How to fix a broken heart: Cardiac disease and the 'multiverse' of stem cell research in Canada

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You have to have a good cell to repair the heart.

(Researcher B)

Stem cell treatments, in many cases, are 'technologies of hope' for patients suffering from a severely disabling, sometimes mortal, health condition (see Brown, 2003; also Leibing and

Tournay, 2010, among others).[1] While in a relatively short period of time the field of regenerative medicine has made major progress – even to the extent of changing the understanding of core ideas within biology – the application of these findings often remains problematic. As Picard (2012) articulates, "progress has been significant in the lab and modest in the clinical world". Nevertheless, in some medical specialities, patients are being treated with stem cells within a climate of the "known unknown" (Webster and Eriksson, 2008), which means that practitioners are relying on different degrees of certainty and safety for the patient. The intervention we focus on in this article – autologous stem cell treatment for cardiac diseases[2] – is considered by scientists to be one of the safest procedures within the field: only a few scholars have voiced concerns over its risks (for example, Main *et al*, 2014). Autologous stem cells – cells from the patient's own body – do not provoke immunological reactions when compared with cells extracted from other organisms, and, as a consequence, regulatory processes are less complex than those targeting more controversial bio-technical materials.

Yet, the debates in this subfield do not touch upon the many ethical/moral controversies that are part of research using embryonic or foetal cells. The 2012 Nobel Prize in medicine, awarded to John Gurden and Shinya Yamanaka for their pioneering work leading to induced pluripotent stem cells (IPS) – adult cells that are reprogrammed into a pluripotent state – illustrates the importance of this kind of research, as it avoids the aforementioned ethical questions. IPS, however, carry their own risks – especially the still unresolved danger of tumour formation (for example, Chen *et al*, 2012) – and some of the initial euphoria surrounding their discovery has since faded.

In contrast to other pathologies, heart disease is not only an urgent public health issue and a major risk factor for a number of other health conditions (Leibing and Kampf, 2013; see also WHO, 2013), it has also been the target of more than 100 international clinical trials, applying stem cell therapies to cardiac patients. The suggestive names of these projects, such as Magic (France), Topcare-CHD (Germany), Boost (Germany), Magic Cell-5 (Korea) and Marvel (the United States), among others, imbue nationalist claims with the promise of almost miraculous cell regeneration.

The specific logic and importance of stem cell treatments, in the case of heart disease, are grounded by the fact that, after a myocardial infarction, conventional pharmacological or surgical interventions cannot repair the damaged and cicatrized muscle tissue; they can only help maintain the less functional organ.[3] Despite advances in surgical procedures, mechanical assistance devices (for example, stents, pacemakers) and drug therapy, more than half of patients with congestive heart failure die within 5 years of initial diagnosis. One researcher we interviewed observed rather pessimistically that: "(…) the faster you get [people] in, the faster we open up the artery, the less the damage occurs, that's the best. But after that, even the

1 'Technologies of hope' are the assemblage of biotechnological processes defined by their promoters as medical tools with the potential capacity to preserve, enhance, or extend life (cf. Leibing and Tournay, 2010, p. 3).

2 For a clear overview of the different stem cell interventions for cardiac diseases see: www.stemcellnetwork.ca/index.php?page=heart-failure ('Heart Failure' by the Canadian Stem Cell Network).

3 In 2009, the final proof of naturally occurring cardiac regeneration was brought by a Swedish team of researchers (Bergmann *et al*, 2009). By staining and tracing heart cells radioactively, the team was able to show a slow regeneration rate of about 0.5–1 per cent in the adult human heart. For the regeneration of the heart in cardiac diseases, however, this natural repair rate is far too low to make a significant difference.

medications (…) don't really make much difference with the actual ejection fraction (…). They don't really repair the heart, they limit the damage, they don't really change it, they don't alter it. So there is no real therapy for that". Heart transplants may be a real alternative in severe cases; however, they involve well-known risks, and there continues to be a shortage of donor organs. Stem cells, on the other hand, specifically support the regeneration of the damaged tissue, with the desired result being the improved functioning of the heart (generally measured by its ejection fraction or 'pumping capacity').

Autologous stem cell treatments for cardiac diseases are not only about 'doable futures', as Eriksson and Webster (2008) have called the hype, hope and promises involved in scientific innovation. In fact, because of the high number of trials that have been run when compared with other pathologies, this kind of intervention becomes, to a certain extent, a concrete – though experimental – treatment possibility, and therefore can be conceptualized as a doable *present* based on a number of certainties. The similar and well established procedure of bone marrow transplants for certain blood cancers reinforces the researchers' feeling that they are getting it right: "So yes, we always point out, when people say 'When is stem cell research going to have an impact in the clinic'?, we can say, 'Well, it is already', because of bone-marrow transplants" (Researcher D).

In line with an approach that one of the current authors has elsewhere referred to as an "anthropology of uncertainty" (Leibing, 2009a) – the analysis of the complex and often partial process of turning uncertainty into a certainty, and thereby legitimizing action within a given context – we want to focus here on how researchers in Canada talk about the apparently uncontroversial clinical trials using stem cells for severe heart disease. These scientists are not the only, but are certainly key players when it comes to articulating authoritative knowledge: it is they who translate and contextualize signs, symptoms, outcomes and analytical processes to different audiences when, for example, they ask for funding, talk to the media, and try to convince patients, other clinicians, and regulatory committee members using their specialized, in-depth knowledge of complex procedures and biological facts (for example, Tournay, 2007). In terms of the breadth and complexity of translating basic science research into clinical applications, we want to focus in this article on one specific aspect: the simultaneity of certainty and uncertainty in the scientists' reasoning and the need to transform, at least partly, uncertain elements into certainty – something that we call the 'multiverse'.

'Multiverse' and Bio-Technologies

> Doublethink means the power of holding two contradictory beliefs in one's mind simultaneously, and accepting both of them.
>
> (George Orwell, *1984*)

Complementary to a number of approaches in STS (Science and Technology Studies) and, more specifically, to a sociology of expectations (see Brown and Michael, 2003; Borup *et al*, 2006), an anthropology of uncertainty is giving space and voice to people who are part of an assemblage of discourses, actions and interactions between humans and non-humans as they relate to emerging bio-technologies and experimental medical interventions. We are talking about people "living in purgatory", as Rabinow (1999) calls the transitory "practiced sites" (p. 4)

in which "diversely stratified and partially incompatible histories temporarily and uneasily come together" (p. 23).

Not surprisingly, a number of social scientists have already discussed emergent bio-technologies, and have described the attitudes towards them as risk (for example, Bharadwaj *et al*, 2006), expectations (for example, Brown, 2003), hope (for example, Leibing and Tournay, 2010), anticipation (for example, Adams *et al*, 2009), ambivalence (for example, Franklin, 2013), and innovation (for example, Nowotny, 2006; Tournay, 2007), among others. A great number of these researchers analyse in detail the complex process of regulation and standardization of hybrid biological matter, such as stem cells. Hogle (2009), for instance, talks about "pragmatic objectivity" within regulatory processes of new biological products, objectivity which is based on "collectively agreed-upon acceptable evidence" (p. 718). Hogle describes the regulatory practices regarding hybrid bio-objects within the field of Tissue Engineering in the United States ultimately as strategies for reaching markets, while relying on different, historically situated objectivities that might make sense in one system, and mean something different or even be in conflict with another regulatory system.

The central point of this article, the synchronicity of certainty and uncertainty, is, as several authors argue, increasingly part of new bio-technologies, but also of 'ordinary' clinical realities. For instance, Mol (2003), in her study on atherosclerosis, shows that, depending on the context, a multiplicity of ontologies exist in which this disease is being experienced and treated. Mol and Law (2002), in the introduction to their edited volume on complexities, further elaborate on the concept of multiplicity; they show the co-existent ways of ordering objects, ideas, routines and structures related to the same clinical condition, saying: "… we discover that we are living in two or more neighboring worlds, worlds that overlap and coexist. Multiplicity is thus about coexistence at a single moment" (p. 8).

Another related concept is what Franklin (2013) calls 'ambivalence' or 'technological ambivalence'. Her reflections on *in vitro* fertilisation (IVF) existing within the tensions of something that has become "both norm and novelty" (p. 34), provides a thought-provoking analysis of how such bio-technologies get embodied by women experiencing this life-changing and deeply troubling kind of intervention. Franklin describes how problems, doubts and controversies are set aside by the fact that IVF has become a normal procedure – 5000 babies later – even though ambivalence is still palpable, partly because the practices related to IVF are much more complex than its promises.

'Multiverse', as we conceive it, is a similar concept; it focuses on synchronicity (and multiplicity) of certain and uncertain elements in scientific practices and reasoning and the importance of reaching a platform of certainty on which responsible action can be articulated and implemented. This platform is not only the result of a strategic manipulation of truths, as several authors argue – although this aspect must not be neglected – it can also, at some point, be a genuine way of speaking truth, an accepted part of which is not knowing (for example, Leigh Star, 1985; Keating and Cambrosio, 2003; Last, 2007; Weires, 2005). Certainty, therefore, especially in the context of emerging bio-technologies, is, to varying degrees, made up of knowledge gaps, ambivalence and doubts. Adams *et al* (2009, p. 247) call this increasing acceptance and normalization of uncertainty "adjusting ourselves to routinized likelihood", while Rose (2007, p. 8) writes about optimizing the "vital future by action in the vital present".

James (1956 [1896]), in his essay "The Will to Believe" , argues that evidence of truth sometimes only reveals itself after one has already committed to believing in this truth

(like joining a research team looking for the cure of a disease). It was James who coined the concept of 'multiverse' in 1895, referring to a moral pluralism within one specific context. Philosopher Bloch adopted this notion in the 1930s; his writings on synchronicity (*Gleichzeitigkeit*) – the co-existence of phenomena with different historical valences (see Bloch, 1985; 1977) – had a major influence on social scientists. Bloch's reflections on synchronicity and multiverse illustrate how the inclusion of older value systems and practices in the construction of the present, alongside a certain resistance to change, was paramount in the acceptance of Nazi ideology within German society. The idea of co-existent temporalities, or layers, within one given time period is central to Bloch's (1991) oeuvre: "Not all people exist in the same Now. (…) Rather, they carry earlier things with them, things which are intricately involved. One has one's times according to where one stands corporeally, above all in terms of classes" (p. 97). His ideas inspired historians like Reinhard Koselleck and Eric Hobsbawm, as well as anthropologist Fabian (1983). Bevernage (2013), in his "belated critique" of Fabian's *Time and the Other*, remarks that what is missing from the book is the aspect of expectation, as well as the acknowledgement that co-existent times (and ideas) need to be understood as a "display of power" – a question of hegemony. Bevernage's critique points to the embeddedness of co-existent temporalities in socio-cultural contexts, and their varying capacity to make truth claims accepted.

We could easily use multiplicity instead of multiverse, especially because Mol and Law (2002) also question the immediate critique of many authors regarding scientific simplifications and innovation as strategic malevolence (often called 'reductionism'). Mol and Law argue that "the question [is] no longer, Do we simplify or do we accept complexity? It becomes instead a matter of determining which (…) simplifications we will attend to and create and, as we do this, of attending to what they foreground (…), as well as what they relegate to the background" (p. 11). It is true that there is an increasing "privatization of risk" (Hacker, 2006; see also O'Malley, 2004 and others): the reliance on profit-oriented, private institutions implicated in the risk management of a variety of products. However, it should also be pointed out that forms of governing people (and objects) vary from one context to another.

This is especially salient in Canada, where economic interests in stem cell research need to be seen within a specific context of collaboration and partial commercialization, controlled by the national Stem Cell Network, Health Canada and – a very recent phenomenon – also by government priorities. Within the last years, there can be observed an increasing demand to commercialize scientific research by the Canadian government, as well as in other domains, such as prisons, the military and in nuclear energy (see Herder and Brian, 2007; Ogbogu, 2008). However, although geographically neighbouring the United States, the politics surrounding stem cell research in Canada are much less economically oriented and less privatized. While Americans in the field of stem cell research face restrictive legislation, and strong political opposition from the conservative wing, they also invest large amounts of money into the development of stem cell products. Between 2002 and 2005, the estimated annual budget of stem cell research was worth US$566 million in public funding in the United States, whereas in Canada only $32 million were invested (Ott, 2007, p. 23). Even though the Canadian public regulations for stem cell research are not as contentious as in the United States, the commodification of biological human material, its 'biovalue' (Waldby and Mitchell, 2006), still raises a number of questions, and the economic power of stem cells remains modest (see Knowles, 2008; but see Mack, 2015 about recent developments in Canada).

The reason why we chose 'multiverse' and not any other concept, is because of its conceptual 'freshness' for studying emerging bio-technologies, especially in terms of its applicability to the aims of this article: we adopted it in order to articulate a discursive platform of certainty, show some of the factors that provide certainty, and demonstrate the way uncertainty is being both acknowledged and, ultimately, transformed into certainty (or bracketed with it), in such a way that actions (applications) can be justified. Different from 'multiplicity', which suggests a numbering, a list of 'worlds' or, 'ambivalence', which ultimately connotes an emotional, intra-psychic stance towards technologies (although its respective authors refer to much more complex and multi-layered phenomena) – it is the beauty and complexity of the image of multiverse that made us suggest this theoretical framework: The notion of multiverse, when used in science fiction and theoretical physics (like string theory), designates 'parallel universes' (for example, Ellis, 2011). The time traveler, an iconic figure of science fiction stories, changes (historical) contexts, but generally carries her embodied knowledge of one universe into the other, while simultaneously becoming 'other'. Likewise, the stem cell researchers we interviewed 'travelled', apparently without issue, among different discursive levels and epistemological claims while speaking with us.

Methodological Overview

We contacted leading stem cell researchers in different cities across Canada; the majority of those who agreed to be interviewed met us in their offices, while a few allowed us to also visit their research facilities – a fascinating world of seemingly chaotic, though in reality well-structured, agglomeration of instruments, machines, humans and sometimes animals. The interviewees were working on different topics within the wider field of stem cell research; some of them specialized in a specific pathology, others on more basic questions of the cell itself, while still others were also involved in questions of regulation and standardization. Our research project is based on several 'waves' of such interviews in Canada; in each one we were focusing on specific aspects of stem cell interventions. Further, we did a focused ethnography in a specific domain of stem cell research, as well as two waves of interviews in Brazil. The interviews we used for this article stem from the first wave, in which we asked more general questions, privileging narrative-style interviews with broad, open-ended questions. Topics covered included the role Canada plays within global stem cell research, the current state of the national research community (conflicts, alliances and so on), the specific contributions the individual interviewees had made to stem cell research, the 'good' cell, issues of funding and commercialization, and the realistic application of said research to animals and humans. Interviews lasted between 25–95 min. Most of the researchers we interviewed allowed us to follow-up in the event that we had more questions.

A standard content analysis has been applied to these interviews, which resulted in themes that we created as umbrella terms under which we could subsume either the researcher's idea of 'doing the right thing' – or of what, at least partly, was working – , and the doubts and uncertainties which had to be overcome. The division we made in this article, first listing those arguments containing certainty, and following this with lists of uncertainties, was not always as clear-cut as it seems in the following text. However, in general, greater uncertainty was more often articulated towards the end of the interviews (see below), so that the structure of

this article follows, to a certain extent, the natural flow of our conversations with the researchers. Further, the following analysis shows that what is certain and what is uncertain sometimes becomes relativized; as the interviews unfolded, new arguments questioned those ones that had been articulated previously (for an example, see 'historical grounding' and 'historical velocity', described in the second part).

For this article, we chose to focus on 4 out of the 15 interviews from the first wave (one female and three male researchers, of whom three were directly involved in research targeting cardiac repair). The reason for using responses from such a limited number of interviews was that it allows the reader the chance to better understand how the same individual can use both 'coexistent' arguments, and discursively work around certainties, within the context of a single interview. All interviewees, from three different Canadian cities, knew each other, and B and C had directly collaborated on a former research project. Nevertheless, each one had quite a different stance on the feasibility of stem cell applications: Researchers C and D (one researcher deeply steeped in clinical work, the other one a basic scientist involved in practices of regulation and standardization) were the most optimistic, while A and B were more apprehensive in relation to what to expect in the near future. Nevertheless, none of the interviewees doubted the promising general idea of regeneration.

Researcher A is a cardiologist and professor at a faculty of medicine at a major Canadian university. This researcher investigates different acute interventions for heart disease, one of them being the use of stem cell treatments (in tissue transplantation).

Researcher B is a basic scientist and professor who does research on cell transplantation and tissue engineering at a major research institute in Canada. He collaborates with groups that apply stem cells to heart disease therapies.

Researcher C is a cardiac surgeon at a major university-affiliated hospital, as well as a researcher and associate professor at the same university. He is able to recruit participants for clinical trials from among his patients.

Researcher D is studying stem cells in fields other than cardiac diseases and has been involved in a number of important committees regarding the regulation of stem cell research in Canada.

Certainties Regarding Autologous Stem Cell Interventions for Cardiac Disease

It is no surprise that stem cell researchers talk about their field of enquiry in a positive way. The sense of being part of a major movement that may revolutionize medical treatments is a source of pride, and, at times, evokes a perception of being on a 'mission': not only are there technical problems to overcome, but researchers must also consider issues such as the public's concern over the ethical aspects of stem cell experiments. Further, the interviewees must combat the decreasing interest that funding agencies and pharmaceutical companies have in financing research, now that the first wave of stem cell hype has passed. This has stimulated researchers to respond in different ways. For instance, the perception that a lack of information is responsible for the public's hesitation in supporting stem cell research provoked one of our interviewees to decide to climb Mount Kilimanjaro to receive more funding for his research. Another researcher described the difficult process of convincing politicians,

who have a limited knowledge of what stem cells are, that research in Canada should be regulated in a more permissive way:

> One of the things that the [Canadian Stem Cell] Network has done is, obviously, to engage patient groups, and disease foundations, because those are *very* interested parties; they are the people who can explain to government why (…) this kind of research is important to Canada. (…) But scientists can't back out of presenting and talking about these issues; *we have the information* on which you can actually make good, informed decisions.
>
> (Researcher D; emphasis added)

The capacity of scientists to translate and simplify their specialized knowledge into a language that less informed individuals (including the interviewing anthropologist) can better understand, and so grasp what is at stake, is based on a number of underlying issues that reinforce the researchers' own certainty that what they are doing is right. The factors that support the interviewees' certainties can be subsumed under four major themes.

Historical grounding

Although innovation can be understood as the pursuit or achievement of more advanced knowledge, its optimal success ideally needs to be anchored in established truths, in the absence of which the novel may seem suspicious and threatening. In the field of regenerative medicine in Canada, for instance, established truths are also geographically anchored: as Canadian contributions have been crucial to the history of stem cell research, Canadian researchers seeking to innovate can feel part of a collective research community with solid and relatively longstanding scientific roots. Although the term 'stem cells' was coined in 1908 – when it was proposed by the Russian histologist Alexander Maksimov (1874–1928) – the clinical discovery of the stem cell is generally attributed to the 1961 paper written by Canadians James Till and Ernest McCulloch (Till and McCulloch, 1961; also Becker *et al*, 1963), in which the authors demonstrated the presence of self-renewing cells in mouse bone marrow. The Canadian Stem Cell Network, formed in 2001, attests to this original discovery on its Website: "… in the year 1961 (…) [t]he existence and properties of transplantable stem cells in mouse bone marrow are established (…). This discovery set the stage for all current research on adult and embryonic stem cells" (Stem Cell Network, 2009).

Local researchers' certainties regarding autologous stem cell interventions for severe heart diseases are primarily based on two kinds of historical grounding: (i) Canada's essential implication in establishing the wider field of stem cell research and, (ii) beginning with Till and McCulloch, the specific use of bone marrow cells – which is now well known and has become established through the long tradition of leukaemia treatment (see note 2). Popular portrayals of bone marrow transplants for leukaemia frequently characterize the procedure as a routine intervention, although its history is made up of "cycles of disappointment" (Martin *et al*, 2008). In the media, dramatic stories are frequently published in which desperate families search for a bone marrow donor (for example, Lau, 2014). These stories generally end – along with underlying messages of salvation – once a donor has been found, yet frequently fail to acknowledge the patient's continued life-threatening struggles after the donation: in truth, interventions continue to be "complex procedures that carry significant risks of serious complications" (for example, NHS, 2014). The risks of these treatments, from infections due

to immunosuppression (leukaemia is treated with compatible donor cells and not autologous cells), are not relevant to the interventions discussed in this article. Nevertheless, it is pertinent to note that part of the popular trust in bone marrow cells is based on this continued depiction of bone marrow cells as having a long history of clinical safety and success, even though this success is in fact far from guaranteed.

There also exists a third kind of historical grounding, which refers to the organ itself. The heart – a "biological celebrity", as Landecker (2007) calls any living matter that becomes famous – is tightly linked to the early history of cell biology. In 1912 – the same year he received the Nobel Prize – the French surgeon and biologist (and eugenicist) Alexis Carrel produced a series of chicken embryonic heart cultures, which became known as "Carrel's immortal chicken hearts". One of those cell cultures (Number 725) fulfilled all Carrel's expectations and eventually became world-famous. It was later shown, however, that Carrel's experiment could not have worked as he claimed it did (see Witkowsky, 1980), but this story can be seen as one of the many *mythes d'origine* of today's treatments for cardiac diseases with stem cells.

The right kind of (non-alienated) cells

In addition to its historical grounding, the use of bone marrow cells for treating cardiac diseases avoids both the complicated ethics procedures and the restrictive laws associated with embryonic stem cell treatments. All interviewees mentioned this point, and especially said that it came up when talking to patients and their families as they were enroled in clinical trials. For instance, researcher B stated: "Well, the first time, when they [the patients] talk about the stem cell treatment, and they can get nervous about that – that's because, in most people's minds, stem cells mean embryonic stem cells". The researchers further explained that the general public often mixes up embryonic stem cells and cloning: "And for us, that's not an ethical problem, because we use the cells from the patient, not embryonic ones. We don't do cloning". "So, 1998, human embryonic stem cells. The year before was the cloning of Dolly: everything got conflated in the public mind" (Researcher D).

Certainty is further linked to the idea of the patient's incorporation of such stem cells; at least once they have received enough information about what 'autologous' means. Not only do these cells avoid rejection found on a biological level; from the patients' point of view (see Leibing *et al*, 2014), the strangeness of embryonic stem cells – living material that is created and sustained in the lab (theoretically indefinitely) – no longer seems so strange when using bone marrow cells. In the case of heart disease, patients learn that their own cells are only out of their body for a few hours (according to the Stem Cell Network, this can even be done in as little as 10 min; see below) before they (or a placebo) are re-implanted on the same day. The patient's acceptance is, as one researcher told us, especially unproblematic when the stem cell application is part of the same (though making it slightly longer) surgical procedure for their heart condition, and not a separate intervention, as is sometimes the case.

Another kind of alienation is avoided by the fact that individuals receiving autologous cells do not question the otherness of the cells, as they may do with cells extracted from strangers – in other words, issues of 'transcorporeality' (Weiss, 1999; Waldby and Mitchell, 2006), including aspects of selfhood, pollution and contamination. These aspects, which we also found emerging in interviews with patients in Canada are frequently used, according to the researchers we interviewed, as a primary line of reasoning when convincing a potential clinical

trial participant; for example: "so when the doctor is trying to convince a patient and says 'No, no, that's not a stem cell. A stem cell, [that's] you, in your own body, in your bones, that's a stem cell, and we're going to take it out, and put it back into you' – so, after you say that, they will say 'No problem at all'; most people would say that" (Researcher B).

Another critical aspect for understanding why bone marrow cells are more frequently used for cardiac repair is their clinical potential. Researcher B, who was involved in early studies, referred to the difficulty of harvesting cardiac cells (procedure), as well as their relatively small numbers (availability) in the beginning, observing that, "at that time, we used heart cells [in rats]. We took, you know, a very simple concept. We used a heart cell to repair the heart. (…) And then, we said 'That's great! We proved the concept. (…) We want to take this knowledge to the clinical application'. (…) After, you know, 1999, we changed from heart cells to the bone marrow cells, because it's hard to take the heart cells".

The 'rightness' of bone marrow cells also needs to be seen within an economic context. Researchers can argue that because autologous bone marrow cells cannot be commercialized, the common critique regarding economic interests, such as Big Pharma influencing test results, is less relevant in this context, and therefore published outcomes are more 'true' than in the context of drug trials. However, the flipside is that the difficult funding situation regarding stem cell research in general are further aggravated by the cell type. Mathur and Martin (2004) summarize the situation within the context of the European research community: "Autologous bone marrow cells themselves have no value as intellectual property. Their commercialization as such is, therefore, impossible (…) unless the treatment process is combined with a patentable preparation or delivery system. Clinical trials (…) will have to be funded by the European Commission, governments, charities, or philanthropy" (p. 189). In this context, one researcher climbing Mount Kilimanjaro makes sense.

Autologous stem cells might even provide too much certainty: Von Tigerstromm *et al* (2012) observe that the Canadian stem cell researchers they interviewed – similar to their colleagues in other countries (for example, Hogle, 2009) – expressed concern about the regulation of clinical trials by Health Canada, which demanded standards not compatible with stem cell procedures, especially with the classification of biological material as either biological or medical entities. The authors argue that some of the products even fall into a "regulatory void", and mention certain autologous products that might not get screened and tested before their application because the use of someone's own cells is apparently unproblematic. In the United States, the owner of a private clinic in Texas that provided (unproven) stem cell treatments argued in court that the procedures qualified as a treatment with a patient's own cells and therefore fell outside FDA jurisdiction. To qualify as such, the cells would have to be 'minimally manipulated' and be implanted for 'homologous use', meaning that they must carry out the same functions in the treated tissue as they do in the tissue from which they are extracted (see Cyranoski, 2013).

In Canada, stem cell applications are discussed, regulated and controlled principally by the Stem Cell Network and Health Canada, which also determine their status within a clinical procedure. For our interviewees, the doubts Von Tigerstrom *et al* found in their interviews were not an issue. The fact that in Canada relatively strict measures and long ethics procedures are implemented, and because the cells were autologous and considered secure, was considered reassuring enough. In fact, a certain degree of normalization, almost banalization, of the procedures was at work, based on the notion of an unproblematic cell. For instance,

one researcher stated that: "*Never* a patient has refused, never! (…) The surgery and the general anesthesia – that worries them, not the cells. They see them as just one more medication. (…) One can die in a surgery, even without stem cells. And what worries *me*, that are the patients who are *extremely* sick … the old ones, 75 years and so, not the cells" (Researcher C).

The right (and quantifiable) organ

Alongside the urgency in public health to combat heart disease (the 'number one killer' in many nations), the heart is also a strong symbol of life. Landecker (2007) refers to this when she talks about the experiments performed by Alexis Carrel at the beginning of the twentieth century: "Although he cultivated all kinds of embryonic tissues, he chose heart tissue to illustrate the possibility of endlessly renewed life, with its highly manifest lifelines – the rather uncanny ability to pulse, stop pulsing, and start again …" (p. 76).

Another argument regarding the heart's symbolic force is made by David Jones in his book exploring the "tangled history of cardiac care". Jones (2013) describes how, before the 1970s, major therapeutic uncertainty faced cardiologists; after this time, however, there began to emerge a "misery of choice" (p. 16) due to the development of a multitude of treatment options, and contradictory accounts regarding each intervention's efficacy. Jones further argues that one reason for the initial importance given to heart disease within public discourse was its association with executives and public people and, therefore with economic and political power – "almost a status symbol" – something that in the 1970s, "motivated unprecedented efforts to improve (…) diagnosis and treatment [in cardiology]" (p. 8).

Besides the heart's strong symbolism, and the dominant role it plays in public health campaigns, targeting the heart with stem cells also yields certainty because it can be listened to, visualized, and measured in concrete pictures, numbers and curves. It is, as Jones (2013, p. 3) writes, "one of the easiest organs to describe". The mechanistic models of what the heart does – the image of a pump is commonly used – was similarly utilized by researchers in our study when explaining how they measure the outcomes of their interventions: the ejection fraction.

> (…) we looked at (…) how much repair do people get after a heart attack. And it's pretty consistent that on average people improve their ejection fraction (…). So a normal ejection fraction is about 50–60 per cent, but after a heart attack it can be down to as low as 20 per cent. But on an average, after a heart attack the average person will improve their ejection fraction from 1 week to 6 months about 4 per cent. So, in our preliminary studies we saw about a 9 per cent improvement, this was not blind, this was just a cohort study.
>
> (Researcher A)

Nowbar *et al* (2014) question this certainty based on measuring outcomes. The authors call left ventricular ejection fraction a "mutable variable" that "in some modalities is easily manipulated innocently by clinicians who have prior beliefs on what a realistic value should be for a particular patient" (p. 5). Nevertheless, the certainty which has emerged from researchers being able to measure outcomes – a slightly higher ejection fraction in some studies was observed when compared with placebo – is the reason for continuing that research, even if it is not known exactly what caused the positive result: "So we are looking at the ejection fraction difference. At the end of this, if we show there's a difference, I don't think we will be

able to say that it's due to regeneration; there are lots of other mechanisms out there" (Researcher A; see note 6).

The logic of simplicity

In the media (but also on other sites targeting the general public), autologous bone marrow stem cells and their therapeutic applications are generally portrayed as safe, and the procedure is described as simple, logical and effective (see, for instance "How stem cells can fix a broken heart – with just one jab: 15-minute procedure could transform lives of patients with heart failure"; Dobson and Keoch, 2015). In their role as knowledge translators, stem cell researchers employ a similar logic of simplicity. The Canadian Stem Cell Network, for example, on their Webpage for patients with heart disease, explains:

> Researchers then isolated the particular stem cells that influence blood vessel and heart growth (…) and – *in a process that took about 10minutes* – injected the cells into the damaged areas of their hearts during heart bypass surgery. After six months, all the patients who had the stem cell procedure were able to pump more blood than the 10 patients who had bypass surgery alone. None of the patients experienced any serious in generals side effects or complications.
>
> (Stem Cell Network, 2009; emphasis added)

Like Researcher B above (we're going to take it out, and put it back into you), the other interviewees also referred to the simplicity of the procedure, especially when discussing the recruitment of patients for clinical trials, and when explaining their research to the unknowledgeable anthropologist (Researcher A was an exception; he referred to some patients' distrust of clinical trials in general). Researcher C's research assistant, a neuropsychologist who recruited patients for the clinical trials, further elaborated on this point: "The difficulty is the inclusion criteria, not convincing the patient. There is no risk, it is quick, and they are part of a revolutionary new technology that repairs instead of … it may lead to getting back the life they had earlier, when the heart was still working normally – most patients are grateful".

Thus, the basic principles of stem cell research are easily communicated. Take as an example the touring science exhibition for children and teenagers conducted by the Canadian Stem Cell Network (SCN, 2014), in which the cells have superpowers and stem cell researchers are portrayed as superheroes "on a mission to the future". However, the simplification of the basic principle is not only a discursive tool for convincing audiences; it is also a fundamental platform for supporting the more complex issues in the field (see below).

Doubts and Uncertainties

> … the core issues in cardiac regeneration remain mysterious …
>
> (Garbern and Lee, 2013)

Temporalities

We began the previous section with the historical grounding of stem cell research, which provided an historical anchorage – certainty – for research and intervention in time, tradition,

and, at least partly, in a process of normalization. However, the injection of bone marrow stem cells into the heart after a cardiac attack has also been described as a "scientific rollercoaster", causing a lot of "excitement and confusion" (Wollert and Drexler, 2009, p. 205), because of the almost frightening velocity of its emergence and transformation. For instance, Researcher B described the development of the field as "very fast", and linked this to the simplicity of the procedure:

> If you look at the heart transplantation, that concept has taken about 25 years from basic research to clinical application.[4] But (…) for the cell therapy, it has moved so fast. This is because (…) *the concept is so simple*. (…) [W]e take the cells from your own body, and they grow in a very clean environment, and then we put them back into your heart. Nothing else is involved. (…) We published our first paper in 1996, and the first clinical study was done, it was finished in (…) 2001. And so it's only six years (…) it's very fast. And then, boom! All the clinical trials started – everything, everywhere.

Dinsmore and Dib (2008, p. 41) arrived at a similar conclusion. They write that "[t]here are currently multiple clinical studies (…) that were only just beginning to be tested in preclinical animal studies a few years earlier. This rapid transition from preclinical to clinical testing is striking and is not typical of the customary timeframe for the progress of a therapy from bench-to-bedside". There is a general belief that because of this "rollercoaster", the velocity of developments within the field of stem cell treatments, that researchers should slow down and consider returning to the fundamental questions – in other words, move from the bedside back to the bench: "I don't think we understand anything really. (…) We are in the embryonic stage of stem cell research", said Researcher A. In a similar vein, his colleague observed a general fatigue in relation to stem cell research, something he linked to the general hype that produced data too quickly and in insufficient depth:

> … the concept is tired, is tiring. It's spent – in the last few years this concept has been over-cooked, over, you know, stated. Now, when the people hear stem cell theory, they think "Oh no, this doesn't work". And, "it's an old concept, and nothing new" (…) by now, it's relatively difficult to get funding, because the field has been over-cooked for a long time.
>
> (Researcher C)

This statement reflects a conceptual 'burnout' (and personal exhaustion, it seems) – what philosophers Stiegler and Stengers describe as anxiety in science. Stiegler (1998) claimed that, arguably, technological innovation is always happening at a more frenetic pace to cultural evolution, in which any new technology is embedded. He perceived this temporal tension to be a possible source of a collective anxiety, but also as a semantic space in which hope and expectations are constructed. Stengers (2013) recently demanded that science slow down,

4 Gabern and Lee (2013, p. 689), differing slightly from Researcher B's description, write that when heart transplantation emerged in the 1960s, the "initial excitement (…) led to over 100 heart transplantations worldwide. (…) However, disappointing results soon followed, with only a quarter of patients surviving more than a few months". This initial hype, and the following 'slowing down' (heart transplants were only taken up again in the 1980s, when the principles of immunosuppression became more well-known), can be compared with the current history of cardiac stem cell trials, although the current hype has not resulted in any known higher mortality, as it did with heart transplantations.

suggesting that it should become what Bruno Latour has called a "matter of concern". The anxiety in science Stengers describes is the pressure of the "knowledge economy", which researchers frequently get caught up in (although they cannot reveal this publicly), and public anxiety is simultaneously fostered, based on the commensurate loss of trust in science. The anxiety we perceived in the researchers we interviewed seemed to be more related to the clash between initial promising results (especially when applied to animals) and the lack of results in humans, set within the context of the powerful pressure regarding academic success and leadership relating to labs, networks and even nations. The recent stories of fraud within the field, such as the scandal targeting the South Korean stem cell researcher Hwang Woo-suk in 2007 or, more recently, the surgeon Paolo Macchiarini (Fountain, 2015), are vivid signs of such ambitions.

The not so simple procedure and the uncertain cell

In contrast to the enthusiastic sentiments expressed at the beginning of the interviews – when we had asked more general questions about this specific research area and its basic principles – towards the end of our conversations, many of the scientists were talking about major doubts, sometimes questioning the whole field. For example, Researcher B explained to us that "I just came back from the American Heart Association. (…) Three or four years ago, everyone [was] working on (…) stem cells, but now (…) not many people are working [anymore] in this field. (…) Because, most people present negative results in the clinical trial or in the research data". The greatest disappointment and source of uncertainty for all interviewees was that stem cell treatments for cardiac diseases in humans did not work as researchers had expected: "I think that with a lot of the therapies that are being done right now (….) we need a better understanding of what is actually happening at the molecular level" (Researcher A). And researcher D told us that "the data from the trials are mixed. The best ones give a small improvement. (…) So, at this point anyway, no bad effects, which is good".

For all researchers, the most challenging questions that arose through the course of their studies were: what is actually happening to the heart when bone marrow cells are injected? And what is the mechanism providing this (limited) repair? "The problem is that we don't know. We don't know. Maybe it's all the answers together: maybe it's a little paracrine and maybe a little regeneration. Maybe a little bit of an angiogenic effect – we don't know, we don't know. Unfortunately we don't know, we don't know"[5] (Researcher C). With surprisingly similar wording, researcher B – who had previously discussed the simplicity of the

5 The three mentioned effects of stem cell interventions are (i) the paracrine effect: many authors now believe that observed effects of stem cell treatments are not because of a differentiation of implanted cells, but to the release of cytokines and growth factors (GFs) by transplanted cells, affecting the viability and recovery of the ischaemic host tissue (see Chimenti *et al*, 2010); (ii) angiogenesis: "Angiogenesis, the growth of new capillary blood vessels in the body, is an important natural process used for healing and reproduction. The body controls angiogenesis by producing a precise balance of growth and inhibitory factors in healthy tissues. (…) Abnormal blood vessel growth, either excessive or insufficient, is now recognized as a 'common denominator' underlying many deadly and debilitating conditions, including cancer, skin diseases, age-related blindness, diabetic ulcers, cardiovascular disease, stroke and many others" (The Angiogenesis Foundation, n.d.); and (iii) regeneration: "Regeneration means the regrowth of a damaged or missing organ part from the remaining tissue. As adults, humans can regenerate some organs, such as the liver (…) and the skin. Unfortunately many other human tissues don't regenerate, and a goal in regenerative medicine is to find ways to kick-start tissue regeneration in the body, or to engineer replacement tissues" (EuroStemCell, 2011).

procedure – told us: "If I knew [what stem cells exactly do in the heart], I would have finished that already. So, we don't know. We don't know. We don't know".

In fact, a first wave of trials in cardiac stem cell interventions, undertaken between 2002 and 2009, yielded mixed results: while some trials reported significant improvements in the patients' heart function, other trials did not bring to light any differences between the stem cell and the placebo groups. Focussing on the promising results from the first wave, in the second wave research procedures were refined and protocols were more standardized among the labs, but still achieved only modest results. All interviewees referred to this lack of success; however, they still found a source of optimism for future research when considering the safety of the intervention. With only a few exceptions, all clinical trials showed no side effects from the procedure; consequently, all interviewees considered 'safety' to be the only certain outcome of the studies, as well as representing a secure platform upon which to further advance the field. With a pedagogical undertone, Researcher C asked the interviewer: "Do you know the most important objective of this study?" He wrote in big letters on a piece of paper in front of him: 'SAFETY'. "After this is shown, it is only a matter of time until we better understand [what is going on]".

In this regard, a recent meta-analysis of stem cell trials for cardiac repair by Nowbar *et al* (2014) explains at least in part why these results were mixed, by referencing their methodological shortcomings. The authors found that, with the exception of 5 (out of the 49) trials, all others showed a number of conceptual errors; and further, the trials that had the most positive results were also those with the highest number of discrepancies. And, while their analysis confirmed and explained, at least partly, the multitude of existing doubts surrounding the mixed trial results, Nowbar *et al*'s study also raised a second concern that was not known either to us nor to our interviewees at the time of our 2011 interviews, it seems: the fact that the safety of the trials was proven and, therefore, taken for granted. Nowbar *et al* concluded that "[t]he safety of bone marrow stem cell therapy is underlined by a large report focusing on this. Unfortunately it too contains many discrepancies, including impossible percentages and conflicts between tables and figures, perhaps because the reassuring findings had to be made available *with urgency*" (pp. 4–5; emphasis added). This statement, which again identifies 'historical velocity' as one culprit in the currently existing uncertainties, may also functionally destroy the most important basic certainty we found expressed by the interviewees: that of patient safety.

What did emerge from our interviews (and the literature) is that stem cell interventions for heart disease are still in need of better standardization procedures for research protocols – a point all interviewees mentioned – but also that there exist deep doubts regarding the type of cell; the number of cells that need to be injected; at what point in time they should be injected and through what kind of procedure; where exactly they should be injected in the heart; what the active element of the injected cells should be; and how to make sure the cells do not migrate and stay alive *in situ*. Researcher A, like the other interviewees, articulated this general set of doubts by saying:

> So they [a research group in Europe] harvested bone marrow from the patients post infarct, differentiated the cells, purified the cells and then delivered them back. And they showed a pretty significant improvement in ejection fraction after a heart attack (…) and they actually showed a difference in clinical events after two years. (…) But in the

same journal there was another group in Europe (…) that actually did the same thing and they showed no benefit. (…) But there were differences in the numbers of cells, how they treated the cells, and so I think that (…) this highlights the infancy of this therapy. (…) And I think that's probably why we're doing this other study, because no one knows what are the cells that are the most important ones. No one really knows how do the cells work, no one knows how many cells do we need, how do we handle the cells, in which point to inject it when is the body receptive to it, I mean there's animal models that suggest that really it's 7 days. (…) One of the difficulties is that 'stem cells' is a very all-inclusive term for lots of different kinds of cells, and I think we don't understand, I don't think any of us understands really which are the most important cells and if we're going to devise a therapy, which cells should we be using.

Nevertheless, when talking about uncertainties, in most cases the researchers linked their doubts to a reasoning that illustrated why they continued to do research in this field. These were 'if only-arguments' in which the interviewees expressed their hopes regarding the advancement of the field in general, a better understanding of biological facts, and the development of more advanced technologies (especially better visualizing or measuring technologies).

If only: The making of certainty

Several mechanisms can be found in the interviews that allowed the interviewees to ultimately transform uncertain elements back onto a platform of certainty and so legitimize continuing to do this kind of research. As noted above, we want to call these mechanisms 'if only arguments', since the majority of them rely on future developments, which concretely impact on current logics of legitimization: (1) The development of more refined and advanced technologies; (2) The development of more advanced insights into biological facts; (3) The substitution of uncertain details by an overall (meta) argument of safety; (4) The recognition of uncertainty as an inherent part of science; (5) The embracing of multi-disciplinarity as an accumulation of different kinds of knowledge; and a (6) A better standardization of procedures.

(1) An important way of dealing with uncertainty is the hope that future technical developments will provide the missing information (in general terms, a *better* standardization, *better* knowledge and so on) (Leibing, 2009b). This kind of reasoning 'imports' the future into the present by legitimizing present action. This point became especially salient when listening to Researcher C, who is doing research with mice and humans and who, at the same time, is a passionate heart surgeon. His argument, which centres on why negative results should be read in a more positive light, emphasizes the aspect of visuality (cf. Dumit, 2004; Franklin, 2013) in line with the bio-geography of cardiac repair:

If one injects the cells, one cannot do it everywhere. One injects them only in a very small territory. The ejection fraction might not change a lot. But if you look at the local ejection, that one gets better. (…) One has to get the global picture. [He draws a heart on a paper]. If one injects into this territory one will see a local or regional improvement, so the heart gets better globally. Many studies just confirm results by using only an echocardiography. That's not good, because if you have an infarctus here, that territory there can recompensate by working a little harder. So it can be that after the intervention

> the ejection fraction is more or less the same. But you have to do it well: you have to look into *this* territory, there where we did the injection. With our echocardiography stemming from nuclear medicine we can even see the finest differences in the inside of the tissues. That's what is different from the others. We see the heart in 3D. It can be that *globally* the heart does not get much better, but *regionally*, the heart is much better.

"You know what that is"? Researcher C continued, pointing at little black dots under glass beside him on the desk. "No? These are mouse hearts. Because in the lab [where] I am working, one can kill the mice – but, of course, we can't do that with humans. If we could look into human tissue as we can do it with animals, one would find the differences [of local effect when compared to placebo]".

(2) A second point is a better understanding of the biology of stem cells. Researcher A, for instance, stated that, "… the more research is done [the more] we're seeing our limitations (…) we need to understand the biology of stem cells better". Researcher B referred to a similar point: the difficulty of translating positive results from animals into humans. His major concern is the aging organism – for older cardiac patients, the naturally occurring stem cells are already diminished, and the patients tend to be living with multiple pathologies, as well as having aging cells and aging tissues:

> When we did the pre-clinical study, we used animals. Those are the young, healthy animals. But, when you take this to the clinical complications, if you can see the patients – they are sixty years old, seventy years old, and eighty years old. (…) So, basically, the (…) young cells have a greater capacity to differentiate into muscle cells. Therefore, they have a greater capacity to repair the heart. (…) The aging patient has less stem cells, and their cells are not working well.

Researcher B is nevertheless hopeful. He argued that "… some people have said the field should be closed. But (…) I personally believe [that there is] great hope for the rejuvenation. So now, we know what the problem is. And we just want to find the way to overcome that". Researcher B is currently working on mechanisms for the rejuvenation of already aged cells, since the application of younger donor cells would again introduce immunological and ethical issues. For him, current trials need to provide, first of all, a better understanding of this basic biological mechanism.

(3) There are principally three 'meta arguments', which together form a relatively solid platform of certainty. Using them requires relying on partial results that then predominate by subordinating and overshadowing doubts and uncertainties: The general notion that these trials are safe and do no harm to patients; the fact that some studies have been able to show a difference in the ejection fraction; and the sense of safety stemming from the support of the Canadian Stem Cell Network and Health Canada, which demand strict ethical procedures. Likewise, Leigh Star (1985, p. 412) suggests that in such a process of subordination "higher-level uncertainties become transformed into lower-level ones". Researcher C above, who argued that safety is the major objective of his study (after before explaining that it was a higher ejection fraction), is now able to subsume a possible lack of results under this meta-argument. For the patient, however, safety is part of the package and a major argument, but the objective that is explained to him or her, and which is hoped for, is better cardiac function.

(4) Three of the four researchers considered their existing doubts to be a legitimate part of science. The argument is that all major innovation has happened either by coincidence or by trying without knowing and that future would show its rightness. As one put it: "did they know when they brought the cholesterol pills on the market? Did they know what they did [to people]"? (Researcher C).

(5) All interviewees referred to a specifically Canadian way of doing research, which is to rely on multidisciplinary collaborations. Because of insufficient funding, a strong sense of collaboration among researchers and clinicians is a significant source of hope for advancing the field, especially when compared with their American colleagues, who can rely on more generous financial resources. This collaborative work, not only joining different disciplines within one research project, but also linking different groups, is the unifying ethos and central value of the Canadian Stem Cell Network and its members. Very revealing, in this regard, is an interview with Michael May, the CEO of the recently formed CCRM (Canadian Centre for Commercialization of Regenerative Medicine) (Mack, 2015), a group that is the result of the current conservative politics of putting more weight on the commercial side of academic research. When the journalist asked the CEO why regenerative medicine has been left behind in terms of development, the interviewee answered: "The bottom line is that regenerative medicine is complicated. It's an expensive process (…) especially at the very early stages, where investors really have abandoned projects". The journalist then asked: "how do you get around, or solve, this problem of doing more with less"? The answer: "I think it can be solved through *collaborative vehicles*. CCRM started with an academic network that was building collaboration and getting access to IP. (…) The system was primed with a very modest amount of money, but now we want to fuel our model with risk capital" (emphasis added).

(6) The need for more standardization was mentioned by all researchers as a possible antidote to disappointing results in cardiac repair (for example, "… but in the same journal there was another group in Europe (…) that actually did the same thing and they showed no benefit"). However, it was not a major point in the discussions, probably because the second wave of current clinical trials is already the result of a relatively long-lasting national and international cooperation among labs, implemented in order to create procedures and outcomes that can be compared.

Conclusion: Lost in Translation

> *L'avenir est la façon nous réagissons à ce qu'arrive, c'est la façon nous transformons un mouvement, un doute dans la vérité.*
>
> (Michel Foucault, 1994, p. 434)

This article is about the discursive struggles and coexistent arguments and claims of stem cell researchers within the specific field of stem cell cardiac repair. In their accounts, uncertainty and certainty are not necessarily opposed, but rather are negotiated and enacted simultaneously. The concept of multiverse has been introduced to express how three complementary ways of thinking about simultaneous but sometimes contradictory arguments can exist within the same scientific realm: (i) The (psychological) capacity of individuals to simultaneously accept and live under different value systems, without necessarily judging this capacity at first

sight (for example, as fraud or manipulation); (ii) The existence of different and co-existent temporalities in science – both in terms of older ideas and as future-oriented expectations and hopes – all of which can be integrated into practices of the present; and (iii) The existence of different, sometimes contradictory, 'epistemic cultures' (Knorr-Cetina, 2006) within one field, and even within one scientist, as well as the *prise en charge* of practices containing uncertainty by different institutions, including regulatory agencies, governments, groups of people and ethics committees, among others.

While at the beginning of the interview the researcher seemed to be more conscious of talking to someone outside of the field, towards the end, when turning to more specific questions, the act of knowledge translation became less evident, therefore allowing for more doubtful observations, paralleling the complexity of the field. The certainties were generally linked to the broad mechanisms of stem cell interventions, which are relatively easily translated and can be especially effectively used when talking to those who are unknowledgeable as well as to funding agencies; while issues related to uncertainty addressed the complexity of regeneration, and generally engage a more specialized audience (see Wainwright *et al*, 2006). However, while all four interviews could be described as containing elements of 'multiverse', the interviewees' overall attitude towards the field was not the same. A and B were more apprehensive than the other two. When interviewing B, his initial negative view of the field (the concept is tiring) suddenly changed when we asked him about his colleagues and their more positive evaluation of the field. B immediately switched his position and claimed that he also held a positive view. Both interviewers in their field journal commented afterwards that they had the impression that B became aware at this moment that his opinions could be published, and that this might impact his funding situation. A, however, doubted the principle of regeneration, thinking that stem cells in humans would "just enhance repair". However, in his opinion, some studies were able to show a significant improvement in the ejection fraction, and that the principle could be shown "were the patients ten years old and had a heart attack". Researcher B always came back to the lack of existing knowledge and the bad funding situation in Canada.

While C is a clinician, as well as a researcher, his certainty seemed to be primarily based on the promissory outcomes of former studies (even if the outcomes were often rather meagre), as well as the desire to help his patients. Several parts of the interview were illustrative of him being on a 'mission'. D, however, who is a basic scientist and not a clinician, was as optimistic as C. While C became 'uncertain' when he went into the details of his research, D acknowledged that there were still many unknown issues, but was very confident that they were close to being resolved. Her certainty was not primarily linked to patients' needs, but on the success she saw in neighbouring fields: "You see, this morning my colleague X was in the newspaper. His research with corneas works".

The sometimes contradictory ways of evaluating the field of stem cell cardiac repair made by the interviewees are not necessarily antagonistic; rather, they can be 'coexistent' realities (Mol and Berg, 1994; Keating and Cambrosio, 2003; see also Mol, 2003) or, as Marilyn Strathern (2004, p. xxiv) once articulated, "certainty itself appears partial". The researchers' 'if only arguments' related their doubts at any given moment to what needs to be known, wearing away and transforming uncertainty through more dominant arguments of certainty and, by doing so, justifying the rightness of more research.

Finally, it seems that the interview also had a transformative aspect, one of conscientization. Researcher C, for instance, at the end of our conversation (having started the interview with an abundance of enthusiasm) admitted that stem cell interventions "might be less expensive in the future, but it's not an alternative to a pacemaker. They're just giving a little extra … Just a little extra".

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