# Chapter 1

## Quo Vadis?

> "Life is, after all, very much the same everywhere," said Miss Marple in her placid voice. "Getting born, you know, and growing up—and coming into contact with other people—getting jostled—and then marriage and more babies—"
>
> —Agatha Christie, *Murder at the Vicarage*

> At issue here is nothing less than taking seriously the question whether a science can depend on something like a circumcision.
>
> —Jacques Derrida, *Archive Fever*

> Seen from the point of view of death, the product of the corpse is life.
>
> —Walter Benjamin, *Origin of German Tragic Drama*

> Why, in short, do we seek, in the mobility of the whole, tracks that are supposed to be followed by bodies supposed to be in motion? A *moving continuity* is given to us, in which everything changes and yet remains: why then do we dissociate the two terms, permanence and change, and then represent permanence by *bodies* and change by *homogeneous movements* in space?
>
> —Henri Bergson, *Matter and Memory*

What are human beings, biologically, and where are they heading? Fossils indicate that human life has changed, or evolved, ever since vaguely human forms appeared several million years ago. Sequences of nitrogenous bases in the human genome also suggest that we have changed even more recently, since *Homo sapiens* became the only species in the genus *Homo* some tens

of thousands years ago. Nothing it would seem, short of extinction, will stop further change, but, by and large, scientists are not thinking about our present status as a species and are hardly contemplating how we might change in the future.

Biologists do not get serious for several reasons about characterizing human life as such and projecting its future. The most compelling reason is that there would be hell to pay from both left and right of the political spectrum. Charges of "Fascist!" would roar from the left, and accusations of "playing God" would fly from the right. Even political moderates might feel that anything remotely resembling a scientific statement on our present condition, to say nothing of a prognosis for our species' future, goes beyond the legitimate province of science. Biologists, therefore, limit their public pronouncements to the realm of nature, alluding to human nature and its evolution by natural selection as a remote consequence of being alive. Biologists wish us *bon chance,* to be sure, but they would sooner abandon us to chance than make serious assessments about our present position and potential.

I am not saying that we should, or can, correct all of our design flaws. For example, the crossing of our nasal and oral passages, which causes more deaths by asphyxiation than is generally realized, seems to have originated in early chordates and is probably too deeply rooted in vertebrate development to be readily altered. We can, nevertheless, improve upon ourselves in several respects, and I do not mean changing unattractive features. For example, birth could be made a lot easier, and a few vestigial structures, such as the appendix (which ruptures with devastating consequences) and breast tissue in males (occasionally the source of a rampant form of breast cancer) might be dispensed with without causing harm.[1] Above all, and what interests me here, is the great prize of achieving immortality. Eliminating old age and death is now within reach.

Imagine what life would be like if we did not get gray, lose hair, suffer tight and fragile skin, cataracts, diabetes mellitus, hypogonadism, osteoporosis, vascular diseases such as atherosclerosis (both myocardial and cerebrovascular), and age-related cancers? Wouldn't it be nice if we lived well and vigorously forever—in permanent, healthy, youthful life! I certainly do not mean growing old forever or even having access to some quick fixes by recall and restart buttons in the event of a crash. I mean a youthful immortality, built in, determined, reliable, and automatic!

I am not talking about believe-it-or-not poultices, miracle cures, and life-enhancing procedures currently in the pipeline for extending life. I leave that hopeful terrain to the perambulation of others.[2] Nor is *Becoming Immortal* an examination of the consequences of immortality for society and culture, of the bioethics of morality or immorality. I am confident that sociologists and

social workers, bioethicists, and moralists will pick up on immortality without my impromptu prodding. My objective here is merely to promote a course of research at the end of which achieving immortality becomes a feasible alternative to aging and death. Mortal *Homo sapiens* forma *mortalis* can give rise to immortal *Homo sapiens* forma *immortalis! Becoming Immortal* shows how.

Most of what I have learned and have to say on making us immortal will come as no surprise to biologists. I have ascertained why, biologically speaking, we are not immortal; why we did not evolve immortality; and why at present we cannot develop immortality. But the history of life on Earth suggests how large, important changes in organisms have come about outside of Darwinian evolution and canonical developmental theories, and how, therefore, a change as portentous as becoming immortal might be achieved in extant forms. My recommendations for a course of research leading to the technology required for immortalization is not a science fiction fabrication. It is a serious attempt to foment debate on "Quo vadis?"

## WHY BECOME IMMORTAL?

My guess is that the inspiration to become immortal is an extension of the awe experienced merely contemplating human life.

> What is the tie which conjoins these several aspects of mind [the human and the infrahuman] so inseparably? What is it else than "urge-to-live"? Human cognition may like the winged horse take at times its flights toward the stars and forget earth. None the less it is harnessed to life's car, whose charioteer is "urge-to-live" sublimed to "zest-to-live." It and its fellow-steeds, endeavour, will, emotion, passion or whatever else we call them pull under the same lash.[3]

Human life is so impressive that aging seems hardly worthy of it, and death seems a criminal affront.

Aesthetics and vanity aside, there is a more practical, and compelling, reason for becoming immortal: to effect prolonged space travel when Earth becomes uninhabitable and we have to abandon our solar system. Human beings will ultimately have to escape from Earth for any of a number of reasons, including those that have caused the mass extinctions of living forms in the past, namely "death from the sky" or "death from the mantle."[4] In our case, a still more likely scenario would seem to be death from ourselves.[5] I might also mention that the Sun will prove the ultimate and irresistible foe to life on Earth. If all goes according to schedule, the Sun will expand and

swallow up Earth in a few billion years, but before that, it will "wipe out the entire biosphere,"[6] and, long before that, the Sun's increased luminosity will end human life.

No matter where the disaster comes from, if we are to preserve human life, we will have to send representatives of humanity to solar systems capable of sustaining human life. That such a solar system exists somewhere in our galaxy is reasonably certain. Where it is, is yet to be discovered. The trip through space to reach this solar system will undoubtedly take hundreds if not thousands of years, even at a maximally feasible velocity. The human beings flying the spaceship will have to be sterile, because reproduction would be disastrous on a space ship with limited resources, and immortal, because accumulated wisdom would permit flight in the face of contingency and monitoring a cargo of mortal human beings in suspended animation. The logistical problems will be enormous, but immortality is nonnegotiable.

Here then is the choice for humanity: Become immortal or accept the inevitable end of humanity. My preference is to make the effort to create immortal human beings in time to move a sizable part of humanity to safe ground.

## HAS LIFE CHANGED?

In an age when cellular is as likely to refer to a mobile phone as a living thing, and clones[7] can be genes or ewes or even bunches of carrots and patches of strawberries on a field, one must be especially vigilant about the meaning of biology's terms. Even death, instead of being one of the two certainties of life (the other being taxes [thank you, Benjamin Franklin]), is now equivocal—*brain dead* is not dead vis-à-vis organs for transplant. Moreover, from the cover of *The New York Times Magazine*[8] to the recesses of academic journals one encounters uncertainty over life's determination by genes versus its regulation by the environment.[9] Has life changed? No, although parameters may have shifted.

Life is the state of existence prior to death. Life is always a precarious condition, maintained in a delicate balance between opportunity and contingency, but, even under the best of all possible circumstances, life is succeeded by death.

Death's inevitability is easily explained. Citing the deplorable statistics for preserving human life in long-term care facilities, the physician and popular-medicine writer, Sherwin Nuland, explains

> [t]hough their doctors dutifully record such distinct entities as stroke, or cardiac failure, or pneumonia, these aged folk have in fact died because something in them has worn out.[10]

Richard Lewontin, the evolutionary geneticist and philosopher of biology, relies on a mechanical metaphor to make the same point:

> [T]he cause of death is that living organisms are electro-mechanical devices, made up of articulated physical parts which, for purely thermodynamic reasons, eventually wear out and fail to function. Different parts wear out at different times in different individuals, and some parts are more prone to failure than others, or are located in the functional articulation at a place that is more critical.[11]

"Old age" and "worn out" are not categories accepted by the Department of Health and Human Services, the Bureau of Vital Statistics, or the World Health Organization, while cardiovascular accidents, cerebral thrombosis (stroke), various forms of cancer, and that old standby, pneumonia, are recognized as terminal events, but death is only secondarily a consequence of acute disease. It is primarily the sequela of a lifetime.

Leonard Hayflick, the doyen of cell-aging research, makes a similar point:

> More than 75% of all human deaths in developed countries now occur in those over the age of 75. If the causes of these deaths are resolved we will not become immortal but we will have revealed how death occurs in the absence of disease. What will be found is that the underlying cause of these deaths is the inexorable loss of physiological capacity in the cells of vital organs—the hallmark of ageing.[12]

And aging results from built-in obsolescence, from the disposability of soma, from the limits of the organism's repair capacity, or from the accumulation of genetic dust-beneath-the-cupboard, but not from aging genes.[13] Aging is not inherited in the ordinary way blue eye color is inherited. Rather, aging is inherited in a covert way—the way enfeebled metarterioles blossom on the bulb of your nose.[14]

## Longevity Research

Possibilities for foiling obsolescence are studied by longevity researchers, and their efforts to push the envelope of life-expectancy outward to its limit have been rewarded. Good health care, especially during one's youth, sufficient nutrition, adequate rest, and time to recuperate from exertion, injury, and abuse have already added years to the average human life-expectancy. One can also buy one or another commodity or service—or not buy other

commodities or services—to good effect. How many more years can be added to the average human lifetime is uncertain, and estimates are all over the map, from no more than 15 years to more than 500 years.[15] But death still looms beyond that limit. Prolonged longevity is not immortality; it is only postponing the inevitable.

Once upon a time, humanity's answer to certain death was Heaven or some such extraterrestrial world, a working hypothesis for the preservation of the spirit.[16] Hypotheses for preserving the body were not equally robust, and solutions to the problem of the body's perishability have eluded all but the most imaginative. Science fiction writers have certainly worked immortality to death without creating anything especially new since Count Dracula. Scientists have not done much better. Even if the Human Genome Project, recently reaching its fruition,[17] allows us to inscribe our sequences of nucleotides (the monomers of deoxyribonucleic acid, better known as DNA) into a database, the encrypted message would not translate into a formula for material immortality—we would not achieve nirvana *in silico*.

The best hope for immortality would seem to be offered by cryonics, a program for freezing the newly dead, or at least the deceased's head, and resurrecting the individual at a future time when death is no longer a threat and when heads may be rejoined to bodies—although access to a headless body would seem to present another problem. Yes, you must die, but not without hope of corporeal revival.

Of course, the premise of cryonics is seriously encumbered not only by problems of revitalization but by uncertainty over restoring a persona. Personality and idiosyncrasies are unlikely to be preserved in ice even at the temperature of liquid nitrogen, and the defrosted body may resist reprogramming with the experience of a previous lifetime.

Alternatively, a great deal of popular literature offers programs for putting off the inevitable as long as possible, if not indefinitely. The fiction and nonfiction writer, Ben Bova, for example, prescribes a route to a semblance of immortality. He accepts the genetic determination of a lifetime but points out "that cancerous cells have found the trick of immortality."[18] Bova rests his case on the bevy of scientific work suggesting that various procedures and products, including improved general nutrition,[19] near-starvation (or caloric restriction [CR]),[20] antioxidants (superoxide dismutase/catalase mimetics),[21] early medical intervention against childhood diseases, rest and relaxation, and castration will allow more of us to achieve the longest possible life-expectancy.

Other programs for prolonging life center on reproduction as either conflicting or convergent with longevity. For example, early birthing and protracted lactation may prolong life by reducing the risk of breast and colon cancer but not without introducing other hazards that tend to reduce life-span.

On the other hand, given the hazards of birthing, increased longevity might be achieved merely by suspending birthing and having fewer offspring. Indeed, the relationship between delayed fecundity and longevity may be so profound that the average duration of a lifetime in future generations will be increased merely by selecting women exhibiting delayed childbearing, as suggested by Michael Rose, one of the parents of Darwinian medicine.[22] Longer lifetimes might be achieved by concentrating genes already in the human gene pool for delayed childbearing.

## The Genetics of Longevity

One very ambitious program for promoting longevity consists of finding genes that cause or prevent aging and, utilizing the yet-to-be-discovered technology of gene therapy to prevent or promote the expression of these genes, thereby warding off their dire effects or enhancing their salubrious ones. The problem with this technique begins with traditional geneticists' habit of identifying normal genes by their opposite members—their mutations. In order to find genes influencing longevity, traditional geneticists look for mutations. In the case of longevity, the relevant mutations would be those that either accelerate aging or extend an individual's lifetime beyond the average life-span for members of the species. The first problem is that

> [e]ven in species where senescence does make some contribution to mortality in the wild . . . any hypothetical "accelerated ageing gene" would be disadvantageous to the individual. It is therefore difficult to see how genes for accelerated ageing could be maintained in stable equilibrium, as individuals in whom the genes were inactivated . . . would enjoy a selection advantage.[23]

On the other hand, several mutations extending an average life-span (among other things) have been discovered in model organisms living in the laboratory.[24] For example, in the fruit fly, *Drosophila melanogaster,*[25] the *chico*[26] and *methuselah* mutants extend life-span; in the round worm, *Caenorhabditis elegans*, *age-1, daf-2,* and other mutants in the insulin-like signaling pathway do likewise, possibly by enhancing the ability to respond to oxidative stress;[27] in yeast, *Saccharomyces cerevisiae, LAG1* and *LAC1* determine mean and maximum number of cell divisions (equated to life-span), *RAS1* is life-shortening, *RAS2* is life-extending; *SIR2* and *SIR4,* containing a specific *AGE* locus, may influence yeast's longevity through transcriptional silencing of genes mediating stress or caloric restriction.[28] Remarkably, *C. elegans,* containing a chromosome IV duplication, including

a *sir-2* locus resembling yeast's *SIR2,*[29] and transgenic worms bearing this locus may live as much as 50% longer than normal adults. The products of the *sir* family of genes may all be involved in the insulin-like signaling pathway coupling longevity to nutrient availability.

In mice (and men?), life-span is influenced by a small number of mutant genes.[30] For example, mutations in the gene encoding the $p66^{shc}$ protein extend the life-span of mice about 30%, and mutants that inhibit the development of the pituitary gland, such as the gene-defective Prophet in Ames dwarf mice, extend life-span approximately 50%. The activities of life-span regulating genes and mutants may be positively correlated with high immune responsiveness, or negatively correlated with metabolic rate (body temperature) and oxidative damage (the mitochondrial free radical theory).

The relevance to human beings of genes discovered in laboratory organisms is certainly a hypothesis worth testing, but only a hypothesis until tested. No doubt genes will influence all the things that keep cells alive or kill them, but larger, longer-lived animals, such as human beings, will have different problems preserving their lives than shorter-lived animals. Longevity will probably depend on genes controlling different enzymes and metabolic pathways, such as antioxidant enzymes and DNA repair pathways.

Quantitative differences between large and small animals illustrate the problem of genetic relevance. Large animals have vastly more cells than smaller animals and maintain some of their latae cell populations by producing enormous numbers of cells per day by cellular proliferation. Unfortunately, cancer cells crop up among the normal cells constantly in production, and some cancers arise in older, larger, longer-lived animals that are virtually unknown in smaller, shorter-lived animals. Unlike short-lived animals whose lifetime may be determined by the preservation of small numbers of cells, large, long-lived animals have to apply

> a brake against the accumulation of the multiple mutations needed for a cell to become malignant. A 70-kg man who lives for 80 years has to be 14,000 times as resistant to developing cancer as a 0.2-kg rat that lives 2 years.[31]

Genes promoting longevity in the rat, therefore, may represent only a fraction of the genes promoting longevity in human beings.

Longevity-gene mutants do not kill an organism by firing a shot, and the normal gene does not prevent an organism's death by outfitting it in body armor. Rather, these genes set processes in motion which, operating through long cascades of actions and reactions, ultimately affect longevity. The hope of gene therapists is to deliver the right human gene to the right

cells while replacing or silencing the wrong genes and ultimately preventing or reversing downstream cellular aging and promoting organismic longevity.[32] The possibility of transferring life-span expanding genes from other organisms to human beings is all the more problematic, since it is not clear whether genes influencing life-span in other animals will operate comparably in human beings.

Candidates for gene therapy are found among sufferers of several inherited aging disorders: genetic instability syndromes, mutants causing aberrations in DNA metabolism, such as *WRN* (null mutations in a helicase[33]) responsible for Werner syndrome (WS or progeria of adults),[34] Rothmund-Thomson syndrome, Cockayne syndrome, possibly Hutchinson-Gilford syndrome (progeria of childhood), and others.[35] The mutations causing these disorders result in the early onset of complex senescent phenotypes (progeria and progeroid syndromes). However,

> [i]t is an oversimplification to refer to these [senescent] disease as "premature ageing syndromes". To do so suggests that they will invariably reveal the mechanisms underlying "usual" or "normal" ageing. But their phenotypic features may sometimes be quite unusual, and some features may result from gross abnormalities in development.[36]

Moreover, genes involved with dementias and other symptoms of senescence which do not show up in progeria are usually associated with physiological activities, such as complex responses to stress mediated by reactive oxygen species (ROS), and hence with tangled interactions unsuitable for gene therapy. In any case, one enters unknown territory with gene therapy and even potent possibilities offer no guarantees.

## "HELLO, DOLLY!" AND SALUTATIONS TO STEM CELLS

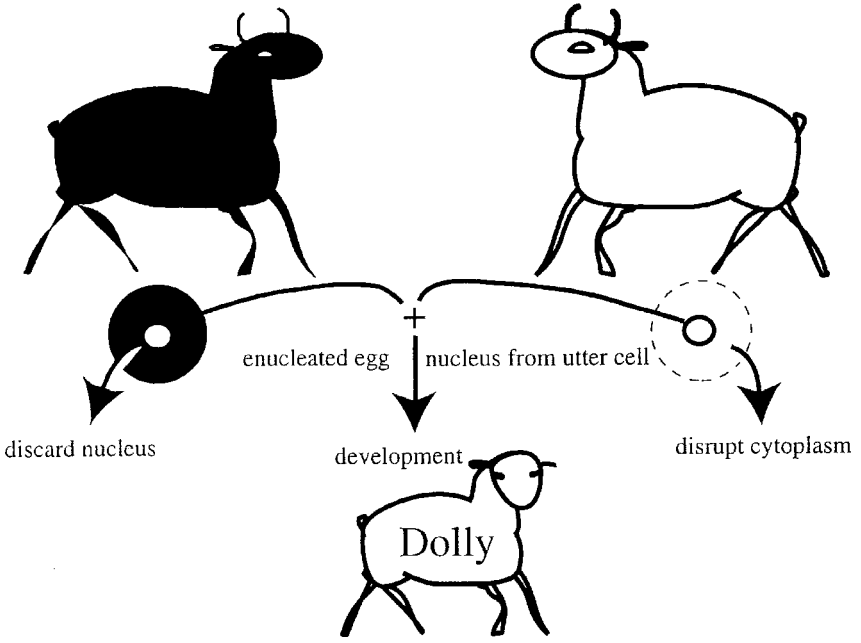
And then came Dolly, cloning, and stem-cell research, providing, in combination, a cure for mortality! This miracle cure does not merely cater to our long-time anxieties over longevity; it closes the gap between body and soul, offering for the first time, genuine corporeal immortality!

Together, cloning and stem cells can work miracles. Separately, they are just pieces of the puzzle, neither alone capable of making immortal organisms. Cloning only promises to replicate organisms (their parts or stem cells), and stem cells are merely self-renewing, pluripotential cells (having the ability to differentiate into other kinds of cells[37]).

## CLONING

The first mammal cloned with a nucleus from a differentiated adult cell was born at the Roslin Institute in 1996[38] and whimsically named Dolly.[39] Speaking genetically, she was a replica of the organism whose cell donated a nucleus.[40] Dolly's nuclear parent was demonstrated morphologically and by high-tech DNA fingerprinting with polymorphic microsatellite DNA fragments. Dolly, the clone, inherited her genetic traits from a pregnant, 6-year old Finn-Dorset ewe killed in 1994 and not the Scottish Blackface which supplied the egg cytoplasm.[41] In all other ways, the pale faced Dolly is as normal as any Finn-Dorset ewe produced by ordinary sexual reproduction, as demonstrated in the Autumn of 1998 by her giving birth to Bonnie and, a year later, to even more lambs.[42]

The Roslin Institute "is a government laboratory, one of a network of institutes throughout Britain that now answer to the Biotechnology and Biological Sciences Research Council (BBSRC) which in turn is one of seven such councils that together form the core and umbrella of Britain's government-supported science and technology."[43] The cultured,[44] mammary gland cell providing the clone's original nucleus was supplied by the biotech startup,



Pharmaceutical Proteins Ltd. (PPL) Inc., and PPL scientists were the "principal investigators" involved in the project.[45]

Dolly was no accident (although success with cloning is rare enough). Her birth was the climax of a series of experiments designed to promote pharming, the harvesting of biologically active materials from livestock. She joined an elite stable of cloned sheep made with nuclei donated by cultured embryonic cells (Megan and Morag, Cedric, Cyril, Cecil and Tuppence), fetal fibroblasts (Taffy and Tweed), and a genetically modified (transformed) culture cell (Polly)[46] carrying the human gene encoding clotting factor IX later secreted in her milk.[47]

Other announcements of cloning with nuclei from differentiated (adult) cells and fetal fibroblasts[48] followed on Dolly's coattails: a calf (Marguerite) in France and eight more in Japan (although only four survived the early antenatal period),[49] mice (Cumulina, named after the cumulus oophorus nuclear donor) in Hawaii,[50] a pig[51] (Xena presumably named for the prospects of using pigs as a source of xenotransplants to human beings) followed by more pigs,[52] and goats[53] if not a monkey.[54] Copycat cloning burgeoned, although frequently reported at press conferences and not in the strictly scientific style required by professional journals. The patented procedure for making Dolly (and hence the patenting of Dolly herself) also provoked turf battles around licensing and royalties, since cloned mammals might prove economically advantageous.[55] The biotech firms sponsoring the cloning of large mammals expect cloning to become as common in the twenty-first century as genetically modified plants were in the closing decade of the twentieth, at least in the United States and the Pacific Rim.[56]

In the public imagination, Dolly became a breakthrough in the struggle against perishability, and many pondered the possibility of extending life through facsimiles. Some simply hoped that cloning technology would make it possible to recreate loved ones from preserved tissue (in the mode of *Creator,* starring Peter O'Toole) from recently deceased children or favorite pets, but, inevitably, self-love conquered, and the idea of perpetuating oneself became a preoccupation of wistful dreamers. Richard Dawkins, the evolutionist and popular science writer, stated his own preference to recreate himself through cloning and challenged the rest of us:

> Mightn't even you, in your heart of hearts, quite like to be cloned? . . . I think I would. . . . My feeling is founded on pure curiosity. . . . I find it a personally riveting thought that I could watch a small copy of myself, fifty years younger and wearing a baseball hat instead of a British Empire pith helmet, nurtured through the early decades of the twenty-first century. Mightn't it feel almost like turning back your personal clock fifty years? And mightn't it be

> wonderful to advise your junior copy on where you went wrong, and how to do it better?[57]

Cloning did not, however, embody the essence of immortality, that is, personal continuity. The microneedle sometimes used in cloning to inject the nucleus of an adult's cell into the cytoplasm of an egg is hardly a fountain of youth, and cloning hardly reanimates the nuclear donor (e.g., the long dead ewe whose udder cell donated the nucleus used in the cloning of Dolly).[58] Cloning is not about rejuvenating individuals. Cloning only replicates them, and then, only as far as their nuclear-genetically encoded traits.

A clone is supposed to be a facsimile of the nuclear-donor, but a human being, clone or not, is inevitably its own person, not the nuclear donor carried over to a new body. In all likelihood, one's clone would develop its own personality, living in its own time and place, even if one tutors one's clone personally. A personality is something acquired over a lifetime, influenced heavily by nurture, experience, and learning, and such a lifetime is unlikely to be transferred to the new body by a mere nucleus (even with a good dose of donor cytoplasm).[59]

Inevitably, individuals are no more likely to see their clones as themselves as they are likely to see their offspring, as currently conceived, as themselves. The break between nuclear donor and clone is just as large as the break between parents and ordinary offspring, especially since the clone would develop *in utero* much the same way as any normally fertilized egg or an egg following *in vitro* fertilization and embryo transfer to a prenatal foster mother or surrogate. Furthermore, no matter how much one's clone looks and behaves like oneself as an infant, one's own ego is likely to balk and leave one unable to identify one's clone with oneself as an adult. In the final analysis or moment, one is unlikely to "go quietly into that gentle sleep" believing that one's clone is oneself.

Dolly also inspired a flurry of ethical controversies, duly raised and aired from the highest echelon of government to the lowest rungs of the tabloid press. These issues were set off by a Geron bombshell when Michael West, chief executive officer of Advanced Cell Technology, announced that a mammalian blastocyst (a preembryo[60]) had developed from a cow's egg (sans its own nucleus) and a human nuclear transplant.[61] The private sector had only been motivated to create bovine/human chimeras for research as a way of economizing, since cow eggs cost $1.00 while human eggs cost no less than $1,000, but the specter of "playing God" would thereafter haunt cloning.

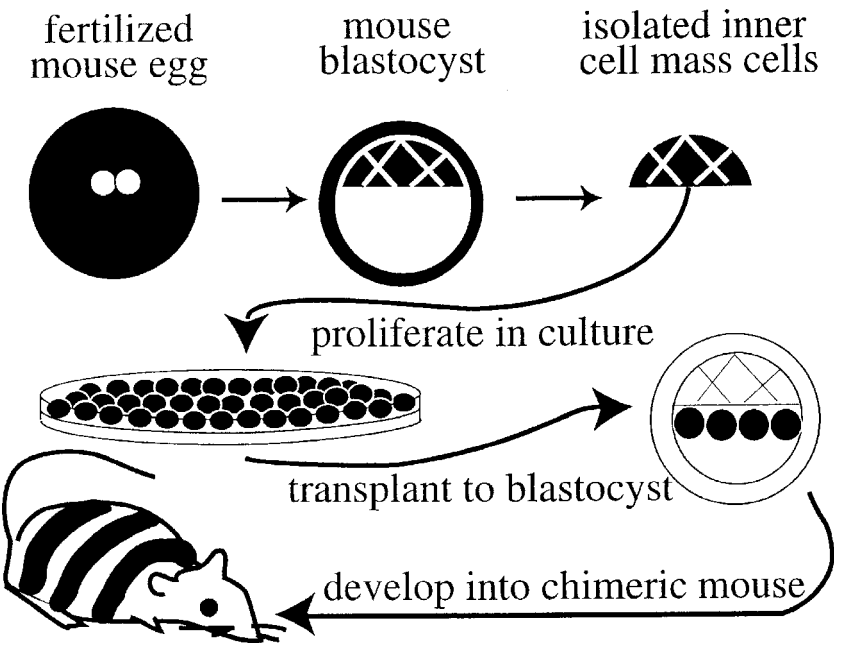
One day, or so it seemed to the casual observer, cloning one's pets and even oneself was as American as apple pie, the next day, cloning was strictly *verboten,* if not a crime against humanity![62] As a consequence, like a meteor careening toward Earth, by 1998 cloning human beings seemed doomed to

follow a trajectory to oblivion. After all, cloning had already been done in fiction and movies (e.g., *Boys from Brazil*), only to be repudiated as a means for preserving "desirable" individuals. Yet, before hurdling to a fiery death, cloning received a boost and became relevant to immortality again. The thrust came from another breakthrough technology in this struggle against perishability.

## Stem cells

Long before stem cells became prime subjects in immortality research, stem cells were studied for their role in normal tissue maintenance.[63] The idea was that individuals were constantly refurbished by stem cells, thereby maintaining life. The constant turnover of cells in the outer layer of skin (epidermis), the inner layer of the digestive track (absorptive cells), and blood and lymphatic systems were known since World War II. At that time, the advent of radioactive elements and labeled materials (especially tritiated thymidine) had made it practical to track cellular turnover.

Diminished production of particular materials associated with some diseases (e.g., insulin and diabetes) suggested that the sufferer's primary defect



might be abnormally low concentrations of replacement-stem cells. The potential of stem cells in therapy seemed enormous, and attempts to use stem cells therapeutically were well underway in the closing decades of the twentieth century: Fetal nerve precursors were transplanted to the brains of Parkinson's disease patients, and bone marrow was transplanted to patients suffering from leukemias, lymphomas, and other cancers.[64]

Most of the fundamental research on stem cells was done on embryonic or embryonal stem (ES) cells obtained from mouse preembryos or blastocysts and raised in tissue culture. These cells could differentiate into virtually any adult mouse cell upon reintroduction into developing mouse blastocysts. But, in the November 6, 1998 issue of the weekly science magazine, *Science,* the team led by James Thomson at the University of Wisconsin with funding from Geron Corporation of Menlo Park, California, announced that it had isolated and cultured human ES cells from 20 of 36 human blastocysts left over from *in vitro* fertilization.[65] Thus, a virtually endless supply of human stem cells became available for research.

The November 10, 1998 issue of the journal, *Proceedings of the National Academy of Sciences,* followed with the announcement by John Gearhart and others at The Johns Hopkins University School of Medicine,[66] likewise with funding from Geron Corporation, that primordial germ cells (PGCs), or germ stem (GS) cells had been isolated and cultured from the gonadal ridges and mesenteries of 5- to 9-week post-fertilization human embryos obtained by therapeutic abortion. These cells not only proliferated in tissue culture, but differentiated into a variety of cell types, including representatives of all three embryonic germ layers.[67]

The Thomson/Gearhart research did more than answer the question of whether human embryos and fetuses contain stem cells. Their research demonstrated that human stem cells could be amplified in tissue culture, theoretically removing the greatest block to stem-cell replacement therapy, namely, the difficulty of obtaining sufficient quantities of high-quality stem cells. The problem of quantity had plagued attempts to re-nervate the substantia nigra of Parkinson's disease patients with dopamine producing cells.

Like the cloning of Dolly, the isolation of stem cells had been accomplished in the private sector, and Geron stock nearly doubled its value following news of the breakthroughs. The United States Congress and parliaments in many countries had driven research on human stem cells into the private sector by placing human embryos and fetuses on the proscribed list of national granting agencies.

The politics of stem-cell research is as murky as the politics of cloning. Human stem-cell research with ES cells derived from preembryos and GS cells from aborted fetuses quickly runs afoul of abortion politics. After much hand wringing, on December 19, 2000, in an open vote, the British House of

Commons approved 366 to 174 new rules allowing scientists to derive and use stem cells from human embryos and perform experiments with nuclear transfer.[68] In the United States, the National Bioethics Advisory Commission recommended easing the strictures on research utilizing human embryos and fetuses.[69] President Clinton partially lifted the ban on cloning and President Bush has decided to allow research utilizing ES cells, although United States scientists will not receive support from the National Institutes of Health allowing them to cull human stem cells from the detritus of *in vitro* fertility clinics. Of course, entrepreneurial scientists will perform human stem-cell research, and the possibility of immortality research through stem cells will soon become global business.[70]

Stem-cell researchers will add ways for increasing longevity with the help of cybernetic devices and electronic prostheses, performing one or another miracle and enhancing well-being for great numbers of individuals who can afford the cost of these technologies. However, stem-cell therapy as such, like other longevity-enhancing devices, only delays the inevitable, and, like cloning, is not in and of itself the long-sought cure for mortality. The panacea for aging, however, is close at hand: It lies in combining the technologies of cloning and stem-cell therapy.

## Combining Cloning and Stem Cells for Immortality

The possibility of biological immortality rests on two premises: (1) *Anyone able to perpetually regenerate, reinvigorate, and replace aged or diseased parts of their body could live in the same body from birth to eternity with their persona intact.* (2) *A clone of one's own cells could serve as a source of embryonic stem cells able to support cellular renewal.*

Neither of the above premises is controversial. The idea of perpetual replacement is as old as the industrial revolution and the manufacture of interchangeable parts. That ES cells could serve as a source of such parts is a new but not too novel permutation on older concepts of stem-cell therapy.

According to the science writer, Gina Kolata, the idea of clones serving as a source of stem cells was first articulated by the Harvard hematologist Stuart Orkin.

> Ultimately, Orkin said, [if] scientists . . . could learn how the egg reprograms a cell's DNA, bringing it back to its primordial state, they might someday be able to force a cell to reprogram its *own* DNA and then differentiate into any sort of cell that the scientists want. That, of course is the most futuristic scenario of all, Orkin warned, but it shows what might someday be possible. That process

of learning to reprogram a cell's DNA would have to begin, however, with cloning.[71]

Indeed, the desire to reprogram the genome had motivated Ian Wilmut's and Keith Campbell's efforts that led to Dolly. In their words, they found ways of "*restoring* totipotency to cell lines that once would have seemed to be differentiated beyond recall . . . creating new embryos from cells that are already differentiated, by reprogramming their genomes."[72]

The novel idea introduced here is that *grafting a clone to an embryo would create a permanent generator of embryonic stem cells and immortalize the host organism* (see Chapter 5 for details). A certain amount of difficulty or hesitance may greet this idea, since little in the history of biology prepares biologists to think synthetically about changing human life. Indeed, biologists can hardly be expected to think about creating new organs and tissues, since the evolution of tissues and organs in organisms is not even explained in standard works of evolutionary theory. Furthermore, standard works of developmental biology sometimes pay attention to correcting errors of metabolism caused by mutations but never pay so much as lip service to the possibility of developing new organs capable of solving old problems.

Little-known studies of parasitism (see discussion of devolution in Chapter 4) suggest how tissues and organs might have originated by fission and fragmentation. These studies suggest that implanting a preembryo in an embryo would be a direct route to providing the developing host with a new organ. Were that organ capable of generating ES cells indefinitely, the host would be capable of living indefinitely.

A clone would seem an ideal source of stem cells for a variety of reasons, not the least of which is the untrammeled tolerance, or self-recognition, of the body for the clone and the clone for the body. Likewise, a blastocyst, or preembryo, would seem the ideal stage for implantation into a developing host, since the portion of the blastocysts known as the inner cell mass (ICM) is the traditional source of ES cells—proliferating cells not yet on their way to differentiate in particular pathways.

The idea of human immortality may still seem like a fairy tale, but if an organ can be created via implantation into an embryo, little else in all this theorizing will be biologically contentious. Cloning and stem-cell research are already the premier topics of immortality research because they can work as sources of immunologically acceptable stem cells. What is added here is merely the idea of implanting the clone and turning it into a permanent source of ES cells, thereby turning the host into a permanent living being.

The solution to the ancient problem of mortality seems in retrospect so simple that one may wonder why biologists have not thought of it before. The

answer resides in biology's historic predilection to ponder old problems instead of new possibilities.

## WHY WE ARE NOT IMMORTAL OR WHAT IS LIFE ANYWAY?

Mortality is part and parcel of biologists' conception of life which goes back to Aristotle in the fourth century B.C. This conception matured materially following the days of idyllic nature, and, in the seventeenth century, some natural philosophers separated themselves from religious philosophers in order to investigate life's mechanisms.[73] Later, eighteenth century nature philosophers declared their allegiance to natural law and attempted to attract acolytes to their rigorous version of life on Earth. Early nineteenth century biologists attempted to offer solutions to life's transcendent problems as well as answers to questions such as what life is doing here, where life comes from, and how it got to where it is now, if not where it is heading in the long term. At the same time, biologists entered the ranks of professional scientists, earning wages and other perquisites for their trouble. Now, at the advent of the twenty-first century, biologists have become the engineers of entrepreneurial enterprises with a little help from their friends, from venture capital, and from those holding the purse strings of national granting agencies and nonprofits.

A synthetic branch of biology never quite germinated from its root and stem. Instead, biologists became mired in a theory of life consisting of three down and dirty parts: 1) flux, 2) discontinuity, and 3) waste. Flux moves the sameness of life from cell to cell and organism to organism, and everything else living things share with each other; discontinuity creates individuals and allows them to gamble and compete or trade off differences with each other; waste is life's great resource, supporting everything within life's capability. Taken together, the three parts of this theory of biological life circumscribe and prescribe mortality. This version of life also encapsulates the obstacles to both thinking about and achieving immortality.

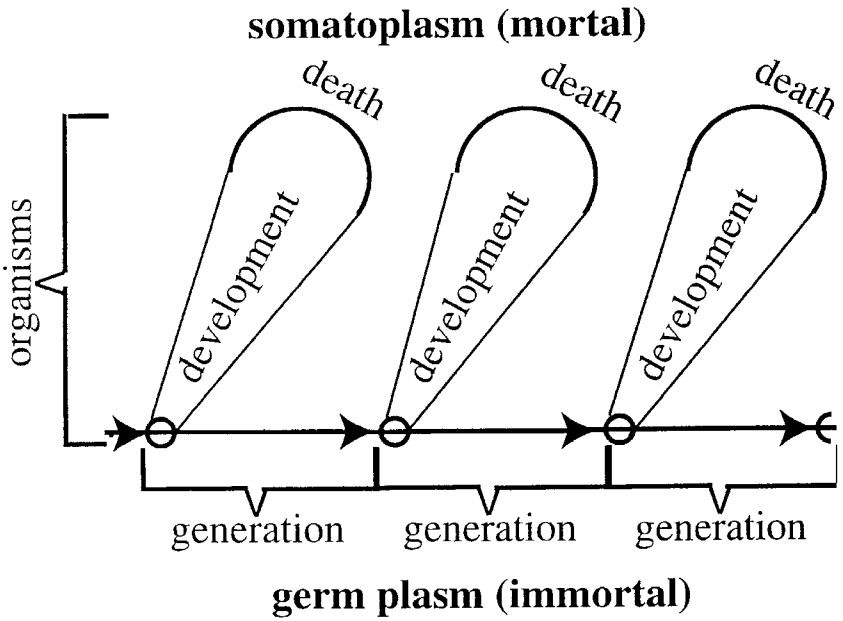
### Flux

Briefly, from the point of view of contemporary biology, life is impermanent. Living things, such as adult organisms, are unstable, and groups of living things, such as species, are transient. Indeed, life's most abiding feature may be its constant flux, for example, the turnover of animals brought about by birth and death. In order to turn the tables on mortality and change us from mortals into immortals, turnover has to be turned into equilibrium. This will

not be as hard as it might seem on first blush, since life's flux, in practice, is continuous.

August (Friedrich Leopold) Weismann (1834–1914), a professor at the University of Freiburg at Breisgau, first appreciated life's flux and continuity in essentially modern terms in the closing decades of the nineteenth century.[74] Weismann's place in history was guaranteed, however, when his language was translated into the vernacular of twentieth century genetics by the Oxford Professor of Zoology, Richard (Clinton) Dawkins (b. 1941).[75] Essentially, living things, or organisms, consist of two elements, one of which, called the germplasm by Weismann, is continuous from generation to generation; the other element, called the somatoplasm by Weismann, is discontinuous, only emerging as an offshoot of germplasm as a mark of succeeding generations. Translated into modern terms, germplasm is a complete set of genes (a genome), and somatoplasm comprises the body of an organism.

Operationally, germplasm passes from parent to offspring and generation to generation in a germ line comprised of germ cells or gametes, commonly eggs and spermatozoa. In contrast, all the cell types making up all the tissues, organs, and organ systems comprise the somatoplasm. It takes its origin from the fertilized egg or zygote and fans out into somatic cell lines in the course



of development. As differentiated cells, eggs or spermatozoa represent unique cell lines. As germ cells belonging to the germ line, they can escape the confines of the organism to reach new generations.

Everyone alive today has acquired germplasm from biological parents who have acquired germplasm from biological parents, and all these biological parents would seem to have acquired germplasm from biological parents back to some time in the Precambrian when sexual reproduction was consolidated in animal reproduction. Moreover, everyone born in the future will have acquired their germplasm from biological parents,[76] and this continuity will last as long as one leaves progeny and one's progeny leave progeny.[77] Clones might seem to be an exception, but their biological parents will inevitably be located one or more generations removed. The quality of continuity in germplasm as opposed to the discontinuity in somatoplasm—popping up in every generation—means that germplasm is immortal, while somatoplasm is not!

Arguably, twentieth century biology consists of deciphering the operations of Weismann's germ- and somatoplasm. The idea of an immortal germplasm has merged with the idea of permanent, particulate conveyors of heredity, known originally as Mendelian factors and rechristened *genes*. Germplasm was virtually ready-made for transformation into self-replicating DNA, but somatoplasm continues to confront biologists with some of life's most bewildering mysteries.

## The Secret of Life

Life's deepest secret, and the one that has preoccupied naturalists and biologists for centuries, is the quality that distinguishes life in all living things from death. If one were to rank biological problems by the status of individuals trying to solve them, this secret of life would be the highest. No end of eminent biologists have discussed their work in terms of this secret and have tried finding its solution.

As late as the 1930s, the physicist-turned-biologist, Max Perutz, thought that "the Secret of Life—in capital letters—consisted of the function of enzymes."[78] Linus Pauling imagined protein as concealing the solution to the "secret of life."[79] Today, the consensus of opinion is that Perutz and Pauling were wrong.

The physicist, Erwin Schrödinger, is generally credited with articulating in 1944 the modern secret of life in his book *What is Life?*[80] although he does not literally use the phrase—it would have been out of character for a physicist. Other words, "conundrum"[81] and "enigmatic"[82] appear, but "secret" escapes him. "Secret" is, nevertheless, implied by the questions and clues around which he organizes his book, a secret, moreover, waiting to be solved by the methods of physics:

> How can the events *in space and time,* which take place within the spatial boundary of a living organism be accounted for by physics and chemistry? (Pg. 3; emphasis original.)

> [I]ncredibly small groups of atoms . . . have control of the observable large scale features which the organism acquires in the course of its development . . . [and] determine important characteristics of its functioning. (Pg. 21.)

> How can we . . . reconcile the facts that the gene structure seem [*sic*] to involve only a comparatively small number of atoms . . . , and that nevertheless it displays a most regular and lawful activity—with a durability or permanence that borders upon the miraculous? (Pg. 49.)

> Are these structures [genes] . . . capable of withstanding for long periods the disturbing influence of heat motion to which the hereditary substance is continually exposed? (Pg. 61.)

> Thus it would appear that the "new" principle, the order-from-order principle, to which we have pointed with great solemnity as being the real clue to the understanding of life, is not at all new to physics (Pg. 87.).

Schrödinger predicts that revelation will come from "the material carrier of life" (pg. 5)—the self-reproducing unit of hereditary information or gene found on the chromosome which he considered "an aperiodic crystal" (Pg. 5) or "solid" (Pg. 65),

> or probably only an axial skeleton fibre of what we actually see under the microscope as the chromosome, that contain in some kind of code-script the entire patterns of the individual's future development and of its functioning in the mature state (Pg. 22).

Furthermore,

> chromosome structures . . . are law-code and executive power—or, to use another simile, they are architect's plan and builder's craft—in one. (Pg. 23.)

Biologists—not to short-change physicists and chemists—have sought to solve life's secret through genes ever since.

*What is Life?* had an enormous impact, especially among war-weary physicists, and was responsible for Francis Crick "leaving physics and devel-