PART II

BIOSCIENCE AND BIOLOGICAL LIFE

ETHICS OF TECHNOSCIENTIFIC OBJECTS

4

STEM CELLS R US:
Emergent Life Forms and the Global Biological

SARAH FRANKLIN

Introduction

Since the late 1990s, stem cell development has become one of the major growth sectors within the global biotechnology industry, and has attracted considerable attention as a site of bio-innovation. Like other ''breakthrough'' areas of bioscience, stem cell techniques have been accompanied by tremendous hype, emphasizing the speed of technological innovation and its ''revolutionary'' potential. A direct media feeder system links developments in stem cell research to the possibility of treatment for severe, disabling, and often fatal conditions – binding stem cell technology securely into a rhetorical fabric of hope, health, and an improved future through increasing biological control. Every country in the world that imagines itself a player in the future of genomics, biotechnology, or what is now being called ''regenerative medicine'' is today busy passing regulation that will facilitate public approval for rapid industrial development of stem cell technology.

The United Kingdom is currently the ''world leader'' in stem cell technologies. As *Business Week* reported in April of 2002, ''In stem cell research, it's rule Britannia'':[1]

> In Britain, home to the world's first test-tube baby and Dolly the cloned sheep, more than a decade of ongoing dialogue between scientists, government, and religious officials has resulted in the most conducive climate in the world for this important new area of scientific research.[2,3]

Both Germany and the United States, the U.K.'s major competitors, are hampered by strong public opposition to the use of human embryos for stem cell research – widely considered to be the most important resource for this area of scientific innovation. France, Spain, the Netherlands, and Sweden have plunged into the stem cell business enthusiastically, as have Australia and Canada. China and Singapore also have burgeoning stem cell industries, but since they are less defined by dominant Western systems of scientific publication, or intellectual property law, their competitiveness is harder to assess. Stem cell research combines human reproductive medicine (in particular, IVF programs) with agricultural applications (such as genetic modification of animals and plants) and traditional areas of biology; in particular, embryology, which, after a lengthy period of being sidelined by molecular biology, has burst back into the frame as a source of essential techniques, such as microinjection, and knowledge, such as expertise in cell cycles and embryonic metabolism. Stem cells offer the prospect of downloading genomics into a wealth of applications, making it the first major post-genomic bio-industry.

There are many emergent hybrid conjunctions that engender the stem cell field. The dominant post-genomic discourse of life's essentially shared molecular architecture (the we-are-50%-genetically-identical-to-cabbage trope of newfound affinities among everything from daffodils to fruit flies) is now increasingly fused with one of biology's oldest and most classical points of reference to describe life's commonalities – the cell. In the new flattened, respatialized, and recombinant genealogical topography of post-genomic designer organisms, life itself is repositioned outside the grid of neatly brachiated channels of ancestry that was formerly the master figure of life as a systematic unity. In place of the tree of life is the post-genomic, post-Darwinian, technique-led *genotopia* of the mix-'n'-match Petri dish, in which life components are assembled in ways that were, until quite recently, considered to be biologically impossible.

It is not so much that the pre-genomic beliefs that life has a structure, or some kind of internal design, have been displaced than that these long-held attitudes to ''life itself'' have been *repositioned alongside* a new enthusiasm for the potential of made-to-order recombinant outcomes. Ideas of naturalness, the inherent, the inherited, and the predetermined are still central vectors of assumed causality in contemporary biotechnological innovation. What has become more prominent is the idea, long established in the field of assisted human conception, and even longer in the field of animal breeding, that ''nature can be given a helping hand.'' Darwin called this ''the breeder's hand,'' and it was more important to the development of his ideas about natural selection than is commonly portrayed. IVF leaflets call it the hand of medicine, or the hand of science, and these ''helping hands'' provide a powerful image of regeneration under technological control, yet which is still being directed by nature's ''own'' dictates.[4]

This chapter explores stem cells as distinctive emergent life forms that refigure traditional understandings of economy, governance, and biology. Although I am focusing exclusively on the U.K., it is clear that the U.K. is responding to the stem cell issue within a global frame. In this, and other senses, stem cells are what might be

called a *global biological*. Their production is a global biological enterprise, but it is also their ''global,'' in the sense of totalizing, projected uses to which this term refers.[5] The idea of the global biological is already manifest in the human genome project, itself a description of a global totality (all of the human genes), the outcome of global cooperation, and a symbol of globalization – much as space exploration, and the image of the blue planet, inaugurated forms of global culture in the last century.[6] The conquest of inner space – the master narrative of genomics – is replete with the same imagery of technological potency, human frailty, and future salvation that framed an earlier century's lunar voyages. Stem cell technology is a prime example of the ways in which the global may come into being as a biocultural condition, as a form of identity, and as a realm of imaginary futures.

At the same time, stem cell technology is also, to mutate slightly Margaret Lock's phrase, a *local biological*. Describing the ''local biologies'' that emerge out of debates about menopause, brain death, and organ transplant, Margaret Lock has emphasized the ways in which the constitution of biological facts, the biological self-evident, or what are considered to be biological conditions, vary significantly according to their locations.[7] Stem cell technologies, as this brief portrait of the British situation attempts to suggest, demonstrate how biological properties are increasingly not only being ''discovered,'' but are being created, in ways that reveal specific national and economic priorities, moral and civic values, and technoscientific institutional cultures.

Regeneration Narratives

A traditional anthropological entry point to begin to evaluate the cultural processes that are being made explicit in the stem cell field are the kinds of origin stories, conception models, or regeneration narratives through which stem cells are represented in both popular and scientific accounts. A typical example is the following opening paragraph from a description of stem cell technology in the European Commission's research and development newsletter, *RTD info*:

> At birth, human beings are made up of approximately 100,000 billion cells belonging to 200 different categories (nerve, muscle, secretory, sense cells, etc.). Each of these groups is able to effect a number of very specialised tasks. As the body develops, the cells multiply by a process of division: when tissues deteriorate or wear out, it is generally the cells in the vicinity of the damaged zone that proliferate and try to compensate for the losses. Over time, however, this regenerative ability is progressively lost and ultimately disappears in many vital organs. Also, when the cells divide they are only able to produce daughter cells that are similar to themselves.[8]

In this origin account, humans are described in terms of their cellular functions, over the course of an individual lifetime. The cells are classified in terms of both quantity (100,000 billion cells at birth) and type (200 different categories). Cellular function is

described in terms of multiplication, division, replacement, specialization, proliferation, compensation, regeneration, development, deterioration, and disappearance. These are the key components of cellular effectivity, which are in turn organized economically, in terms of production and loss. Vitality is the outcome of successful replacement of cells, and age, or diminished vitality, results from the waning of this capacity. Significantly, regeneration alone is neither sufficient to produce beneficial outcomes, nor is it always a ''good'' in itself: successful regeneration requires the maintenance of appropriate specialization.[9]

The added-on concluding sentence, ''Also, when cells divide they are only able to produce daughter cells which are similar to themselves,'' draws attention to this ambiguity of regeneration: more of the same is both good and bad, enough and not enough. The axes of regeneration and deterioration, and identity and difference, are both represented by the figure of the unilineal descent group, comprised of daughter cells. The next paragraph explains why the search for both dutiful and deviant daughters has proven to be so important:

> This is why the discovery of the role and properties of stem cells (known as *multipotent* when they can form several types of cells and *pluripotent* when they can form all of them) brings new and exciting prospects. Tissues formed from cells so specialised that they are virtually unable to be renewed could—if damaged—be ''reconstructed'' through the addition of a sufficient number of stem cells. In any event, that is the underlying idea of what is hoped is a new field of medicine in the making: regenerative medicine.[10]

Here, some of the functions of cells are spelt out in terms of the desirable and undesirable equations through which the viability, and profitability, of stem cell economics are being imaged and imagined: in a steady state, multiplication-plus-specialization, and division-minus-variation, equate to positive growth; however, this can transform into a state of deterioration, in which multiplication-plus-specialization (variation or no variation) equates to limited growth (or cessation). It is because specialization equals deterioration (over time) that a new source of renewable, specialized cells equates to *positive growth in perpetuity* – the ultimate bio-outcome.

Stem cells are important *because they are exceptional*. They are, according to the article cited above, ''the exceptional exception'' precisely because they offer unique regenerative capacities:

> Stem cells are a double exception to the rule of cell specialisation – hence their interest. Not only are they able to reproduce identically (and exceptionally quickly) throughout their lives but, more importantly, they are able to differentiate to form several (sometimes in very large numbers) distinct cell types.[11]

Stem cells, then, generate interest because they are multi-talented multipliers. ''Not only do they reproduce identically,'' but they ''are able to differentiate.'' In this account of stem cells, they are doubly valuable because they are a ''double exception to the rule of cell specialisation.'' This makes them both doubly useful, and exceptionally interesting.[12]

What is evident in even the briefest descriptions of stem cells are emergent models of human life in which who we are, and what we are made up of, can be extracted and utilized in ways that are not only about the reuse of existing parts, *but their redefinition*. The redefinition of the human as a quantity of cells with different qualities is then further elaborated in terms of the ability to break down cellular capacities into specific functions, *and to redesign them*. The ways in which this emergent global cellular functionality is at once technologically assisted and ''natural'' repeats a common conflation, but in a new guise. At this early stage of stem cell research, a dominant language of cellular capacity is closely linked to the extraction of specific functions and effects. Extracted from the body, cellular functionality has become a field of property speculation, in the sense that cells are seen both to *have* new formal properties, and to *be* valuable as new property forms; that is, as various forms of biocapital. The language of engineering and design, applied to the fundamental units of the body – cells – offers the prospect of bespoke life forms which can be used to augment various kinds of life as we know it, including our own.[13]

In these ways, the RTD description of stem cells is typically global, referencing a global (all encompassing) set of future applications, and a global view of humanity (all of whom share a universal biological condition). Stem cells are also regionalized and localized in the description of several European projects at the close of the article, accompanied by a portrait of Eurocord, Europe's umbilical cord blood bank based in Paris: ''Europe seems determined not to miss the stem cell train. The European Union already funds – to the sum of 27.4 million euro – 15 research projects involving 117 laboratories in countries from Finland to Portugal.''[14] A description of the specific cell types under investigation, such as hematopoietic cells (the precursors of blood cells), completes the *compression of scale* from worldwide, panhuman applications of stem cell technologies, to major economic regions (the EU), to specific national projects, to distinct cell types, from which cell lines will be purified. The literacy that allows a movement, unfolding, or a ''making sense,'' within and across all of these differently scaled contextual registers is also part of what is meant by the global biological.

Cellular Capacity

In classic biological terms, ''differentiation'' has always been associated with temporal progression and with the acquisition of form and shape. Together, these processes result in the development of both organisms and species, and it is to the mechanisms of generation, growth, and development that most of biological thought was directed until the advent of molecular genetics. ''Differentiation'' is a term derived from embryology and used to describe the way in which a body acquires specific parts out of a single undifferentiated whole. It describes the ways in which cells acquire specialized functions, and ''to differentiate'' is defined in the *American Heritage* dictionary as ''to undergo a progressive developmental change to a more specialized form or function. Used especially of embryonic cells or tissues.''[15]

At the close of the 19th century, in his now-famous treatise on ''The Continuity of the Germplasm,'' August Weismann asserted that all the genetic material is contained in the cell nucleus and he forcefully rejected the idea of inheritance of acquired traits in any form.[16] Weissman had already explicitly stated that ''heredity is brought about by transmission from one generation to another of a substance with a definite chemical and, above all, molecular constitution.''[17] By the mid-20th century, following the discovery of the structure of the double helix by Watson and Crick, Weismann's continuity theory was recapitulated with even greater molecular authority in Crick's ''central dogma'' of molecular genetics, which stated that RNA makes DNA makes protein. This dogma expressed, in molecular terms, an affinity between differentiation and development that emphasized the one-way, irreversible, and progressive nature of both evolution and cellular specialization, which were united by the coding function of DNA.

According to the historian of biology Ernst Mayr, Weissman believed there were two possible relationships between genetic material and individual development.[18] Either all of the genes were divided up during embryogenesis, and then ''turned on'' to direct each specialist part of development, or all of the genetic material was contained in each cell, but was selectively activated to produce cellular specialization, or differentiation. Although evidence was established during Weismann's lifetime of continuity of the chromosomes, it was not until the 1930s that this idea came to be more widely accepted.[19] Shortly following the rediscovery of Gregor Mendel's experiments in 1900, according to Mayr, the embryologists Theodor Boveri and Walter Sutton began to combine genetic arguments about hereditary transmission with new kinds of cytological evidence, founding the subdiscipline of cytology. Bridging the gap between theories of hereditary transmission and the role of hereditary material in the process of individual development, Boveri and Sutton are historically credited with having offered the first substantial evidence of ''the individuality and continuity of the chromosomes,''[20] which later became known as the *Sutton–Boveri chromosomal theory of inheritance*.[21]

Whiggish histories of biology such as Mayr's rely heavily on the assumption of a progressive reconciliation of elementary components of biological thought over time, leading to the eventual alignment of very broad approaches, such as evolution and embryology, so that an overall (Darwinian) complementarity is achieved. However, it is precisely the kinds of gaps described by Mayr that separated the researchers concerned with heredity-as-inheritance and those who investigated the relationship between inherited material and development in the early 20th century which have been redefined, and in many ways broadened, with the advent of molecular genetics. Today, fewer biologists have a general zoological approach to living systems, and many more have highly technical specialities that require very different kinds of interdisciplinarity; for example, between computation and biology. From this perspective, it is not so surprising that some of the fundamental laws and properties that shaped the emergence of modern biology, and indeed had become nearly sacrosanct, are undergoing substantial revision.

The increasing unity between ideas about development, differentiation, and cell division reached what may have been its culminating coherence in the late 20th century. In symphonic harmony, these processes were all seen to work together to a very considerable degree and, in a sense, reproduced each other in their movements. Despite obvious problems with Darwinian models, highlighted by provocateurs such as Steven Jay Gould, evolution, inheritance, and development worked within a system that favored recapitulation of certain key principles and forms. An economy of loss governed all of them. Evolution is, in Darwinian terms, dominated by extinction. Most species fail, and it is only the few successful adaptees who are favored by the hand of natural selection, all of whom are linked within a single system of descent that connects everyone to shared common ancestors, who survive. Similarly, differentiation is produced by the loss of cell functionality, specialization being conceived as an irreversible tapering off of genetic potential as an organism develops from simple to complex.

Stem cell technology offers not only to compensate for the losses inherent in cellular specialization, such as aging, disease, or organ failure, but to reverse them, and introduce an economy of growth in perpetuity. Stem cells are not only imagined as a supplementary source of tissue, but as a technology that can reprogram the cell in a way that transforms what were formerly thought of as its inherent one-way tendencies to decline into capacities for unlimited production. Stem cell technology, therefore, is not only offering new, lucrative, and ''exciting'' ways to harness the productive powers of the cell: what is most ''interesting'' about stem cell technology is that it is offering *a new means of creating them*.[22]

The Dolly Technique

In the experiments that led to the birth of Dolly the sheep, Ian Wilmut and his team at the Roslin Institute in Scotland made one of the major discoveries that has led to the development of the stem cell industry when they confirmed that the nuclear DNA of an adult cell could, in effect, be ''reprogrammed'' to go back in time and become totipotent, as if it were an embryonic cell, capable of forming all of the tissues in the body. Before the birth of Dolly the sheep, this was considered to be biologically impossible, because it contradicted one of the most fundamental laws of biology, namely the one-way process of specialization. Wilmut's team discovered that it is the very powerful cytoplasm, or cellular soup inside of the ovum, which, as he put it, ''tells the DNA what to do.'' The egg cell used to make Dolly came from a Scottish Blackface sheep, and was, like all mammalian egg cells, 100 times larger than the mammary (adult) cell, from a white Finn Dorset sheep, with which it was fused.[23] The idea was to ''trigger'' the Finn Dorset DNA to make a sheep identical to its nuclear genetic mother (a ''clone''). In sheer physical terms, the Blackface egg overwhelmingly dominated the cellular environment of the two cells once they were fused together with a jolt of electricity, which dissolved the cell wall of the microinjected Finn Dorset mammary cell. Wilmut describes the egg cytoplasm

as a kind of super-computer that ''reprogrammes'' the DNA of the mammary cell to recommence development *as if it were an embryo* (see Figure 4.1).

Reversing the usual determinism attributed to DNA as the ''blueprint'' or master plan for cellular development, Wilmut's findings introduced an entirely new principle into reproductive biology, which is that DNA can, in a sense, be reactivated.

Wilmut was undoubtedly overstating the case when he concluded from the Dolly experiment that we have entered what he calls ''the age of biological control'' in which, in effect, nothing is ''biologically impossible'' anymore. However, as he states in the following passage, that term has certainly become a more unstable guarantee:

> As decades and centuries pass, the science of cloning and the technologies that flow from it will affect all aspects of human life—the things that people can do, the way we live, and even, if we choose, the kinds of people we are. Those future technologies will offer our successors a degree of control over life's processes that will come effectively to seem absolute. Until the birth of Dolly scientists were apt to declare that this or that procedure would be ''biologically impossible''—but now that expression seems to have lost all meaning. In the 21st century and beyond, human ambition will be bound only by the laws of physics, the rules of logic, and our descendants' own sense of right and wrong. Truly, Dolly has taken us into the age of biological control.[24]

In overstating his case, Wilmut deliberately ups the ante of moral responsibility in the area of biological innovation. The implication of his statement is that the idea that something is biologically impossible is not going to be a very reliable guide in the future, and should not be cause for complacency. As a highly socially concerned and publicly active scientist, Wilmut is not being grandiose so much as urging caution, and expressing his eagerness to promote more substantial social,

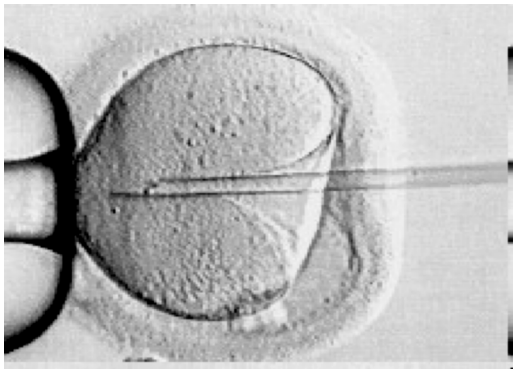

Figure 4.1 Microinjection of a human egg cell. In this image, which I argue elsewhere has become iconic of what I am calling in this chapter ''the global biological,'' a new topography of ''life itself'' is characterized by the flattened focal frame of the cell's transluscent interior, out of which protrude the two ''helping hands'' of science: the suction, or ''holding'' pipette, and the microinjection needle, the source of new genealogical flows.
Source: Sue Pickering

ethical, and political discussion of how science should be regulated in the future, because, as he sees it, science is opening doors faster than anyone might have expected.

Wilmut's finding has led to considerable debate about the importance of the Dolly experiment within the scientific community itself. Wilmut and his own team would be the first to admit the term ''clone'' is very unhelpful, both because it is inflammatory and because it is scientifically inaccurate. Dolly would be a ''proper'' clone if she had been produced from *the adult cell alone* – a possibility the Dolly experiment may bring closer, but which it came nowhere near achieving. Since Dolly was created from a fusion of two cells, she is not accurately described as a clone – only the fact that her nuclear DNA came from one parent supports this view. More technically, the question of differentiation, and what happened to it, exactly, during the Dolly experiment, remains unclear. Initially, Wilmut and his team described the process by which the Finn Dorset mammary cell was ''reprogrammed'' as ''dedifferentiation,'' because it was no longer functioning as a specialized mammary tissue cell, but as a germ cell. This was the ''reversal'' the Dolly experiment was seen to confirm. However, Wilmut has since suggested that ''dedifferentiation'' is the wrong term, since he suggests the Dolly experiment shows that adult cells do not ''differentiate'' irreversibly to begin with, and that specialization does not preclude recapacitation of ''lost'' functionality.[25]

While the importance of the Dolly technique remains in dispute, it has been widely interpreted as a formidable feat of biological experimentation that, at the very least, points toward dramatic new possibilities for harnessing cells as productive units. What has become the agreed position is that the technique used to make Dolly, somatic cell nuclear transfer, now shortened to cell nuclear transfer, or CNR, is extremely useful and promising. Already several versions of CNR have been developed, and a major battle over patenting its various components is under way. Attempts to replicate the Dolly experiment have been undertaken all over the world, on various species, many of which have been successfully ''cloned.''[26]

Economically, the success of the Dolly technique, and its implications for stem cell technologies, have been seen to offer the greatest commercial potential yet of any of the post-genomic bioindustries. The Human Genome project was never imagined to be very profitable itself, but was justified as a strategic investment in the development of biotechnology. Initially, diagnostic tests created from the ability to target specific genes were imagined to be a major consumer market, and to an extent this has been the case – for example, with Myriad Genetics' breast cancer test, on which it holds a patent. Gene therapy, another major application, has proved far more clinically challenging than initially imagined, and has led to several highly publicized and controversial deaths. Stem cell technology – with its enormous range of applications – has been seized upon by the biotechnology industry as a highly desirable R&D investment area. If we are not yet in the age of ''biological control'' envisaged by Wilmut, life is nonetheless substantially altered after Dolly.[27]

British Biology

Summarizing the scientific developments I have just described above, the British House of Lords Select Committee Report on stem cell research, published in February 2002, claims that:

> Until recently it has generally been considered that in mammalian cells the process of differentiation is irreversible. However, it has been demonstrated in animals that it is possible to reprogramme (''dedifferentiate'') the genetic material of a differentiated adult cell by CNR. Following this seminal finding, many studies have also suggested that adult stem cells may have greater ''plasticity'' than previously suspected: they may be reprogrammed to give rise to cell types to which they normally do not give rise in the body. The potential of specialised cells to differentiate into cell types other than those to which they normally give rise in the body is little short of a revolutionary concept in cell biology. It has significantly increased the possibilities for developing effective stem-cell based therapies.[28]

In this description, the term ''dedifferentiation'' is retained, and equated with reprogramming, and the term ''plasticity'' is used to describe what is revolutionary about the CNR technique. Closely following scientific accounts of stem cell technology and nuclear transfer techniques, such as those provided by members of the Roslin Institute, the House of Lords' description of the basic biological ''breakthrough'' behind stem cell research endorses the view that it offers radical new possibilities, and emphasizes their therapeutic potential.

The House of Lords Report offers a thorough consideration of stem cell research and concludes that it should be ''strongly encouraged by funding bodies and the Government'' in the U.K.[29] Research on human embryos is described as ''necessary, particularly to understand the processes of cell differentiation and dedifferentiation'' and the report endorses the CNR technique, stating that ''there is a powerful case for its use . . . as a research tool to enable other cell-based therapies to be developed.''[30] The report recommends the establishment of a British stem cell bank to be ''responsible for the custody of stem cell lines, ensuring their purity and provenance''[31] and it concludes that existing mechanisms for regulation of research, and mechanisms for procuring informed consent from donors, are sufficiently robust to accommodate the new developments in the area of stem cell research.

The House of Lords would not have appointed a Select Committee to consider the issue of stem cells were it not a matter of significant national concern, while, in keeping with over 15 years of debate on related matters in Parliament, the outcome of the Committee's deliberations is extremely permissive – indeed almost radically liberal.[32] It is a more comprehensive and substantial endorsement of stem cell research than has been produced in any other country, including Sweden or the Netherlands, which also have very liberal legislation in this area.

Although the Committee acknowledges that it was only able to give limited attention to the role of commercial interests in stem cell research, it devotes an

entire section of the report to this concern, and acknowledges that it has ''been aware throughout that commercial interests could, and to some extent already do, play an important role in the development of such research.''[33] It also acknowledges that ''biotechnology is a growth industry,'' citing an Ernst & Young report that by the end of 2000 ''the total value of Europe's publicly quoted biotechnology companies stood at 75 billion Euros, compared with 36 billion Euros a year earlier.''[34] The Committee adds that

> According to a separate report, the United States, which has the largest number of companies in this field, market capitalisation of publicly quoted biotechnology companies fell over the same period (from $353.8 billion to $330.8 billion), but the number of public companies increased by 12.6%, and in the two years to June 2001 biotechnology stocks outperformed internet stocks on the Nasdaq index.[35]

These references, along with acknowledgment that the U.K. ''has by far the most public biotechnology companies'' in Europe, and that ''investor interest is considerable and evidently based on the assumption that future profits may be significant'' confirm the extent to which the British government recognizes the importance of economic growth in the biotechnology sector as a national priority. This is further underlined by reference in the House of Lords report to China and Singapore, which ''provide examples that deserve special mention'':

> In China the government has encouraged a number of universities to invest heavily in stem cell research. In doing so universities have attracted not only public funds but investment by private companies like the Beijing Stemcell Medengineering Company. Leading Chinese researchers are often U.S.-trained and have links with American laboratories. In Singapore, the Economic Development Board has provided initial finance for the Singapore Genetics Programme; it is said that by 2005 some $7 billion dollars will have been invested in relevant research. In both China and Singapore there is concern with ethical issues but also an interest to maintain the competitive advantage gained by light regulation.[36]

Between the lines of this description clearly lies a recognition of the intensely competitive economics of the global biotechnology sector, as well as a recognition of possible tension between ''concern with ethical issues'' and ''the competitive advantage gained by light regulation.''

To date, the U.K. has successfully promoted its highly regulated but unusually permissive biotech R&D environment by emphasizing its stability, in large part due to high levels of public confidence in the government's ability to regulate developments in the life sciences. This scene was largely set through the debates over IVF and embryo research that began in the mid-1980s, and resulted in the establishment of the Human Fertilisation and Embryology Authority (HFEA) in 1990. Public confidence in the HFEA remains high, and the combination of high public trust and robust regulatory guidelines is a competitively advantageous recipe for long-term R&D, which the British government is keen to protect and maintain. That a technique

developed by an agricultural research facility largely concerned with livestock breeding has in such a short time become the lynchpin of an emergent global biotechnology industry, which, because it increasingly relies on human, not ovine, embryos, will soon come under the regulatory aegis of a Licensing Authority established to oversee reproductive medicine in the U.K., returns us to the theme of the complex hybridities, conjunctures, and mobilities that emerge in the stem cell field.

Stem Cell Futures

As part of an ESRC-funded ethnographic study of preimplantation genetic diagnosis in the U.K., conducted between 2001 and 2003, I interviewed Austin Smith, one of the U.K.'s leading stem cell scientists, in Edinburgh in March 2002.[37] An important finding of this study was the extent to which issues and concerns about stem cells had become intertwined with the cloning debate, genetic diagnosis, genetic screening, and the regulation of assisted reproductive technologies such as IVF during this period.[38]

The Centre for Genome Research, of which Smith is the Director, is based in an enormous science campus, on West Mains Road, a mile north of the city center. The historic campus is a hodge-podge of vast scientific facilities, varying in their architecture from 19th-century zoological collections housed in ornate stone edifices to logo-emblazoned ready-made warehouses large enough to house an Olympic-size swimming pool. Austin Smith's facility is vintage British public sector, with acres of linoleum, nondescript furnishings, and a plain, functional decor. He is a small, boyish figure with large blue eyes and an air of calm precision. He speaks so slowly and clearly, enunciating so precisely, it would be possible to transcribe his words as he spoke them.

I was unaware at the time of the interview, on March 7, that less than a week later, on March 13, Austin Smith would be the senior author of one of two articles published by the journal *Nature* casting doubt on many of the dramatic findings claimed for stem cell research.[39] If I had known this, I would have asked some additional questions. As it is, the *Nature* article sheds an interesting light, all the same, on his comments about stem cells.

Having previously interviewed Ian Wilmut, and conducted fieldwork at the Roslin Institute 15 miles south of Edinburgh (and also part of the university), I was particularly interested in the ''dedifferentiation'' question. Wilmut had suggested to me that he no longer considers the term appropriate, although, as the House of Lords Report demonstrates, it continues to be widely used, and has become a term that is in some ways defining of the CNR technique:

> SF: In terms of the language of what's happening to the cells, Ian Wilmut says that initially he used the term ''dedifferentation'' but then he came to feel it was an inappropriate term, because they didn't differentiate to begin with, and I wondered what you think about that term?

AS: Well, dedifferentiation means to me, its fairly precise meaning is just a loss of differentiated character of a cell, or of a group of cells, but it's of the same cell. So I don't think dedifferentiation actually has anything to do with cloning. It's totally inappropriate to use that word. But people did use it for a while, for a little bit, at the start, because they really didn't know how to describe the effects. But reprogramming is the correct terminology . . . Once you start doing a nuclear transfer experiment it's not the same cell, so I don't think you can talk about dedifferentiation . . . They didn't have cells, not in nuclear transfer. They're talking about this idea that there might be adult stem cells that could make other types of cells. So then it's a transdifferentiation, well, it is if it occurs.

The term ''transdifferentiation'' is the one preferred by the Royal Society, the U.K.'s leading scientific association, whose contribution to the stem cell debate in the form of their published literature uses that term throughout. For Smith, it is not possible to analyze any differentiation process ''in itself'' *once a cell has been combined with another cell*, which is what the Dolly technique involved. The fact that you have mixed a cell with another cell, to create a cell fusion, by definition, in his terms, means that you can no longer speak about cellular properties, since you are talking about a multicellular process.

As it turns out, this is exactly the message Austin was hammering home in the *Nature* article, which, by many, is considered a ''blockbuster'' for the industry.[40] Working with mouse cells, Smith and his colleagues mixed fluorescent embryonic (ES) cells with bone marrow and brain cells – that is, they mixed (totipotent) embryonic cells with adult stem cells (multipotent progenitor cells). This experiment precisely mimicked earlier research that had concluded that adult stem cells could be made to ''go back in time,'' just as the Dolly mammary cell had apparently done. However, although the adult stem cells in Austin's experiment *appeared* to revert to the ''blank slate state'' of early embryos, it was revealed by further testing that they had simply *merged* with the ES cells, creating cells with two sets of chromosomes – one effectively ''masking'' the other. According to Robert Lanza, Medical Director of Advanced Cell Technologies in Worcester, Massachusetts (the main competitor to Geron-Bio-Med, the merged Geron/Roslin company that now holds the license to the Dolly technique), Smith's research ''calls into question almost all of the data generated using stem cells.''

Here again, the difference between how cells behave when they are merged and how they operate as single units, or as lineages of single cells, is the main target of Smith's concern. This raises a broader issue about which he spoke at some length during our interview, known as ''characterization'':

SF: In terms of getting a cell line that is *characterized*, that would be one that reliably produces a type of cell that will hold its identity and can be identified as having particular kinds of traits, is that what you would say?

AS: Yeh, I mean, well obviously there are many, there will be many levels to characterization. I mean it's up, it's different for different purposes for the scientist. You might want to set different thresholds, or criteria. I mean I think you'd really have to give me a specific example for me to be able to say, well, look.

SF: Yeh, OK, well, when we were at a medical conference in London on the day the stem cell licensing announcement was made, there was a lot of discussion about how many human embryonic cell lines there are, and people were saying there are about 60 or 70 that are registered, and maybe now there are ten more from Sweden, and one of the leading IVF practitioners stood up and said well there may be that many cell lines but only a very few are *characterized* and *none* of these are in the UK?

AS: Well, now, the answers are more [laughter], they're a little complicated. Firstly, there are some cell lines in the UK, but they haven't been made here, the cell lines have been brought in from the US. But there are not, er, there are not cell lines yet that have been produced in the UK. So the issue of the 64 cell lines basically comes up because what the NIH did, er, the 64 is basically a made-up number. It was a device to get a green light for stem cell research. And so the NIH issued a call for people to register. So people basically registered if they, er, had any ideas they thought they might be making embryonic tissue: because then if they did get anything it would be registered. That's why the ''64 cell lines'' has to be treated with a pinch of salt. Some of these organizations may subsequently come up with cell lines, or they may yet do, and they will be able to make out that they had them at the time of registration, so that's one issue. Some of them just don't exist, and are just a prospective thing. The other characterization issue is cell lines or cultures that were in the process at that time, but which may not have gone onto lives as cell lines. And since a lot of it is not published, there is really no way to know what the *status of those lines is*. Again, you know, people will just inflate the numbers so a lot of these things will not transpire to be cell lines. So this is where it gets even more complicated, because how do you characterize the cell lines without any available data? All of the groups are assigning slightly different properties to cells. Until you have a reasonable number of competent researchers who are not tied up with issues about companies, until you can do some proper comparative evaluations, *you can't really say this is hard science*. You can't say this is what the fundamental properties of these cells are as opposed to what you would call their individual polymorphic properties.

According to Smith, in other words, it is very difficult even to say what cell line characterization will be, because so many cell lines have such a speculative future. Even if they are well established, they may not continue to reproduce reliably. At this stage, he reported in our interview, ''you can set criteria, but they would be arbitrary.'' Since different researchers are using different culture methods, it is very hard to standardize, on top of the fact there are so few human cell lines to compare. Looking back at the history of murine cell lines, Smith pointed out that it took ten years to learn best how to culture them, and another ten to decide how to characterize them. ''People just seem to have forgotten all of that,'' he noted.

The apparent stability of the ''blank slate state'' adult stem cells that Smith used for the *Nature* article reproduces an *effect*, an experimental *artifact*, that led to what Smith considers to be a possible source of major scientific error. Through a kind of experimental mimicry, Smith and his team sought to expose the kind of premature claims that could impede progress in achieving either standardized culture methods or anything like stable criteria for the standardization of human cell lines. In Smith's

view, the history of standardization of mouse cell lines sets a noteworthy precedent – it was not an achievement that occurred either quickly or very efficiently.

It is not surprising it is difficult to standardize cells that are being cultured into lines *precisely because* they are ''exceptional,'' or even ''doubly exceptional.'' While Austin Smith's concerns about the industry are substantial, and his *Nature* article is an elaborate staging of ''what can go wrong,'' it is also clearly aimed at making the industry more robust and accountable, and thus building it on a stronger foundation. Significantly, the experiment also demonstrates the danger of assuming research can go forward using only adult stem cells – a major argument used by the anti-embryo research lobby to restrict stem cell research to adult cells alone, precisely on the basis of their newfound ''plasticity.'' Hence, although it is highly critical of other studies, Smith's research is clearly protective toward the research field in general.

Cell Cultures

Among the multiplicities of stem cells are their identities as scientific, corporate, national, and public entities – in all of which capacities they are both unstable and contested. As individual lines, they have an ambiguous existence in relation to their collective future as either a research tool or as life forms. The cell lines that will eventually emerge into an orderly, characterized, typologized, patented, licensed, regulated, and marketable collection, such as the stem cell bank proposed in the U.K., will comprise a unique population of immortal, human life forms, whose existence, or origin, is technoscientific, organic, and historical.[41] Like genes, they currently elude stable characterization, in several senses of that term. At the same time, they have become a powerful global biocultural population, the imagined future of which already exercises a strong shaping force on scientific research, health priorities, commercial investment, and technological innovation. Learning how to ''culture'' stem cells has an additional meaning at the level of a report such as that prepared by the House of Lords, which, like the feeder cells necessary to grow cell lines, is creating fertile social and political soil for their successful cultivation. Cultivating public opinion in order to create a robust climate for bio-commerce turns out to be one of several generative activities out of which stem cells will be hot-housed into fruition.[42]

In striving to depict the ''cultures of technoscience'' out of which stem cells emerge as one of many multi-talented progeny, it is necessary to move beyond the ''culture of no culture'' that Sharon Traweek established as a kind of ground zero for the ethnography of laboratory life.[43] We have become increasingly familiar with the assemblages and artifacts with ''lives of their own'' that populate the process of technoscientific innovation. We have also come to take for granted the ease of pointing out the nature–culture hybrids that make a nature–culture distinction less and less meaningful. It may be that Paul Rabinow is right; it is no longer very meaningful to refer to culture at all, any more than it is to imagine we are now in ''the age of biological control.''[44]

However, if either biosociality or bioculture, or for that matter biocapital, are to become more robust analytic concepts, with which a certain amount of critical work can continue to be done in either a sociological or an anthropological vein, we might want to think about ''culturing up the culture medium,'' as it were. Borrowing the trope of traffic in analogies from Strathern's work on new reproductive technologies, it may be worth thinking about how the culture concept ''travels back'' *out of* the Petri dish. It is, after all, culture in the sense of cultivation, or horticulture, from which anthropology borrowed the term to begin with.

In that case, cell cultures ask for both an ingredients list and a recipe for preparation. The stem cells ''in culture'' at the moment are being ''fed'' by the production of norms, principles, values, and laws, as they are also being ''nurtured'' by venture capital investments, media coverage, and public-sector funding. Certainly stem cells are being carefully tended by highly trained scientists, who are trying to teach them basic obedience lessons in state-of-the-art laboratories from Singapore to Silicon Valley. They are being watched over carefully by presidents, prime ministers, and innumerable professional organizations concerned with their welfare, their rate of population growth, and their international travel arrangements. Few offspring have their provenance, ancestry, reproductive behavior, or genetic composition more carefully scrutinized by highly trained custodians.

Like the enormous populations of frozen embryos that have become official legal entities, with protected status under the law of most countries, stem cells and their immortal progeny are increasingly becoming part of public, national, and civic culture. Like Dolly, they will eventually have names, and some will undoubtedly go on to enjoy worldwide celebrity and commercial success. In addition, they are destined to become parts of future people, carrying the genetic identities of their founder cells into new kinds of organic union with the as-yet unborn organ failure cases of the next generation.

The cellular trajectories marked by the passage of stem cells into the future forge a corporeal path out of scientific desire in ways that challenge existing current models of biological scale, temporality, and form. Moreover, human embryonic cell lines are ''related'' to us by genealogical and genetic links that challenge the meaning of relation, or relative, in the same way they establish excessive connections among themselves. Their lack of calibration awaits proper, and proprietary, denomination, according to criteria only their future systematic comparison will yield. For this reason, and all of the others, stem cell lineages are inevitably curious doppelgangers for their human cultivators, whose existences are being mutually transformed by new kinds of biocultural connections.

Appendix A

In one of the most concise accounts of embryology currently available, combining medical, historical, and evolutionary issues under one cover, the British embryologist Lewis Wolpert

provides a definition of stem cells that clarifies the difference between stem cells and embryonic stem cells, as well as the two types of daughter cells:

> All the cells in the blood come, remarkably, from just one special progenitor cell – the multipotential stem cell. The essential nature of a stem cell is that it is self-renewing and, as its name implies, the source of other cells. When the stem cell divides, one of the two daughter cells may go on to give rise to other types of cell, whereas the other daughter cell remains a stem cell, capable of dividing again and always giving one daughter to diversification. Thus a characteristic feature of stem cells is this asymmetry; one daughter keeping the stem cell character, the other proceeding along a pathway of diversification. In principle, because stem cells are self-renewing, they are, unlike the cells they generate, immortal.[45]

Notes

1 Kerry Capel, ''In Stem-Cell Research, It's Rule Britannia,'' *Business Week Online*, April 4, 2002, p. 1.

2 Ibid., p. 2.

3 The article goes on to claim that ''Britain is the only country on the globe with a regulatory structure in place that provides a clear road map for both public- and private-sector research on embryonic stem cells'' and points out that the U.K. will house the world's first stem cell bank – issues I will be discussing in more depth further on in this chapter.

4 Sarah Franklin, *Embodied Progress: A Cultural Account of Assisted Conception* (London: Routledge, 1997); Marilyn Strathern, *Reproducing the Future: Anthropology, Kinship, and the New Reproductive Technologies* (Manchester: Manchester University Press, 1992).

5 In describing the post-genomic shift from structural to functional genetics, Keller cites geneticists Hieter and Boguski's definition of functional genomics as: ''the development and application of global (genome-wide or system-wide) experimental approaches to assess gene function by making use of the information and reagents provided by structural genomics.'' See Evelyn Fox Keller, *The Century of the Gene* (Cambridge, MA: Harvard University Press, 2000), p. 7. This is not strictly a definition of how stem cells are being used, but there are strong family resemblances, and this is one of the ways in which I am using the idea of the ''global biological'' in this chapter.

6 Sarah Franklin, Celia Lury, and Jackie Stacey, *Global Nature, Global Culture* (London: Sage, 2000).

7 Margaret Lock, ''Deadly Disputes: the Calculation of Meaningful Life,'' in *Living and Working with the New Medical Technologies*, M. Lock, A. Young, and A. Cambrosio, eds. (Cambridge: Cambridge University Press, 2000); Margaret Lock, *Twice Dead: Organ Transplants and the Reinvention of Death* (Berkeley: University of California Press, 2002).

8 European Commission, ''Stem Cells: Promises and Precautions,'' *RTD info* (Brussels) 32, 2001, p. 4.

9 Hannah Landecker, ''On Beginning and Ending With Apoptosis: Cells and Biomedicine,'' in *Remaking Life and Death: Toward an Anthropology of the Biosciences*, Sarah Franklin and Margaret Lock, eds. (Oxford: James Currey, 2003), pp. 23–59.

10 European Commission, ''Stem Cells,'' p. 4.

11 Idem.

12 ''Stem cells'' is a confusing term because it refers both to *embryonic cells* (ES cells, which are taken from early, undifferentiated embryonic tissue) and to *undifferentiated progenitor cells* derived from specific types of tissue (such as blood and bone marrow). ES cells are considered to be ''totipotent'' – i.e., capable of producing any tissue in the body – whereas stem cells taken from blood or marrow are ''multipotent,'' meaning they can form most, but not all, tissue types. ES cells are the ''ultimate'' stem cells, but, in a sense, they are not really stem cells at all, since that term more accurately describes the undifferentiated progenitor cells that produce specific cell types. See further in Appendix A.

13 Linda F. Hogle, ''Life/Time Warranty – Rechargeable Cells and Extendable Lives,'' in *Remaking Life and Death: Toward an Anthropology of the Biosciences*, Sarah Franklin and Margaret Lock, eds. (Oxford: James Currey, 2003), pp. 61–96. It is important to note that the productivity of stem cells is described in terms of mimicking, copying, or duplicating the *in vivo* functions of cells. In this way, cellular modelling, or simulation, forms part of a structural coupling: it is the *in vitro* version of an *in vivo* process. I have not developed in this chapter the question of what kind of productive economy results from this structural coupling, but I have explored elsewhere the ''Warhol effect'' of cloning on the traditional biological model of development as growth and differentiation, arguing that the mode of production cloning inaugurates is digital. See Sarah Franklin, *Dolly Mixtures: Cloning, Capital and Immortality* (forthcoming).

14 European Commission, ''Stem Cells,'' p. 7.

15 *American Heritage Dictionary*, 3rd edition (1992), p. 521.

16 August Weisman, ''The Continuity of the Germplasm,'' in *Das Keimplasma* (Jena: Gustav Fischer, 1892).

17 August Weisman, *Essays upon Heredity* (Oxford: Clarendon Press, 1889), p. 167.

18 Ernst Mayr, *The Growth of Biological Thought: Diversity, Evolution, and Inheritance* (Cambridge, MA: Harvard University Press, 1982).

19 Ibid., p. 749.

20 Ibid., p. 747.

21 A useful and comprehensive source of information on embryology can be found at the virtual embryo website (http://www.ucalgary.ca/UofC/eduweb/virtualembryo/index.htm).

22 The way stem cells are being redefined as productive mechanisms brings to mind comparisons to early industrialization in the north of England; for example, in the way rivers came to be seen as energy sources, and could be redesigned through sluices and weirs to drive waterwheels.

23 The mammary cell from the Finn Dorset sheep came from an animal that had died six years previously, and whose cells had been frozen in culture by PPL therapeutics, which both funded the Dolly experiment and contributed many of the materials for it, including cells. PPL is housed next to the Roslin Institute, just outside the village of Roslin, in what has become the Roslin Science Park. Roslin Biomed was founded as a public–private partnership to pursue commercially profitable research, and it is Roslin Biomed that later merged with the Geron Corporation in the United States, to which they have granted an exclusive license to the patented Dolly technique.

24 Ian Wilmut, Keith Campbell, and Colin Tudge, *The Second Creation: The Age of Biological Control by the Scientists who Created Dolly* (London: Headline, 2000), p. 17.

25 I first interviewed Ian Wilmut in 1999, which was the first time I had encountered this questioning of the dedifferentiation terminology. Since that time, Roslin has become

increasingly involved in stem cell research using human embryos, and they are likely to play a significant role in the application of their highly developed micromanipulation technology for sheep eggs to human embryos in the pursuit of basic understanding of cellular processes such as differentiation.

26 Royal Society, *Stem Cell Research and Therapeutic Cloning: An Update* (London: The Royal Society, 2000); Royal Society, *Stem Cell Research: Second Update* (London: The Royal Society, 2001).

27 Ironically, the ways in which experiments designed for sheep-breeding have led to the development of a huge industry for the replacement of human tissue fulfills one of Marx's many claims about the lessons to be learned from sheep-breeding in Scotland during the Highland Clearances, notably that "the British aristocracy, who have everywhere supersseded man by bullocks and sheep, will, in a future not very distant, be superseded, in turn, by these useful animals." See Karl Marx, "The Duchess of Sutherland and Slavery," *The People's Paper* no. 45, March 12, 1853.

28 House of Lords Select Committee on Stem Cells, *Stem Cell Research* (London: HMSO, 2002), p. 13.

29 Ibid., p. 48.

30 Ibid., pp. 48–49.

31 Ibid., p. 50.

32 The recent debates are very similar to those that took place in the late 1980s in their combination of elaborate discussion in great detail of embryology, and highly liberal, even radical, permissiveness. See Franklin, *Embodied Progress*; Sarah Franklin, "Making Representations: the Parliamentary Debate of the Human Fertilisation and Embryology Act," in *Technologies of Procreation: Kinship in the Age of Assisted Conception*, J. Edwards, S. Franklin, E. Hirsch, F. Price, and S. Strathern, eds. (London: Routledge, 1999), pp. 127–165.

33 House of Lords, *Stem Cell Research*, p. 32.

34 Idem.

35 Idem.

36 Idem.

37 The current project, which is being undertaken in collaboration with Dr. Celia Roberts in the Department of Sociology at Lancaster (who also took part in this interview), is primarily aimed to produce an ethnographic portrait of the changing role of genetic selection within reproductive choice by studying the technique of PGD at two of the U.K.'s leading PGD centers.

38 See Sarah Franklin and Celia Roberts, *Born and Made: An Ethnography of Preimplantation Genetic Diagnosis* (Princeton, NJ: Princeton University Press, forthcoming, 2005).

39 Qui-Long Ying, Jennifer Nichols, Edward P. Evans, and Austin G. Smith, "Changing Potency by Spontaneous Fusion," *Nature* 416, 2002, pp. 545–548.

40 I would like to thank Linda Hogle for longstanding and ongoing assistance and very reliable information on the stem cell field during the writing of this chapter, and other papers, on this topic.

41 The ways in which the identities of stem cell lines vacillate between a discourse based on origins, or lineage, and ownership, or provenance, extends many of the arguments developed in *Global Nature* about what Donna Haraway calls a "shift from kind to brand." See Sarah Franklin, Celia Lury, and Jackie Stacey, *Global Nature, Global Culture* (London: Sage, 2000); and Donna Haraway, *Modest_Witness@Second_Millennium: FemaleMan meets*

OncoMouse (London: Routledge, 1997). It also raises important issues about property and creation, such as those that have been the subject of Marilyn Strathern's most recent work on "emergent forms." See Marilyn Strathern, "Emergent Relations," in *Scientific Authorship: Credit and Intellectual Property in Science*, M. Biagioli and P. Galison, eds. (New York: Routledge, 2003); also Marilyn Strathern, *Property, Substance and Effect: Anthropological Essays on Persons and Things* (London: Athlone Press, 1999).

42 I have written elsewhere about the ways in which the Geron Corporation has "built in" a cultural/ethical component to their cell lines, in a variation of this generative, or fertilizing, effect. See Sarah Franklin, "Culturing Biology: Cell Lines for the Second Millennium," *Health* 5(3), 2001, pp. 335–354.

43 Sharon Traweek, *Beamtimes and Lifetimes: the World of High Energy Physicists* (Cambridge, MA: Harvard University Press, 1988).

44 Paul Rabinow, *French DNA: Trouble in Purgatory* (Chicago: University of Chicago Press, 1999).

45 Lewis Wolpert, *The Triumph of the Embryo* (Oxford University Press, 1991), p. 94.