From Core Set to Assemblage:
On the Dynamics of Exclusion and Inclusion in the Failure to Derive Beta Cells from Embryonic Stem Cells

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In this paper, we examine the controversy surrounding the Lumelsky protocol (which potentially could have transformed the procedures for differentiating embryonic stem cells into beta cells for diabetes treatment). The protocol is analyzed initially using Collins' core set model to show how the controversy over epistemic claims was resolved (and the Lumelsky protocol deemed to be a failure). This approach is then contrasted to an analysis in terms of scientific 'assemblages' characterized not by the resolution of epistemic controversy, but by the 'irresolution' or openness of social associations amongst scientists. We suggest that scientists who jumped on the 'Lumelsky bandwagon' can be rehabilitated, partly because of the recognized chronic uncertainty in the stem cell field. Thus, alongside the judgement, resolution and exclusion mapped by core set analysis, there is 'understanding', irresolution and inclusion suggested by 'assemblage analysis'.

Key words: core set, assemblage, stem cells

This paper provides an analysis of the dynamics of a dispersed scientific 'assemblage' concerned with the differentiation of embryonic stem cells into insulin-producing beta cells.[1] Specifically, we present a preliminary examination of the resolution of the controversy surrounding the Lumelsky protocol – a protocol which, it was claimed, could convert embryonic stem cells into beta cells. Announcements about the Lumelsky protocol had an enormous impact, because it seemed to point to a way of producing a potentially inexhaustible supply of beta cells for the treatment, and ultimately the cure, for Type I diabetes. As we shall see, the epistemic resolution of this controversy was that the Lumelsky protocol was generally deemed to be a failure. However, paralleling this process of epistemic resolution, we argue, was an ongoing process of 'irresolution', where social possibilities and potentials were, by and large, kept open. We de-

scribe the former process of epistemic 'resolution' through Collins' (1985) classic terminology of core set and experimenters' regress, in which after resolution, scientific factions become excluded from the core set. By contrast, the process of 'irresolution' connotes a sort of diffuse inclusion which allows for the possibility of future connection between the 'outsiders' and 'insiders' of the core set. In elaborating this argument, we draw upon Wynne's (2003) critique of Collins' 'propositional' core set model by way of the emergent sociology of expectations (Brown and Michael, 2003).

Stem cell research is an excellent example of the uncertainty that characterizes controversial science (Collins and Pinch, 1998). In what follows we demonstrate this by applying Collins' related notions of the experimenters' regress and the core set in a case study of contested science. Collins' strategy, and ours, is to use quotations, gleaned from documents and interviews, with scientists involved in controversy in order to demonstrate that experimental data in themselves do not wholly determine when an experiment counts for or against a particular scientific hypothesis or theory. For example, if findings from an experiment are not replicated in another lab, the original group will often argue that this is because their procedures were not properly followed:

> In controversies, it is invariably the case that scientists disagree not only about results, but also about the quality of each other's work. This is what stops experiments being decisive and gives rise to the [experimenters'] regress. (Collins and Pinch, 1998: 3)

The experimenters' regress is the product of judgements on the competence of scientists, the equipment used, the meaning of the experiment and so on. All of these may be contested and the regress can only be broken through negotiations within a relatively small core set of researchers. This core set is expert and active in generating and resolving scientific controversies within their field of science, through social consensus. Collins' most famous example of these social practices is his 30 year study of the controversy of gravity waves amongst a core set of physicists (Collins, 1975; 1985; 2004), where the relevant arguments included "a morass of judgements on personal honesty, technical competence, institutional associations, style of presentation and nationality" (Lynch, 1993: 88). Following Collins, one of our key aims is:

> To study those moments when what seems strange and new is being turned into what seems ordinary. Turning the strange into the taken-for-granted is what science does in its laboratories, its conferences, its publications, and its publicity. A sociological understanding of science, then, means mastering science after the fashion of a scientist, but it also means being able to step back far enough from that world to enable new 'forms of life' to be topics as well as accomplishments. (Collins, 2004: 747)

Now, in expanding on the notion of the core set into more 'public science' arenas, Collins (Collins and Evans, 2002) has attempted to demarcate the ways technical or contributory expertise might be differentiated from other forms of expertise (e.g. interactional). However, Wynne (2003) has argued that this account rests on the privileging of propositional truth (for example about the impacts of a particular innovation such

as nanotechnology) to the exclusion of the analysis of the political and cultural assumptions embedded in such propositional knowledge claims. In other words, for 'public science', the technicalities of knowledge claims embody assumptions about the ways questions are framed and thus the way knowledges are valorized, not least those of lay constituencies whose frameworks of knowledge might be radically different (see Leach et al., 2005).[2]

In the present case, we take a cue from Wynne's critique to examine how the resolution of a particular controversy within stem cell science—specifically, the establishment of a consensus around the failure of the Lumelsky protocol for the differentiation of embryonic stem cells into beta cells—entails both propositional knowledge claims and more diffuse social 'stakes' within the scientific 'assemblage'. In particular, we will argue, the discrediting of the protocol marks not only the breaking of the experimenters' regress and the triumph of a given faction within the core set, it also reflects and mediates continuing research associations into the future. In other words, and this is central to this paper, the *exclusion* of the now discredited faction of the core set accomplished through the *epistemic closure* of the controversy is paralleled by leaving *socially open* the possibility of future *inclusion* of that faction – inclusion in the form of associations that can range from formal collaborations through to continued informal dialogue.

On this score, we draw upon recent work within STS on the role of expectations in structuring technoscientific endeavour (Van Lente, 1993; Brown et al., 2000; Brown and Michael, 2003). However, we depart from this literature by paying attention less to explicit future scenarios than to the way scientists' accounts presuppose inexplicit, vague or open futures occupied by social possibilities (for example, collaboration or dialogue).[3] As we shall show, in the present case, the exclusion wrought by discrediting others rests partly on accusations of their 'jumping on the bandwagon'; yet this is counterposed to the 'understandability' of such bandwagoning because of the nature of the field. In a context of high and chronic uncertainty, bandwagoning is socially understandable and thus 'forgivable': it is this that allows for the possibility of subsequent re-inclusion.

In what follows we will provide a brief background to the science, followed by an account of the controversy over the Lumelsky protocol and its eventual, generally accepted, failure. In keeping with Collins' analytic, we note that this failure partly rested on establishing experimental criteria that were credibly attainable only by particular scientists (beta cell specialists). However, if in the process the experimenters' regress is broken, and the core set reconfigured, those who 'jumped onto the Lumelsky bandwagon' can have their credibility endangered. These 'others' are still however, part of the scientific assemblage that is studying the differentiation of stem cells. We propose that what enables their continued credibility is the way in which the scientific field is generally characterized – a characterization that takes note of high chronic uncertainty. This uncertainty makes understandable their bandwagoning. We illustrate this chronic uncertainty with numerous accounts of the routine problems that beset the experimental differentiation of stem cells into beta cells. In concluding, we summarize our assemblage perspective on the stem cell field, and draw out some further differences between core set analysis and analysis in terms

of assemblages with a view to developing future research avenues.

Scientific background

Arguably, stem cells have huge potential in the fields of tissue engineering and regenerative medicine as, in principle, they hold the capacity to produce every type of cell and tissue in the body (Lanza et al., 2004a; 2004b). They promise a medical revolution in the treatment of cardiovascular disease, neurodegenerative diseases such as Alzheimer's and Parkinson's, cancer, diabetes, and the possibility of the replacement of organ transplants with stem cell transplants. In 1998 a seminal paper described the *in vitro* growth of human embryonic stem (hES) cells derived from the inner cell mass of the early blastocyst (Thompson et al., 1998). Stem cell biology has evolved over the last seven years and it is currently one of the most rapidly developing areas within the life sciences (Blau et al., 2001; Kiessling and Anderson, 2003; Rippon and Bishop, 2004). The two defining features of stem cells are that they can reproduce themselves, and so in principle a few cells can produce large numbers of daughter cells, and they can differentiate into many different cell types. Bone marrow transplants for leukaemia are the best known clinical example of (blood) stem cells ability to repopulate a complex environment with a huge number of cells with different functions (Gearhart, 2005). The hope is that one day it may be possible to do something similar for other acute and chronic diseases, such as diabetes, by using one or more of adult, foetal and particularly embryonic stem cells in what could become a revolutionary new era of regenerative medicine (Lanza et al., 2004a; 2004b).

Diabetes mellitus has been identified as "one of the main threats to human health in the 21st century" (Zimmet et al., 2001: 782). In the UK 2 % of the population have diabetes and treatment accounts for 10% of the total healthcare budget (Wass and Shalet, 2002). The main therapy for insulin-dependent (Type-1) diabetes is insulin replacement. Essentially, Type-1 diabetes involves autoimmune destruction of the insulin producing beta cells which, until the discovery of insulin and the subsequent development of insulin therapies, resulted in death from uncontrollably high levels of blood glucose (Bliss, 1984). The beta cells are the main cell type within the more complex islets of langerhans cells which make up the endocrine part of the pancreas. Within these islets other cells produce other hormones, for instance alpha cells produce glucagon, and delta cells secrete somatostatin. It is extremely difficult to separate the beta cells from the rest of the islets, and there is strong evidence that the spatial arrangement of beta cells within an islet results in a coordinated and more effective secretion of insulin (Gray, 2002).

Recently, significant advances in the transplantation of human islets into patients with Type-1 diabetes have largely removed the insulin dependency of these patients (Shapiro et al., 2000; Ryan et al., 2005). Shapiro's pioneering work in this area, particularly his 'Edmonton protocol' for islet transplantation, has led to a significant global interest in islet cell transplantation. His centre in Alberta has recently been awarded $25 million dollars to develop their islet transplant programme, with the largest ever grant given by the JDRF (Juvenile Diabetes Research Foundation). However, the application of this increasingly routine therapy is severely restricted by the very limited availability of human

islets. Currently human embryonic stem (hES) cells are thought to offer the most promising potential source of beta cells for islet transplantation (Itkin-Ansari and Levine, 2004; Rother and Harlan, 2004).

There has been considerable recent enthusiasm about the potential of hES cells to provide material for the islet transplant therapy of diabetes, but so far this has translated into little peer reviewed, published information (Jones et al., 2004). This is largely because scientists have found it very difficult to reliably drive differentiation of hES cell populations towards an endocrine phenotype (Bonner-Weir and Weir, 2005). The key scientific question that beta cell biologists are currently asking is, "are hES cells likely to offer a useful starting material from which to generate *in vitro* mature, functional beta cells for islet transplantation?"

It is now established that mouse ES cells can differentiate into cells with an insulin-expressing phenotype, either by genetic manipulation or by permitting spontaneous differentiation followed by culture under selective conditions (Jones et al., 2004). It has, however, proved much more difficult for scientists to generate insulin-expressing cells from hES cells, although preliminary human embryonic data (Burns et al., 2004) and published reports (Assady et al., 2001; Segev et al., 2004) suggest that hES cells will spontaneously differentiate into an insulin-expressing phenotype, albeit at a low frequency. Experiments are therefore designed to discover whether the purported beta cells express the genes and proteins related to a beta cell genotype, and to assess the functional phenotype of insulin-expressing cells. In other words, do these bioengineered cells have the genetic makeup required to be beta cells, and if they do have the correct genes, are they producing the proteins needed for these cells to function as beta cells?

With this backdrop in place, we can now, after a brief overview of our methods, move on to the specificities of the controversy surrounding the emergence of the Lumelsky protocol.

Methodological note

The present paper draws on a broader study of translational research, that is, the interactions between 'the bench and the bedside', particularly the prospects and problems of stem cell therapies and cell transplantation in the fields of diabetes and liver disease. The corpus of data from which this present study draws is comprised of the main published documents in specialist and general scientific journals; ethnographic observation in labs and at scientific and medical conferences of 'stem cell science in action'; two ethics discussion groups with scientists and clinicians; and over 60 interviews with scientists, clinicians and key stakeholders in both the UK and the USA. However, over and above documentary evidence, here we primarily draw on interviews with seven biomedical scientists who work in one leading beta cell/stem cell laboratory in England (Scientists 1-7). That these scientists are seen to be part of the core set of beta cell scientists is evidenced not only in their extensive publications, but also by the fact that two members of the laboratory attend 'keystone meetings' of the world's top 100 beta cell scientists. We also draw on six other senior scientists, who, as directors of Beta Cell / Stem Cell Labs in the US and UK are key players on the field (Scientists 25 (US), 26 (US), 28 (US), 43 (UK), 45 (UK) and 49 (US)). To preserve anonymity we do not include the specific titles of scientists.

The interviews we conducted lasted between 1-2 hours, took place within the laboratory offices and with permission, were taped and transcribed. Open-ended questions and an informal interview schedule were used, in order to encourage scientists to speak in their own words about their experiences. Transcripts were analyzed by content for emergent themes (Weber, 1990), which were then coded (Strauss, 1987). The research team discussed the data and analysis which enabled different perspectives to be incorporated, and added to the richness of the analysis.

While the sample of actual interviews is small, the representativeness of the data is partly grounded in the other more informal observations that were made over the course of the research. [4] Having noted this point of triangulation, we necessarily do not make strong claims about the validity of the analysis, not only because of the small sample (which is a chronic feature of much qualitative work), but also because the interpretative tradition presupposes that analyses will be contingent and constitutionally open to revision (see Potter and Wetherell, 1987; Silverman, 1993).

The Lumelsky protocol controversy

The Lumelsky protocol: 'stem cells are coaxed to produce insulin'

The revolutionary Lumelsky protocol from Ron McKay's neural stem cell lab at the NIH (National Institutes of Health, USA) was published in *Science* under the headline, 'stem cells are coaxed to produce insulin' (Lumelsky et al., 2001). The seminal nature of the Lumelsky paper is captured in the rhetorical flourishes of an accompanying editorial comment in *Science*:

> In a boost for scientists who hope to turn the potential of undifferentiated stem cells into *medical miracles*, researchers have found a way to produce insulin-producing cells from mouse embryonic stem (ES) cells. There is a ready-made demand for anyone who can achieve such *alchemy* in human cells: millions of patients with diabetes… An unlimited source of cells that can produce insulin in response to the body's cues would… be a *hot commodity*. (Vogel, 2001: 615, our italics)

The paper was highly significant as Lumelsky et al. (2001) showed that the several cell types of the endocrine pancreas could be generated from ES cells *in vitro*, and that ES cells could be made into pancreatic islets. Their aim was to adapt their successful strategy of making neural cells from mouse ES cells (Lee et al., 2000) to produce pancreatic endocrine cells. Rather than genetically modifying ES cells, their approach was to attempt to reproduce a simplified variant of the chemical stimulations that occur in embryonic development, especially those that are thought to be key influences on 'driving a cell down the beta cell pathway'. After five days of adding and removing a cocktail of growth factors they evaluated the cells using several routine biological procedures which are consistently used within molecular biology to demonstrate gene and protein expression (Alberts et al., 2002).

Prior to the Lumelsky publication, the scientists in our UK beta cell lab had been influenced by the Edmonton protocol for islet cell transplantation:

> If you could regenerate beta cells you could effectively cure diabetes, as simple as that… So this new [Edmon-

> ton] protocol where they have described the transplantation of islets with a much less aggressive immuno regime [Shapiro, 2000] stimulated the interest in the proof of the principle. If you could make beta cells or islets from some other source, a much more abundant source, then you could cure diabetes and that's where stem cells came in because they are pretty much the only sensible option to make insulin secreting cells that you could transplant into the diabetic in enough numbers so that it becomes a viable therapy. (Scientist 2)

However, the Lumelsky paper resulted in an important change of direction for them:

> We got into stem cell research after the Lumelsky paper [2001] was published because it was an obvious area that everybody was going to get into because it was the big chance to cure diabetes… What has happened is funding in science has become more and more a people bandwagon, so there were a few people working on ES cells trying to turn them into beta cells and suddenly it becomes popular, the government ring fenced funding for it, the diabetes charities really want the science to work so they fund it, then scientists get into it and then they find they can't actually do it so what will happen, I predict but I could be wrong, is that the research interest will dwindle but there will still be a body of scientists who probably were there in the first place and who will continue to do it. Again I think because the prize is so enormous if somebody could actually do it. (Scientist 3)

Within this field there is a gulf between the apparent ease with which revolutionary new findings are heralded in seminal papers, and the findings from other labs which have tried to replicate and extend these initial experiments. This tension is captured in four short quotations below:

> You read the literature and it seems easy. (Scientist 5)

> The Lumelsky paper…was a little bit of a misguided paper because it wasn't well reproduced, but it was probably good in terms of impetus, it got a lot of people doing this. (Scientist 4)

> It's very hard in this kind of area to know whether the results that have been published are genuinely reproducible, that the effects that they are describing are attributable to the experimental procedures and aren't being affected by other randomly occurring factors. (Scientist 6)

> So it was quite difficult, and I think we've probably come to the conclusion that the Lumelsky protocol is rather complicated and perhaps there may be some other protocol that could be better used, but what that would be right now, I guess we don't know! (Scientist 45, UK)

These quotes all reflect elements of the scientific research game, what Bourdieu (2001) calls *illusio*: is the game worth the candle? Is this a field of science that scientists should invest their time, resources, staff in? Scientists within this field participate in enacting the tension between optimism and pessimism, or as one leading American beta cell biologist puts it:

> The field of generating new beta-cells from stem cells… is still in its infancy. Each new report has been met with a mixture of excitement and skepticism. (Bonner-Weir, 2003: 10)

This reflects the normal practice of scientific publication where, following publication of an important paper, other groups of scientists will try and replicate or, more typically, refine the initial experiment:

> What almost always happens is somebody will publish a very interesting paper, everybody thinks "Wow that's amazing!" or "I don't believe that!" depending on where you would come from, and then everyone tries to repeat it… You don't really know what to believe or what not to believe, and we have the feeling that to actually believe something we need to do it ourselves, so we have repeated a lot of the things that people have published and found that we can't do that, or that we can get similar results but it's not for the reasons that they are claiming, it's because maybe we are not actually making beta cells, we are making some sort of embryonic tissue that expresses the same things as beta cells. You have to be very careful with what you are claiming, and then you get to where the people who published the original paper will come back with some other model that supports their original paper because people don't want to say "Oh no, I was wrong!" And that's often the way it works. (Scientist 2)

This quote provides a clear example of the experimenters' regress in action, illustrating how judgements are made about, for example, the competence of scientists and the meaning of the experiment. It illustrates the way in which this core set is active in generating and resolving scientific controversies within their field of science, through the negotiations which can take place over contested claims. The Lumelsky et al. (2001) paper is also a good example of the ways in which key publications change the research directions of the network of scientists within an international core set of scientists.

In the context of such competition, however, there is always the possibility of being accused of 'bandwagoning' – of pursuing the prize irrespective of the weaknesses of the original finding or protocol (even if these only become generally 'apparent' after the resolution or closure of the controversy). The following quotes indicate the ease with which the discourse of 'jumping on the bandwagon' is available:

> When that Lumelsky protocol came out, the world and his dog jumped on the bandwagon, trying to reproduce it in various ways. And loads of people had a load of problems. (Scientist 43, UK).

> The Lumelsky paper made it look like there was a default pathway. A few steps, a few stages, all bing, bing, bing, and you get beta cells. No! And now there are a whole lot of laboratories working on it. There's been a whole lot of money spent on it, and a lot of people were coming up with things that express a little bit of insulin. And a lot of people were hyping their work. We're more than uncomfortable with it. (Scientist 25, USA).

> In 2001 [following publication of the Lumelsky protocol] everybody said, 'Oh look, they do it almost by default!' [ES cells become beta cells]. That's

> been now shown not to be the case [in 2005]. That makes a big difference in the mindset for a lot of people and how you approach this field… I think people were expecting to get to the clinic much faster. (Scientist 26, USA).

> [Scientists] dropped everything and tried to repeat and extend their [Lumelsky] protocol. And the protocol was wrong. So it's a disaster. (Scientist 28, USA).

This 'bandwagoning' discourse can amount to an attack on the credibility of the 'bandwagon jumpers'. As we shall see, the Lumelsky protocol was indeed 'found' to be faulty. To the extent that this places the credibility of scientists under pressure, there is a need somehow to recover the situation if one is to continue to work credibly. However, as we shall see, this recovery is partly made possible by the fact that to 'jump on the bandwagon' is 'understandable'.

Melton debunks the Lumelsky protocol

The Lumelsky paper came from McKay's lab at the US government funded NIH, and US restrictions on hES cell science meant that in 2000 they did not have access to cells of a quality to do meaningful experiments with (Weissman, 2002). In 2004, however, Doug Melton at Harvard—but working in his privately funded Howard Hughes lab—astonished the scientific world with a paper in the *New England Journal of Medicine* which documented his lab's success at creating 17 new hES cell lines (Cowan et al., 2004). Melton, a developmental beta cell biologist, offered to reproduce the Lumelsky protocol in human rather than in mouse ES cells. However, the subsequent one page paper from Melton's lab, by Rajagopal et al. (2003), effectively debunked the Lumelsky protocol, and is a vivid illustration of the production of scientific scepticism. One of our scientists summarized three aspects of the skepticism of those working at the intersection of stem cell and beta cell biology:

> One, people who work on stem cells probably know how difficult it is and are skeptics; two, because out in the front line of research area no one is just sitting there saying "Oh right, that's fine, great results, yes we believe you, that's fine, you've solved our problems"; three, scientists are like everyone else, they hate it when someone else beats them to it… You are more likely to criticize something that's going to be very exciting and get a lot of attention… than someone working on more routine problems. (Scientist 1)

In essence, the Melton lab demonstrated that rather than the cells producing insulin, insulin was being absorbed from the culture medium and then secreted by cells. The problems of gene expression in this pair of experimental reports from the McKay and Melton labs is a theme expanded upon by one scientist who has spent three years working on Lumelsky style protocols:

> What the Melton Group showed was that most of the insulin that's been secreted by the cells has been taken up, and really the sort of level of insulin gene expression that they were getting was really quite low, approaching what you'd find as a random occurrence, because if you grow stem cells as a cluster…you can get stem cells that make insulin, but it's not many… You really need to show that you have got a lot of cells making insulin, that those cells are making a large amount

> of it, and also that you have got other beta cell markers expressed as well, because there's no use in having insulin expressed if it can't be packaged and secreted appropriately. (Scientist 6)

This last point, of the importance of experiments demonstrating the appropriate packaging of insulin so that it may be physiologically secreted, is the essence of a range of recommendations designed to eliminate problems from future experiments that purport to show that ES cells can produce insulin. Rajagopal et al. (2003) suggested that a combination of several methods is required for reliable analysis of insulin production in ES cell progeny. In short, Melton's group raised the bar of what counts as the minimum scientific evidence within this field. This approach is common in science. For instance, Guillemin made the laboratory standard of detecting the hormone TRF [thyrotropin releasing factor] so high that only two labs in the world had the equipment and expertise necessary to conduct the experiments (Latour and Woolgar, 1986). Melton's five additional lab tests require considerable expertise in beta cell biology, making it very difficult for anyone outside the core set of beta cell biologists, including McKay's neural stem cell group, to perform credible experiments in this area. Scientist 3 summed up the impact of the Melton critique on the beta cell field:

> We know that the initial Lumelsky paper sparked this all off was based on an error. The cells weren't making insulin, they were taking it out [of the culture medium], we knew that before that was published, because we couldn't find any gene significant expression…so it was clear there was something wrong with the protocol…and Melton realised this and Melton had the brains to publish it in *Science*. So that knocked off the first paper [Lumelsky et al., 2001] and then it undermined a whole series of papers which had been submitted and were obviously in press. There was a big gap, a delay, where people had followed the Lumelsky protocol with minor variations, and you can write all those papers off immediately… Scientifically you can write those off because they are based on flawed protocols. So the ones that aren't based on those protocols, the general result tends to be, "we have reproduced this, that a small number of cells will differentiate to an insulin genotype but it's not clear what the phenotype of the cells is in our opinion. We think that the cells are doing it themselves rather than responding to any external stimulus, but that's just our lab's spin on it." (Scientist 3)

This section illustrates further ways in which this core set actively manages scientific controversies within their field through, notably, the exclusion of other scientists from these negotiations. However, such exclusion on one highly specialist level does not preclude inclusion on a broader level. In terms of the debate between Collins and Wynne outlined in the introduction, if the proposition entailed in Lumelsky is now 'found' to be false, the tacit assumptions built into the proposition serve in enabling the broader scientific assemblage to 'go on' in that those scientists who reacted to the Lumelsky protocol with a 'Wow that's amazing' and who are seen as jumping onto the 'bandwagon' are nevertheless not wholly discredited. Indeed, in a context of chronic uncertainty where no-one knows how to direct the differentiation of embryonic stem cells into beta

cells, jumping on the bandwagon becomes understandable. In what follows, we trace some of the key uncertainties that bedevil this field.

Chronic uncertainty and the possibility of inclusion

> I don't want to be a Cassandra and say that it's never going to happen. The reality of it at the moment, the way the science of stem cells is very difficult… I think we know very little, and that's why we are having trouble directing them. (Scientist 1)

In this quote we are presented with a profound sense of the uncertainties dogging stem cell research. In this section, we present interview data structured in terms of four juxtaposed problems with stem cell research. The aim here is to counterpose the account of rise and fall of the Lumelsky protocol of the preceding section with an examination of some of the varieties of chronic uncertainty within this field. Our purpose is to show how such uncertainty can serve as a common ground which can keep alive the connections between (that is, the assemblage of) the 'victors' and the 'vanquished' of the Lumelsky protocol controversy.

Problems with cell culture

Scientists in this lab worked on mouse, rat and hES cells, as well as rat and human foetal stem cells. The biomedical science techniques required for growing and experimenting with this range of stem cells and beta cells are similar. However, hES cells were seen as being particularly difficult to culture:

> The characterization of cells that come from stem cells is the same for each different tissue source. We are exposing them to the same experimental techniques… [hES cells] grow so slowly as well, they take a lot longer to get the tissue number to the level of material that we need to actually do functional testing on the cells. (Scientist 2)

In all of our interviews with stem cell scientists, in this UK lab and elsewhere, this process of the culture of hES cells is seen as an art as much as a science. Scientists often spoke of the importance of having 'green fingers' or 'golden hands' (Knorr-Cetina, 1999), particularly when selecting staff for particular tasks relating to hES cells:

> We wanted somebody who we knew was good at tissue culture looking after our precious little babies [hES cells]. (Scientist 3)

Scientists argued that the variation in the cells, the plasticity of the cells and their propensity to differentiate into cells that are no longer ES cells, contributed to the difficulty of reproducing experimental results:

> Some experiments aren't reproducible anyway. Something happened, for some reason you don't know why it happened on that particular day, somebody used a different batch of cells and you get those results and you try to reproduce them and you don't. (Scientist 4)

> Studying these cells is so different to studying other differentiating tissue, because it is so plastic and you don't know whether the cells that you started with two passages [ES cells must be divided and transferred to a new culture dish every few days: the process of passage] ago are actually giving

> you the same cells that you are using now. (Scientist 6)

In the two quotes above the variation in laboratory materials leads to what scientists' describe as non-reproducible experiments. In other cases, scientists put down their difficulties to the inherent complexity of beta cells themselves.

> But actually to do the research is very difficult. It is not easy by any stretch of the imagination. And the likelihood of a positive outcome has to be years and years away, if at all, to be honest. I think that beta cells are a particularly difficult line to follow because it's a complex cell. (Scientist 45, UK)

Here, then, we have sketched out a chronic uncertainty within this research programme. This uncertainty is further underscored when other considerations are taken into account.

Problems with spontaneous differentiation of cells

All of the scientists we interviewed argued that ES cells differentiate into other cell types spontaneously. In other words, scientists are measuring the results of a natural process that they cannot control, rather than an experimentally induced process that they are in control of:

> We have shown that we can see beta cell genes being expressed from stem cells, but really it's nothing that we do to them. They have this spontaneous capacity to show some elements of a beta cell geneotype, and I'm sure you [SW] have asked this question before, 'Well, if you looked for cardiac cell markers in the same cell populations would you see them?' We haven't looked for them, but I am pretty certain the answer would be yes. (Scientist 4)

In this quote we see how scientists only see what they are looking for – in the case of this lab, beta cells. This is an example of "the 'framing' of scientific discourse… that literally makes some objects accessible and others invisible" (Doyle, 1997: 6). The following quote illustrates the central importance of the tacit and verbal nature of scientific research:

> We had this problem of spontaneous differentiation all the time, and after a while I realized, well, actually probably nobody uses the cultures that are 100% pluripotent [able to change into almost any type of cell]. Probably everybody has a certain level of differentiation.
> SW: *So the assumption is that they are working with pure cultures even though in practice they are not? Is that fair?*
> Yes I would think so. It's just not really something that's been addressed at all. I realized this when I took a trip to [another lab] and we went in a lab where they have done a lot of ES cell work and I looked at some of their cultures and a lot of them were *more* differentiated than the ones that I had been using in my study! But it's a sort of shady area that people don't really tend to talk about. (Scientist 6)

Problems with in vitro developmental biology

As we have seen, the approach of both the McKay and Melton groups was to try to reproduce the 'embryonic environment' in the lab, to see whether ES cells could be turned into islet cells. However, the scientists we interviewed saw this strategy as problematic:

> I am skeptical about it working *in vitro* as it's such a complicated system and it's not just about transcription factors, switching on another one - it's switch on, switch off, right timing, right factors and the right mix at the right time and can we do that *in vitro*? (Scientist 4)

The major problem was seen as a lack of scientific understanding of the processes of stem cell and beta cell development:

> I think the principal problem is that we just don't understand the process of development in the pancreas. It's so enormously complicated, and we know quite a lot about which genes are switched on and off during the process, but we don't know actually what switches them on and even if we did know, I'm not sure that you could really reproduce that *in vitro* because it's the embryo, a dynamic changing system whilst *in vitro* methods tend to be static… The main hurdle probably is that we just don't have enough understanding of stem cells and of embryonic development in general, but then even if we had a completely full understanding of how the pancreas develops I don't think we could replicate that. (Scientist 6)

The problem of a lack of appropriate biological markers through which to track the transformation of hES cells into beta cells was seen as a priority for unravelling some of the complexities of embryonic development, although the gulf between what is known about mouse ES cells and hES cells was also highlighted:

> I think you do perhaps need to understand the whole process both of differentiation initially, how you get from the non beta cell to a beta cell, what steps are involved in that process of differentiation. The first important thing to have is some kind of marker for different stages of differentiation. These are known in the mouse but there is virtually nothing known about the way that cells differentiate in humans, whether they go through a similar process, because there do appear to be substantial differences in, say, foetal differentiation which is starting to come out in comparisons. (Scientist 5)

Problems with people and 'the area'

Alongside the problems with the material and the procedures, there are problems with people. Our scientists, on reflecting upon the field were keenly aware of the way that in seeking to convert stem cells to beta cells, colleagues were liable to over-hype findings, as one scientist put it in relation to the initial celebrations around the Lumelsky protocol:

> It's because people want it to work. And if it had been true it would have revolutionised lots of things. (Scientist 3)

Allied to this, such problems with people arise because of the limitations to their expertise:

> Melton came out and says this (the Lumelsky protocol) is wrong, and he was absolutely right! So I think that has helped to raise the standard for what do we call a beta cell. And I think that people are beginning to appreciate the importance of all techniques like RT-PCR to really show that amino acids produce proteins, and a lot of people are using very sophisticated imaging techniques – but they are not experts. So they are misinterpreting, and a lot of people are experts up to

> a point, but not in a particular methodology, so they measure something, but maybe it's the wrong measure. (Scientist 49, USA).

In this context, many of our scientists see one of their key roles within this field as that of deflating some of the scientific hype that often surrounds the prospects of stem cell science (Braude et al., 2005). This critical perspective is grounded in their own stem cell experiments:

> Most journal editors would fall over themselves to get hold of a human embryonic stem cell paper, but as for positive results that depends on your spin, or would depend on how far you want to stretch your data to fit your hypotheses. A lot of what we publish could be construed to be negative'ish in that we're trying to temper some of the hype, we're trying to provide the other side of the coin to what some people have been claiming in some of their publications. So positive results, negative results, it depends on what way we stand. (Scientist 2)

Our respondents, in summing up the current state of the field, severally pointed to the chronic uncertainties:

> The whole area is a bit of a muddle actually. There are holes in all of the studies. (Scientist 5)

> Scientifically, the potential that stem cells had three years ago hasn't been fulfilled, but it could be, and if it was it would be such a big prize that I think people are going to continue in this area for a while. What happens to scientists is they get very disillusioned, and so if something is hyped up and hyped up that you work on for three years and you don't get anything that's logical, sensible, reproducible or publishable it tends to fall out of favour, and stem cells and diabetes are at that stage at the minute. So nobody believes much of what has been published, and people are very critical of grant applications and stuff like that with stem cells. (Scientist 3)

> SW: *So how do you think stem cells might change beta cell biology and diabetes?*
> That's a question if you had asked me probably three years ago I would have given you a more positive answer, but at the moment I don't think they will. Three years later we have got nothing that looks like a beta cell… I think generating the data is difficult and it's very easy to generate negative data but nobody wants to hear, "I tried something else and that didn't work!" (Scientist 4)

If these uncertainties technically militate against beta cell derivation from stem cells, they also point to other possibilities (e.g. the genetic modification of stem cells) but such a move, in turn, generates ethical and social uncertainties.

> I've only worked in this area for three or four years and there are not many people who have worked in stem cells for diabetes longer than that, because the interest only really came in five or six years ago. But in that short time, to begin with I was quite excited about it, I really thought, this is good stuff, this has amazing potential. That's been slightly tempered just by my experience, of our own work but then also speaking to other people, and going to conferences and seeing what people are able to do, people with huge amounts of money and facilities. They haven't really got any further down

> the line than we were 18 months ago. Having said that I still do think that probably ultimately one day there will be a cure that people are waiting for. I just think that maybe it requires genetic modification, mainly the cells need to be genetically changed before you actually are going to be able to get a cell that behaves enough like a beta cell. That then requires a wholesale change of ethical thought as to whether you can put some genetically modified cell back into a human, and that's going to take years and years of legislation. (Scientist 2)

Conclusion

In the preceding section, we have presented a series of accounts of the chronic uncertainty that bedevils stem cell research, not least that concerned with the differentiation of beta cells. These data have been presented in this way in order to contrast with the section on the Lumelsky protocol which was characterized by a narratively dramatic, linear structure of apparent success followed by accepted failure. This is a narrative structure typical of core set analysis (but also applicable to other analytics within the sociology of science, notably actor-network theory; see Michael, 1996). The question posed of this form of analysis is: how do those who jumped on the 'Lumelsky bandwagon' remain credible scientists – or have their standing 'rehabilitated'? The section on the chronic uncertainties of the field aims to reflect the complex layers of uncertainty in the field with which stem cell scientists must deal. It suggests that running alongside the dramatic narrative of seeming success and evident failure is a morass of experimental work whose success and failure is profoundly and chronically uncertain. This can be likened to an assemblage where scientists are making all sorts of attempts to develop workable experimental systems – attempts which while still reactive to the competitive structure of science, might also entail other sorts of associations.

If in the core set analysis in which scientists compete for the epistemic high ground, certain scientists were 'discredited' because of the propositional findings against the Lumelsky protocol, in the more diffuse assemblage of chronic uncertainties, to jump onto the Lumelsky bandwagon is socially 'understandable'.[5] In other words, parallel to assessments of epistemic correctness or incorrectness—that is about the propositional or substantive content of knowledge—mapped by core set analysis, are feelings of 'social understandability' under conditions of chronic uncertainty. To put this another way, alongside the judgement, resolution and exclusion mapped by core set analysis, there is the 'understanding', irresolution and inclusion suggested by 'assemblage analysis'. If the former documents the 'punishment' of those who have failed in a controversy, the latter points to the ways in which they may be 'forgiven'.

There are obviously echoes here of Gilbert and Mulkay's (1984) classic analysis of empiricist and contingent repertoires, and we can usefully draw on their work to highlight what is distinctive in the present paper. As is well known, they noted that empiricist repertories were applied to self, and contingent to 'others' (opponents in a controversy), and certainly our respondents followed a similar pattern. However, Gilbert and Mulkay also noted that contradictions arose, where the contingent repertoire was necessarily applied to self when it became evident that one had made mistakes in the past. The resolution to this contradiction (the application of

both empiricist and contingent repertoires to self) was managed through the Truth Will Out Device in which nature ultimately ensured that the empiricist prevailed. In the present case, the 'contingent' repertoire is applied to self 'in principle' as it were, because our respondents did not jump onto the bandwagon, but they might have done if circumstances had been slightly different. Indeed, they might be on a bandwagon at the present moment, but will only know it in retrospect, though they can certainly acknowledge the possibility.[6] In a sense then, the present paper attends to the obverse of the Truth Will Out Device, the 'but for the grace of god' presumption – "it could have been me (or my lab) on that (the Lumelsky protocol) bandwagon". Thus, in contrast to the necessity entailed in the Truth Will Out Device (nature will always ensure the truth's emergence), the 'but for the grace of god' presumption reflects the probabilities of making mistakes (or rather the lucky escapes).

Finally, we can, rather more speculatively, suggest two further differences between analyses oriented respectively toward core sets or assemblages. We draw out these differences as prompts to future thinking about how to explore scientific research processes and dynamics.

The first concerns the narrative form taken by core set or assemblage accounts. The core set analysis in accounting for the resolution of the experimenters' regress, 'concludes' a narrative. What of those who were 'defeated'? As is well known, they may 'continue' on the outside of the core set (by and large marginal to the 'real action'), or they take up the now predominant knowledge and retain a position within the core set. That is to say, the end-state of the core set narrative portrays a world inhabited by insiders and outsiders. There is a dramatic reconfiguration of the assemblage into the included and the excluded. By comparison, the assemblage model provides for a much murkier model in this case of stem cell research – where people from opposing factions' continue dialogues, form alliances, develop collaborations and so on and so forth in a process of 'irresolution'. Here, the epistemically 'victorious' accept the defeated not *in spite of* their epistemic mistakes, but *because of* their 'social understandability' – their strategies are understandable under such conditions of uncertainty. In this latter case, the account is not structured by a dramatic narrative of contest and victory-defeat, but by a sort of continuing diffuse or potential connectivity.[7]

The second related point concerns the divergent models of time that inform the contrast between core set and assemblage analyses. For the former, time proceeds linearly along a line on which are sequentially arrayed the past, present and future. Overlying the movement between these phases is a dramatic narrative in which, typically, a claim is staked, factions form, one faction triumphs, the other fails. This sort of temporality is, of course, typical of modern western societies (see Kern, 2003; Nowotny, 1994). By way of contrast, the assemblage model draws on a more topological sense of time (Serres and Latour, 1995) in which the linear version is seen to be one out of many ways in which 'events' combine and arrange themselves. As Serres puts it:

> No, time flows in a turbulent and chaotic manner; it percolates….this time can be schematized by a kind of crumpling, a multiple, foldable diversity" (Serres and Latour, 1995: 59).

In relation to the assemblage model, we can suggest that it might be fruitful to explore the usefulness of 'topological' temporality.[8] What would an account that treats respondents' representations of the past, present and future non-linearly look like? At the very least, we might hope that it casts some light on the more circuitous dynamics—the continuing diffuse or potential connectivity, as we have phrased it above—that characterize scientific assemblages.

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Notes

1 We use the term assemblage here, derived from Deleuze and Guattari (1988; see also Martin, 1998; Irwin and Michael, 2003), to denote both the heterogeneity of what might have otherwise been called the scientific 'community', and also the complex processes by which shifting alliances and fissures are enacted amongst scientists (and also with non-scientists) to produce what from a more traditional perspective might seem to be 'odd' combinations. On this latter score our use of the term assemblage echoes that of Latour (2005: 9), unsurprisingly given that he too tacitly references Deleuze and Guattari in his suggestion that 'actant rhyzome ontology' might have served as a more adequate replacement for the term 'actor-network theory'. We especially applaud Latour for his use of the verb 'reassembling', not least for evoking his debt to the process philosophy of Whitehead, a debt he shares with Deleuze. While we use the noun 'assemblage' this is always with the understanding that this be read processually: the assemblage is always in the process of assembly (see Halewood and Michael, in press).

2 We can also note that the core set can be expanded to incorporate matters 'beyond' the propositional or the epistemic, not least those concerning ethics (see Michael and Birke, 1994; Hedgecoe, 2006).

3 This brings to mind Greg Myers' (1989) classic account of the use of *politeness* in scientific articles to stake radical claims while not appearing to threaten the positions of other scientists in the field.

4 Two of the researchers (SW, CW) also observed and interacted with the scientists in meetings, in the lab, and at seminar and conference presentations. Informal conversations with scientists took place in all these settings. In addition, one of the researchers (SW) participated in nine lab workshops for postgraduate biomedical scientists, learning various laboratory techniques.

5 The meaning of 'understandable', 'understanding' and 'understandability' as used here clearly has an affective dimension – it connotes empathy, or sympathy. As such, it resonates with Michael's (2002) second version of understanding (in his review of the public understanding of science literature) as 'apprehension' (as opposed to comprehension and prehension). This is not to say that core set analysis does not engage with the affects of scientists.

6 This dynamic is reflected in what Brown and Michael (2003) have contrasted as prospecting retrospects and retrospecting prospects.

7 Indeed, despite the classic SSK methodological tactic of seeking insight by studying controversy, this arguably obscures more subtle configurations and dynamics of the scientific 'assemblage'.

8 Needless to say, topological temporality has been subjected to criticism – see Connor (2004).

References

Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K. & Walter, P.
2002 Molecular Biology of the Cell. Fourth Edition New York: Garland Science.

Assady, S., Maor, G., Amit, M., Itskovitz-Eldor, J., Skorecki, K. L. & Tzukerman, M.
2001 "Insulin production by human embryonic stem cells". Diabetes 50: 1691-1697.

Blau, H. M., Brazelton, T.R. & Weimann, J. M.
2001 "The evolving concept of a stem cell: entity or function." Cell 105: 829-841.

Bliss, M.
1984 The Discovery of Insulin Chicago: Chicago University Press.

Bonner-Weir, S.
2003 "Stem cells in diabetes: what has been achieved." Hormone Research 60: 3-10.

Bonner-Weir, S. & Weir, G. C.
2005 "New sources of pancreatic Beta-cells." Nature Biotechnology 23: 857 – 886.

Bourdieu, P.
2001 Pascalian Meditations. Polity Press: Cambridge.

Braude, P., Minger, S. L. & Warwick, R. M.
2005 "Stem cell therapies: hope or hype?" British Medical Journal 330: 1159-1160.

Brown, N. & Michael, M.
2003 "A sociology of expectations: retrospecting prospects and prospecting retrospects." Technology Analysis and Strategic Management 15: 3-18.

Brown, N. & Rappert, B. & Webster, A. (Eds.)
2000 Contested Futures. Aldershot: Ashgate.

Burns, C. J., Persaud, S. J. & Jones, P. M.
2004 "Stem cell therapy for diabetes: do we need to make beta cells?" Endocrinology 183: 437-443.

Collins, H.
1975 "The seven sexes: a study in the sociology of a phenomenon, or the replication of experiments in physics." Sociology 9: 205-224.
1985 Changing Order. London: Sage.
2004 Gravity's Shadow: The Search for Gravitational Waves. Chicago: Chicago University Press.

Collins, H. & Evans, R.
2002 "The third wave of science studies: studies of expertise and experience." Social Studies of Science 32: 235-296.

Collins, H. & Pinch. T.
1998 The Golem. Second Edition Cambridge: Cambridge University Press

Connor, S.
2004 "Topologies: Michel Serres and the shapes of thought." Anglistik 15: 105-117.

Cowan, C. A., Klimanskaya, I., McMahon, J. et al.
2004 "Derivation of embryonic stem cell lines from human blastocysts." New England Journal of Medicine 350: 1353.1356.

Deleuze, G. & Guattari, F.
1988 A Thousand Plateaus: Capitalism and Schizophrenia. London: Athlone Press.

Doyle, R.
1997 On Beyond Living: Rhetorical Transformations of the Life Sciences Stanford: Stanford University Press.

Gearhart, J. (Ed.)
2005 Stem Cells: Nuclear Reprogramming and Therapeutic Applications (Novartis Foundation Symposium). New York: Wiley.

Gilbert, G. N., & Mulkay, M.
1984 Opening Pandora's Box: A Sociological Analysis of Scientists' Discourse. Cambridge: Cambridge University Press.
Gray, D. W. K.
2002 Pp. 305-325 in "An historical overview of the development of cellular and islet transplantation." Hakim, N., Straata, R. & Gray, D. W. K. (Eds.), Pancreas and Islet Transplantation. Oxford: Oxford University Press.
Halewood, M. & Michael, M.
In Press "Being a sociologist and becoming a Whiteheadian: concrescing methodological tactics." Theory, Culture and Society.
Hedgecoe, A.
2006 "Pharmacogenetics as alien science: Alzheimer's disease, core sets and expectations." Social Studies of Science 36: 723-752.
Irwin, A., & Michael, M.
2003 Science, Social Theory and Public Knowledge. Maidenhead: Open University Press/McGraw-Hill.
Itkin-Ansari, P. & Levine, F.
2004 "Sources of beta-cells for human cell-based therapies for diabetes." Cell Biochemistry & Biophysics 40:103-12.
Jones, P.M, Burns C. J. & Persaud, S. J.
2004 "Beta-cell replacement technologies: the potential of stem cells for transplantation therapy of Type 1 diabetes." Drug Discovery Today: Therapeutic Strategies: 213-217.
Kern, S.
2003 The Culture of Time and Space 1880-1918. Cambridge, Mass.: Harvard University Press
Kiessling, A. A. & Anderson, S.
2003 Human Embryonic Stem Cells: An introduction to the Science and the Therapeutic Potential. Boston: Jones & Bartlet.
Knorr-Cetina, K.
1999 Epistemic Cultures: How Sciences Make Knowledge. Cambridge, Mass.: Harvard University Press.
Lanza, R. et al. (Eds.)
2004a Handbook of Stem Cells. Volume 1 Embryonic Stem Cells. Elsevier: Amsterdam.
2004b Handbook of Stem Cells. Volume 2 Fetal & Adult Stem Cells. Elsevier: Amsterdam.
Latour, B.
2005 Reassembling the Social: An Introduction to Actor-Network-Theory. Oxford & New York: Oxford University Press
Latour, B. & Woolgar, S.
1986 Laboratory Life: The Construction of Scientific Facts. Princeton: Princeton University Press.
Leach, M., Scoones, X., & Wynne, B. (Eds.)
2005 Science and Citizens: Globalization, and the Challenge of Engagement. London: Zed Books.
Lee, S.H, Lumelsky, N., Studer, L., Auerbach, J. M. & McKay, R. D.
2000 "Efficient generation of midbrain and hindbrain neurons from mouse embryonic stem cells." Nature Biotechnology 18, 6:675-9.
Lumelsky, N., Blondel, O., Laeng, P., Valeslo, I., Ravin, R. & McKay, R.
2001 "Differentiation of embryonic stem cells to insulin-secreting structures similar to pancreatic islets." Science 292: 1389-1394.
Lynch, M.
1993 Scientific Practice and Ordinary Action: Ethnomethodology and Social Studies of Science Cambridge: Cambridge University Press.
Martin, E.
1998 "Anthropology and cultural study of science." Science, Technology and Human Values 23: 24-44.

Michael, M.
1996 Constructing Identities: The Social, the Nonhuman and Change. London: Sage.
Michael, M.
2002 "Comprehension, apprehension, and prehension: heterogeneity and the public understanding of science." Science, Technology and Human Values 27, 3: 357-370.
Michael, M. & Birke, L.
1994 "Animal experimentation: enrolling the core set." Social Studies of Science 24, 1: 81-95.
Myers, G.
1989 "The pragmatics of politeness in scientific articles." Applied Linguistics 10, 1:1-35
Nowotny, H.
1994 Time: The Modern and Postmodern Experience. Cambridge: Polity Press.
Potter, J. & Wetherell, M.
1987 Discourse and Social Psychology. London: Sage.
Rajagopal, J., Anderson, W. J., Kume, S.,
Martinez, O. I. & Melton, D. A.
2003 " Insulin staining of ES cell progeny from insulin uptake." Science 299, 5605: 363.
Rippon, H. J. & Bishop, A. E.
2004 "Embryonic stem cells." Cell Proliferation 37: 23-34.
Rother, K. I. & Harlan, D. M.
2004 "Challenges facing islet transplantation for the treatment of Type 1 Diabetes Mellitus." Journal of Clinical Investigation 114: 877-883.
Ryan, E. A., Paty, B. W., Senior, P. A.,
Bigam, D., Alfadhli, E., Kneteman, N. M.,
Lakey, J. R. & Shapiro, A. M. J.
2005 "Five-year follow up after clinical islet transplantation." Diabetes 54: 2060-2069.
Segev, H., Fishman, B., Ziskind, A. & Itskovitz-Eldor, J.
2004 "Differentiation of human embryonic stem cells into insulin producing clusters." Stem Cells 22: 265-274.
Serres, M. & Latour, B.
1995 Conversations on Science, Culture and Time. Ann Arbor: Michigan University Press.
Shapiro, A. M. J., Lakey, J. R. T., Ryan, E.
A. & Korbutt, G. S.
2000 "Islet transplantation in seven patients with Type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regime." New England Journal of Medicine 343, 230-238.
Silverman, D.
1993 Interpreting Qualitative Data: Methods for Analysing Talk, Text and Interaction. London: Sage.
Strauss, A. L.
1987 Qualitative Analysis for Social Scientists. Cambridge University Press: Cambridge.
Thompson, J., Liskovitz-Eldor, J., Shapiro, S., et al.
1998 "Embryonic stem cell lines derived from human blastocysts." Science 282: 1145-47.
Van Lente, H.
1993 Promising Technology: The Dynamics of Expectations in Technological Developments. University of Twente: Delft.
Vogel, G.
2001 "Developmental biology: stem cells are coaxed to produce insulin." Science 292: 615-7.
2003 "Stem cell research: same results, different interpretations." Science 299: 363.
Wass, J. & Shalet, S.
2002 Oxford Textbook of Endocrinology and Diabetes. Oxford: Oxford University Press.

Weber, R.
1990 Basic Content Analysis. London: Sage.
Weissman, I. L.
2002 "Stem cells - scientific, medical, and political issues." New England Journal of Medicine 346: 1576-1579.
Wynne, B.
2003 "Seasick on the third wave? Subverting the hegemony of propositionalism." Social Studies of Science 33: 401-418.
Zimmet, P., Alberti, K. & Shaw, J.
2001 "Global and societal implications of the diabetes epidemic." Nature 414: 782-787.

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