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Stem Cells:
Stories of a Hot Situation

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Stem Cells: Stories of a Hot Situation

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Introduction

In his influential essay on markets, *An essay on framing and overflowing* (1998), Michel Callon writes that "the growing complexity of industrialized societies [is] due in large part to the movements of the technosciences, which are causing connections and interdependencies to proliferate". This paper is about technoscience, and about the proliferation of connections and interdependencies created by it.

More specifically, the paper is about stem cells. Biotechnology in general has the power to capture the imagination. Within the field of biotechnology nothing seems more provocative and tantalizing than stem cells, in research, in medicine, or as products.

Already, I have hinted at one cause of the stem cells´ powers of fascination: the fact that it is equally research-subject, product, therapeutic medicine, but also myth (stem cell), and much else. The stem cell is a tiny object with the capacity to link many networks that was previously unlinked - a tiny object able to take on many shapes.

In the vocabulary of Michel Callon, whom I quoted above, the point is that the framing of a market (or any other `field´/`sphere´, I would argue) is costly and rare, and that overflows are the norm rather than the exception. Callon´s analytic vocabulary is simple and effective, and allows you to rapidly make meaningful points about very complex phenomena. The terms picked up from Callon´s text that are most central here text, are the following.

Framing/overflowing:

When creating a market, actors try to `frame´ it, thus making it context-free, and shielded from the outside world. However, writes Callon, frames will always leak, or overflow. The very idea of the frame relies on the context, from which it tries to free itself. If the inside of a frame was really cut off from the context the inside would loose all legitimacy and efficiency. Scientific language would become meaningless, standardized equipment would disappear, etc. Overflows are the rule, rather than the exception.

Hot/Cold Situations:

As mentioned, overflows are the rule in all framing-processes. But overflows can have different meanings. Callon makes a distinction between `cold´ and `hot´ situations, which indicates situations characterized by different types of overflows.

In cold situations there is wide-spread agreement about overflows: "Actors are identified, interests are stabilized, preferences can be expressed, responsibilities are acknowledged and accepted." (1998: 261)

In hot situations, on the other hand, "… everything becomes controversial; the identification of intermediaries and overflows, the distribution of source and target agents, the way effects are measured. These controversies, which indicate the absence of a stabilized knowledge base, usually involve a wide variety of actors. The actual list of actors, as well as their identities, will fluctuate in the course of the controversy itself and they will put forward mutually incompatible descriptions of future world states" (Callon, 1998: side 260).

Callon argues that the technosciences has made our society increasingly hot, and made the hot situations increasingly difficult to cool down – "i.e. arrive at a consensus on how the situation should be described and how it is likely to develop.".

The case of stem cells seems to be exceptionally `hot´, so hot that an all-encompassing description is impossible – and not only for pragmatic reasons. The situation moves so fast, that such a description would always be outdated. Instead, I have chosen to tell stories and anecdotes of "the proliferation of connections and interdependencies". In other words, this paper tries to offer some

angles on the hot situation, looking to specify different types of framing, overflows, agents and interests. The stories will be mainly Danish, but as Callon rightly notices, in hot situations "the local and the global are in constant interactions" (262), and therefore my framing the scene as strictly national would be futile.

1. Story:

Classifications and practices: How legal became illegal and existent became non-existent

Stem cells are classified in (at least) three different ways, the three systems together constituting a complex 3-dimensional matrix:

First, there are the three developmental stages of the cell that are becoming increasingly known to the public: the embryonic stem cell, the naval-cord stem cell, and the adult stem cell.

It is legal to do research on stem cells from up to 2 week-old embryos. After that the practice becomes illegal, which makes the embryonic stem cell non-existent (as a research subject) after the 2 first weeks. The stem cell re-emerges approximately 8½ months later as a naval-cord stem cell. The naval-cord stem cell exists for fifteen minutes after the birth of a child. After that the blood coagulates, and the stem cells are no more. The stem cell next reappears as an adult stem cell, found in the bodies of adults and children, for instance in blood marrow, producing new blood cells.

In a research-specific frame, the stem cell exists only very briefly in its potent early stages. The first gestalt, the embryonic stem cell, is taken out of existence by law, whereas the second gestalt, the naval-cord stem cell, is eclipsed by the blood's immanent characteristics (coagulation). The brevity of the early stem cells´ existence makes the harvesting of them a central crux. This will become obvious in the stories to come.

Second, there is a differentiation made on the basis of the specificity of the stem cell. The differentiation is made between totopotent stem cells, pluripotent stem cells and multipotent stem cells.

Totopotent stem cells can become any human cell, which means that these are the earliest cells of the embryo. Some argue that it is in fact only the fertil-

ized egg that can rightfully be referred to as totopotent. Pluripotent stem cells can become different cells in different types of tissues, while multipotent stem cells can become different cells of the same tissues.

This classification is in some ways coincident with the classification above, but it has central differences as well: The classification of toto-, pluri- and multipotent stem cells is not intrinsically connected to the development the `host-organism´. For instance, experiments are being made, trying to have multipotent stem cells (for instance from adults) develop `backwards´ and become pluripotent stem cells.

Third, is a developmental differentiation – not an organism-specific development, as was the case above, but a cell-specific development. This is a differentiation between stem cells, progenitors and precursors. Progenitors and precursors are not considered stem cells, but immature cells that are maturing into one specific cell type.

The distinction between stem cells and the different types of immature cells is relatively new. This makes the differentiation between stem cells, progenitors and precursors a historical as well as a developmental one:

The term "stem cell", and the differentiation between stem cells, progenitors and precursors, has been around for a long time in some parts of the scientific community, for instance within haematology, but is rather new in others. In neurobiology in the 90s, for instance, scientists worked with foetal tissues that contained all the different types of immature cells – stem cells, progenitors and precursors. But it was presumed that the tissues mainly contained precursors. It was not until later that it was discovered that these tissues did in fact contain actual stem cells.

Until then, the work of transplanting foetal tissues was described using the term `precursor cells´, not `stem cells´. It was not until the simultaneous discovery of the presence of stem cells, and the increasing use of the term stem cells in the public, that the use of foetal tissues were made into a problem. Until then, says a researcher in the biotech-industry, quoted from memory: "it was relatively unproblematic to get permission to perform this kind of research, using tissues from aborted foetuses. These foetuses were typically more than 6 weeks

old. Now, it is heavily disputed whether we can use fertilized eggs for research".

When the term `stem cell´ connected the last and the first classification system described here, it also meant that the research practice described by the researcher above became connected to a political practice – i.e. the prohibition against using stem cells from embryos more than 2 weeks old. The cells from older foetuses that had been used for research suddenly disappeared. This disappearing act also meant that working with stem cells from 6 – 10 week old aborted foetuses went from being ordinary practice to being illegal.

2. Story:

Embryos: How childlessness is connected to stem cell research

Embryonic stem cells for research comes from one single source; surplus fertilized eggs from IVF clinics. The connection between these two seemingly separate frames are created in the following way;

Since September 1st, 2003, it has been legal to do research on embryonic stem cells. The research takes place using eggs that are up to 2 weeks old. Accordingly, researchers need human eggs. This is not an item you come by easily. Not only are they embedded deeply in the female body, they are also entities that are surrounded by parental love, both individual and generalized. The eggs can only be legally acquired from surplus fertilized eggs from IVF treatments. Also, nations with strict regulations (such as Denmark) import stem cell lines from other nations with less strict regulations (such as Sweden).

IVF treatment is becoming more and more common. Experts estimate that between 10 and 15 percent of Danish couples are infertile, and approximately one child in 20 are the result of IVF treatments. (Weekendavisen 23. juli, 2004)

In IVF treatments we witness the rare situation of human eggs being taken out of the female body. In a petri-dish, several of them become fertilized. However, there are health risks for mothers as well as children connected multiple preg-

nancies, and therefore a maximum of two eggs are placed in the womb of the mother. In the petri-dish 4 – 5 eggs are left. What to do with them? Throw them away? Give them to another infertile woman (illegal in many countries, Denmark one of them)? Or how about donating them to science?

On August 27th 2004, Nature published the results made by a group of researchers at the Center for BioEthics at the University of Pennsylvania. They had been addressing this exact question: what happens to the surplus eggs? The group had only studied American surplus eggs, but the answers are interesting nevertheless: 16% of the clinics did not get rid off the eggs in any way. They stored them in freezers indefinitely. Another 3% of the clinics avoided making surplus eggs at all. The rest of the clinics – the majority - did a variety of things: some gave the parents the eggs to take home, some burn them as biological waste, some had funerals for the eggs, with or without the attendance of the parents. But the majority of the clinics donated the eggs to research, with the consent of the parents.

And these, of course, are the eggs we are interested in; they form the fragile but powerful link between the IVF clinics and stem cell research that determines the future of stem cell research. How is that?

One example, which came close to ending stem cell research in Denmark completely, is the following: In the beginning of 2004, Danish Minister of Health, Lars Løkke Rasmussen, made a bill proposing to allow surplus IVF-eggs to be kept in storage for 5 years. Until then, Danish surplus eggs had only been allowed to be kept for 2 years. That meant that if parents wanted a second child using the first `batch´ of eggs, thus sparing the woman the hardships of hormone treatments, they would have to decide when the first child was just 1 year old. Hence the amount of surplus eggs was relatively large. However, if parents were allowed to wait 5 years until deciding whether to have a second child, many more would use that opportunity. Changing the law in this way would in effect stop stem cell research in Denmark, or have all Danish stem cell research

be based on eggs imported from abroad. Incidentally, this part of the bill was not passed.

This story's overall point has been how two frames – IVF treatment and stem cell research - is connected through the rare entity of the human fertilized egg found outside a human body. This connection also allows a range of ethical and moral issues tightly associated to the embryos to overflow the IVF frame and literally flood the would be frame of stem cell research.

3. Story

Children & Critical Disease: How stem cells and ethical dilemmas confronted Danish laws

When 10-year old Danish boy, Jason Valsted, was diagnosed with the rare hereditary blood disease fanconi anaemia, there was little hope of treatment. All international donor databases were searched to find a bone-marrow donor that fitted Jason, but none was found.

Another possibility was transplanting naval-cord stem cells from a sibling to Jason's bone marrow. But having such a compatible sibling be born seemed as far away as finding a donor. Not any sibling would do. Jason already had two siblings, neither of whom had tissues compatible with Jason's. Therefore, the sibling had to be created using IVF techniques combined with selection of the fertilized eggs, a procedure illegal in Denmark, although legal in many other countries, for instance the UK and the USA. According to Danish law, it is illegal to sort eggs, except when looking for a few very rare diseases. Logically, it is also illegal to sort the eggs according to specific types of tissue, compatible to the tissues of an older, albeit dying, sibling. The point is that humans should not be made as spare parts for others. Thus, although it was in principal possible to make a donor for Jason, it seemed very likely that Jason was going to die of his disease.

However, the story attracted much attention in the media, and after heavy debate, the minister of health decided to dispense of the law, and give Jason's

parents permission to go to USA to start the treatment. However, the attempt to inseminate Jason's mother failed, and all hope of curing Jason was gone.

But in 2003 the impossible happened; A compatible donor, a 43 year old British man, was found for Jason, who had bone marrow transplanted on the 16th of June 2003.

After the story of Jason a few other media-stories concerning deadly sick children in need of donor siblings followed: 4-year old Savannah developed a hereditary bone-marrow disease. In the wake of the Jason-story the minister of health dispensed of laws and her parents were send to America, to start reproductive treatment.

The changes in the law made in connection to the cases of Jason and Savannah were for critical, hereditary diseases. Thus, a new problem arose when young Patrick became ill with a disease that was critical, albeit not hereditary – aplastic anaemia. In spring of 2004 yet a new law was accepted making it legal to conduct infertility treatment combined with selection of eggs in cases where the newborn would be a donor of older siblings suffering of critical illness.

This story is obviously about new and unexpected connections between diseases, medical research, IVF techniques, politics and individual families. But it also about IVF techniques making connections between time-frames that were earlier kept strictly apart: the present and the future. When looking for donors, one has to look in the national and international donor-databases of present donors. The cases of Jason, Savannah and Patrick shows how IVF-techniques and selection of eggs expand the possibilities to include future donors. The connection between the presently sick and the donors to be, create oppositions between entities that were never opposed or even connected before: suddenly one has to decide: Which is the greater ethical offence - sacrificing the dying to protect the unborn? Or sacrificing the rights of the unborn to save the dying? Are you on the side of the not yet living, or the not yet dead?

5. Story:

Biobanks: How to sell stem cell therapy before it exists

Bio banks are by no means a novel concept. We all know blood banks, for instance. But recently, overflows from the frame of bio banking has challenged the attempts of framing stem cell research. Or, rather, attempts have been made to frame stem cells as marketable products, while others try to keep stem cells `pure´ of mercenary interests.

All over the world companies have been offering to extract blood from the naval-cords of newborns and to store the blood into the future, hoping and expecting that medical research would make it possible to save the then newborns using stem cells from their naval-cord. In Denmark, naval-cord banking was introduced in 2000. Since then an increasing number of parents have bought the service, reaching 4% in 2004 (Jyllandsposten, August 5th, 2004).

The arguments to have blood from your child's naval-cord stored by a private bio bank are many. Here formulated by a young mother to Ekstra Bladet, on November 14th , 2004:

"Even if the researchers still cannot say anything conclusive about the chances of curing diseases, I was never in doubt that Hannibal's stem cells were to be drawn and frozen […] I would feel like a poor mother, if he were to get a serious disease as a grown up, and I had had the opportunity of securing his health now, 20 years earlier. But hadn't done it."

The arguments against the private biobanks are weighty too: A doctor from Rigshospitalet, specializing in stem cells, says in the same article:

"There is no doubt that the potential of stem cells is amazingly big. But the chances that you will need your own stem cells are minimal. Today we do not know whether stem cells from a sick patient carries the sick genes. There-

fore, it will make more sense to have a stem cell bank, which everyone deposits naval-cord blood in. Rather than the stem cells only following the one child, the blood will be usable by others with compatible tissue. That is already the way it works abroad."

Another newspaper has another doctor make a different argument against the private bloodbanks:

"The information given by Copygene [a private bio bank] is not correct. They say that it is a unique opportunity to draw stem cells, but the truth is that the amount of stem cells found in the naval-cord is only enough to treat a child of 1 or 2 years of age, and in that age you do not develop Parkinson's disease. So yes! It borders on confidence tricks." (Information, 15. September 2004.)

Interestingly, the doctors speaking on the subject in the media are unanimously against the private bio banks. They are arduously trying to cut the connection between their work with stem cells and the service sold by the bio banks. At the same time, what the bio banks are selling is the hope that the same doctors will come up with miraculous cures against diseases. And if this possibility is even remotely possible, what parent would say no? As indicated in the quote from the young mother; only a poor one.

Thus, the doctors try to keep the frames of medical research apart from the frame of bio banking-market, while the bio banks try to connect the two.

But the complications do not stop here: The bio banks' attempts to associate themselves with the frame of serious medical research only goes so far. The following is the story of how a bio bank actually claimed that what they were selling was <u>not</u> a health-service:

In the fall of 2004, the naval-cord banking company, Copygene, founded by controversial business man, Klaus Riskær Pedersen, started advertising for their services on TV. Much to the indignation of competing company, Stem Care. Stem Care had earlier approached Minister of Health, Lars Løkke Rasmussen,

allegedly to have a confirmation that such commercials were illegal due to the Danish prohibition against advertising for "health services":

> "We have no problem with Copygene. But we are afraid that the area will appear as frivolous and mercenary. It is the beginning of a slide where the horror-scenario are supermarket-commercials" (Politiken, September 3rd , 2004)

Copygene managed to convince the authorities that they were in fact not selling or advertising a "health service" thereby making the very insecurities connected to stem cell research an argument working in favour of them, rather than against them.

This story is an extreme version of the paradoxical connections between stem cell research and markets that is an important reason why the situation is as hot as it is:

First, we saw how doctors defended the stem cell frame from being associated with private bio banks, which are in essence selling the hope of positive results of the doctors' work. Without this hope, the doctor's work would be futile. Hence, the doctor's work hinges on the usability of their work – the promise of miraculous cures. This usability also means marketability. Hence, experimenting with stem cells can be said always to be also producing stem cells. Making a product that can be sold and bought. Thus, the pure frame of basic stem cell research sought created by the doctors essentially depend on that which they try to distance it from; the market.

Secondly, we saw – paradoxically – how one bio bank renounced the claim to a connection to the doctors – and thereby logically also renouncing the bio bank's market's connection to a product. At least the company Copygene earned the right to advertise for their services on TV by arguing that what they were selling was <u>not</u> a health service. This, of course, makes their enterprise absurd, and the other bio bank mentioned in the story, Stem Care, makes a different point. They renounce that the market they are trying to frame is mercenary, thereby trying to strengthen the connection to the doctors, and hence the prod-

uct. Thus, paradoxically, their framing of a market hinges on renouncing its market-like characteristics.

The End

Hot and Cold: How to end stem cell controversy

The above stories have, I hope, shown that the stem cell phenomena is a hot situation, par excellence. The vocabulary of framing and overflowing supplies a figure of understanding the chaotic movements of a forum as hybrid as this one.

The anecdotes amply shows that the field of stem cells, stem cell research, stem cell therapy and stem cell products is rich with examples of phenomena that are continuously shifting shapes, and networks in which relations are continuously made and unmade, intentions and actions that create curious and unexpected effects in networks that were thought to be outside the frame. We have seen a variety of agents trying to frame stem cells in a particular fashion. Interestingly these agents have not all been commercial ones, and the frames have not always been markets. Although Callon has formulated the concepts of framing and overflowing specifically regarding markets, it is obvious that the terms of framing and hot/cold situations are not specific to market-like phenomena. The general idea of framing can be used in much broader contexts.

Not only does the concept of the `frame´ seem more broadly applicable than indicated by Callon, the concept of `overflow´ seem also to work in more that one way. Callon writes that frames flow over spilling negative or positive effects onto the surrounding context. However, it seems from the stories told here, that not only do frames flow over, just as often contexts flow over into frames. Much of the work done by the actors in the stories seem to be as protecting the fragile frames they are trying to build from overflows from without. The frames seem as often to be flooded as to spill over.

Returning from the analytic vocabulary to the stem cell phenomena: At the outset of this paper, I stated that stem cells constitute a hot situation par excellence. So, do they?

Yes, at the moment they do. It seems that the extreme hotness is created by two types of connections build in to the stem cell. The one is the connection between markets and research, the other is the connection between medicine and embryos.

First, research in stem cells is always about therapy. The usability of the cell to cure terrible diseases is the reason of the focus on stem cells. The usability of the cells, and the fatality of the diseases in question makes the stem cell a potentially very pricy object. Thus, the idea of its future use, and thereby the profitability of the market created is intrinsic to stem cells as research objects. This connection allows frames around `research´ and `market´ to overflow and be flooded no end.

Second, the situation is made hot by a connection that not only opens frames, but tears them down completely: the link between stem cells and embryos. This link is made by political and research practices which makes embryos the all important source of stem cells for research. At the same time, the embryo is embedded in thick layers of flesh, myth, emotion, religion… Thus, the centrality of embryos for stem cell research means that issues that are `outside´ this would-be frame, is also always central to it.

The connections build into the hybrid object of the stem cell as research subject; markets, science, embryos and medicine makes framing it impossible. Framing the stem cell as part only of a market, of science, of medicine, etc. would take it apart. The hybrid nature is not only about how it is used, the hybrid is build into the stem cell itself. We are not only talking hybrid forums, but hybrid objects.

Of course, this does not mean that the stem cell situation will necessarily always be as hot as it is now. The situation can be made colder or hotter still, depending on the source of the stem cells. Let us consider, for instance, what happens if the link from stem cells to embryos is broken. In fact, we don't have to imagine – others have done that for us:

Many scientific voices have pointed to the possibility of having adult stem cells give rise to other types of cells outside of their origin. This would be a way

of "realizing medical gain without ethical pain" (Nature 2002). If adult stem cells could be made as potent as embryonic stem cells the connection between stem cells and embryos would be broken, and thereby the ethical, moral, and religious dilemmas would be disconnected allowing the situation to cool down considerably.

Another possibility to uncouple embryos from stem cells comes from the naval-cord. Not from blood but from the naval-cord itself. In the tissue of the naval-cord is a substance called Wharton's jelly. Wharton's jelly secures that the naval-cord does not collapse, stopping the supply of oxygen and nutrition to the foetus. In Wharton's jelly many simple stem cells have been found, stem cells that have potential of developing into e.g. brain tissue and nerval tissue. (http://www.innovations-report.de/html/berichte/biowissenschaften_chemie/bericht-15818.html) Researchers claim that it is a real possibility that the stem cells from Wharton's jelly could partly replace the stem cells obtained from embryos. (P1: Videnskabens verden. 2. oktober, 2004). This line of development would logically cool down the situation too.

Not all future scenarios shows the situation cooling down. There is yet (at least) one way of uncoupling the embryos from stem cell therapy: therapeutic cloning, which is legal for instance in the UK. This, however, leaves the situation hotter than ever.

When performing a cloning you empty an egg of hereditary material, and insert a cell into it. It then starts to divide. In the lab, researchers try to make the new cells grow into a specific type of cells – heart, kidney… In this way it is possible to make lines of stem cells that matches the tissues of the sick person exactly. You no longer depend on the relative compatibility of siblings made by selecting eggs.

Therapeutic cloning may be a way of securing stem cells for research and therapy, but as indicated it is by no means a way of cooling the situation down: The beginning of the process described above, the emptying of an egg and injection of a different human cell, is the same as in a different , and much more con-

troversial type of cloning: reproductive cloning. And the science fiction-like vision of actual human cloning makes this way of achieving the coveted stem cells as hot as using non-cloned embryos.

Concluding, the hotness of the stem cell situation is created by tiny technoscientific objects that are hybrid in their very base and created through connections between heterogeneous networks. The stem cell is intrinsically natural biology, and equally intrinsically technology. It is the hybrid objects and the immanent connectivity that makes the situation surrounding them almost inevitable hot.

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