and bureaucratic practices could productively be applied to the patent application in order to explore the way in which scientific and legal notions of validity are negotiated in the work of crafting the text.

As stem cell research starts producing greater financial and therapeutic value, the identities and interests that Canadian stem cell researchers actualize in their labs, enabled by their institution's research management apparatus, may yet become greater matters of public concern. Legal disputes over intellectual property will surely arise and the trajectories of many actors will intersect in multiple and unforeseeable ways. Stem cell science is an expert and moral terrain where much is still unknown and whose politics are shifting towards more common cause with other emerging biomedical sciences. In presenting one's analysis of such a situation, to paraphrase ethicist Dr. Patel, all one can do, morally, is not attribute completeness to one's model.

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