

LE Magazine November 2003

REPORT

Cellular Immortality

An Exclusive Interview with Stem Cell Pioneer Michael D. West, Ph.D.

Dr. Gregory M. Fahy



In his new book *The Immortal Cell*, Dr. Michael West describes the meaning of cellular immortality and the implications of the “time machine” of therapeutic cloning for life extension. The following interview with Dr. West was conducted by Dr. Gregory M. Fahy.

Life Extension: *Dr. West, your book is not about one subject, but many. It's the story of how the biology of immortality may eventually conquer the biology of aging, and what happens when science moves faster than political and religious leaders can accept. It's an impassioned philosophical statement about life, death, and immortality. What was your purpose in writing it?*

Dr. Michael West: I wanted to communicate why stem cell technology is so important from both a scientific and a personal point of view. On the science side, I hoped to communicate the excitement of the research community about the embryonic stem cell—the immortal cell, a cell capable of branching into any of the cell types in the body and effectively treating today's “incurable” conditions, including aging. On the personal side, I can imagine the day when thousands of people with various diseases, particularly age-related diseases, can benefit from these discoveries.

LE: *What impact do you think the book may have in promoting greater understanding of and public support for therapeutic cloning?*

MW: My hope is that the book will explain why scientists working in the field are so impassioned about moving the technology forward rapidly—why, from our perspective, therapeutic cloning is an ethical and appropriate use of technology. There's been so much disinformation circulated by the opposition that I think it's important to clearly voice what we see as the facts, to allow readers to make up their own minds as to where they stand on the issue.

LE: *In your book you say that embryonic stem cell research is going to “unleash one of the fiercest battles between religion and science in recent history.”*

MW: I think the backlash in the religious community stems from one primary and one less significant reason. The primary reason is that this is seen as fresh ground to fight over in the abortion debate. The abortion debate, at least in the U.S., has been largely stalemated. Now enters the embryonic stem cell. These cells come from the embryo when it is still a microscopic ball of cells that has not yet begun to develop, has not attached to the uterus, and is not a pregnancy. The “pro-life” community sees this as an opportunity to win the abortion debate. If they could cause a new law to be passed that would ban the use or production of cells from pre-implantation embryos, then they would have achieved a checkmate in the abortion debate, because if the pre-implantation embryo has a right to life and cannot be destroyed, then certainly a developing fetus in a woman's uterus—an actual developing human being—could not be destroyed for any purpose either.

A second reason I think some members of the religious community have attacked embryonic stem cell technologies is use of the word “immortal.” By “immortal,” we mean that these cells are not programmed to age and can replicate indefinitely. They have potential immortality in that they're part of the reproductive lineage of cells that connects the generations. This is the result of the nearly magical ability of germ-line cells to escape the inevitable aging of the body. In my book I call the germ-line cell the immortal cell. But use of the word “immortal” to describe these cells at the root of the immortal substratum of life, and to envision their use to fight the eternal battle against aging and death, may seem to intrude into what has historically been the province of religion. This talk about science potentially being able to extend the life span, or even about the possibility of immortality itself, is threatening to some people.

LE: *It doesn't seem logical that a law against therapeutic cloning and a law permitting abortion can co-exist. But can't the view of a fetus as a person and the view of a pre-implantation embryo as not being a person co-exist in principle?*

MW: Orrin Hatch, the Republican senator from Utah and an ardent advocate of the pro-life position, made an effort to understand the issues behind therapeutic cloning. He interviewed researchers in the field and requested scientific papers. And after, as he described it, a thoughtful and prayerful consideration of the issues involved, he came out in favor of therapeutic cloning. He argued, as we do from a scientific perspective, that a microscopic ball of cells that has not yet begun to develop, that has not yet individualized—that is, that has not yet committed to being one person, or two—is not a person for the purpose of writing law.



LE: *It's encouraging that Sen. Hatch was able to travel that journey, but a lot of your opposition seems to come in the form of sloganeering and jeering.*

MW: It does seem that use of the word “immortality” has resulted in more derisive rhetoric than thoughtful commentary. The most disappointing aspect of this debate for me has been the loud and hardened opposition to therapeutic cloning from some individuals and groups. When you talk to those individuals, it becomes clear that they are not interested in discussion. Their minds are already made up. When you then force the debate, what you often see is a rapid descent to inflammatory language—saying scientists want to make embryo farms, or worse, comparing me and other researchers to Osama Bin Laden or Dr. Mengele.

The issue is worthy of a far more respectable debate. Even our critics admit that these technologies at least have the potential to offer cures or new therapies for many thousands of people suffering from degenerative diseases. This debate should be about compassion, reason, and how we can best serve our fellow human beings. It should not be about getting votes or using this as a political football to win election or to look good on the floor of the U.S. Congress.



LE: *The House of Representatives recently voted to ban your research. Where is the political trend going in the near future?*

MW: There's the recent, nearly unanimous recommendation from the American Medical Association to back therapeutic cloning, the recent stance of the New England Journal of Medicine encouraging submission of manuscripts relating to therapeutic cloning, and the formal recommendation from the National Academy of Sciences (the formal body that advises Congress on matters of science and technology) advocating moving forward on therapeutic cloning. I find it very difficult to imagine that the U.S. Senate, the most deliberative body in the world, could pass a law that would ban a medical technology that could impact the lives of 3,000 people a day who could potentially be treated with technology like this. But we'll have to wait and see. I think, certainly, the momentum is on our side, increasing in force every day. There's a steady stream now

of scientific publications supporting the importance of the technology.

LE: *Let's move from politics to your philosophy of life. Please take us back to a moment when you had a sudden flash of insight while visiting the graves of your grandfather and father.*

MW: One day at my hometown cemetery, seeing the graves of previous generations that led up to me, I realized that the sun would rise on a day when not only my father, who I loved dearly, but all the people who live with me and who I love desperately also will have their names etched on tomb-stones. That day will come, as certain as the sun rising tomorrow.

At that moment, I recognized something that I had noticed earlier in my life, but with a force I had never experienced before—that I hate death. Death reduces all meaning to zero. And it is the antithesis of our love for one another. I realized at that point that it would be not just the highest calling of mankind, but my own calling, to apply every resource I have, all of my skills in science, to a continual effort to try to combat aging and death, as difficult as that may be.

I'm convinced that, in this century, we will largely understand the molecular mechanism of the clock that resides within us, ticking away and leading to the degeneration and aging of tissues. I'm convinced that human creativity and ingenuity are going to inevitably turn those insights into novel technologies that, at least to some degree, can intervene in aging. Not simply to extend the human lifespan, but also to add quality in our remaining years.



LE: *Let's now turn to your discussion of August Weismann's view that the very first stable cell was immortal and that aging arose as an adaptation by previously immortal cells.*

MW: Reproductive cells, by definition, cannot have dead ancestors because cells come from cells and life comes from life. It's the continuum of cells that has connected all the generations of life on this planet for billions of years.

Life is immortal in the sense that the germ-line, which is not a human life but can be considered human life itself, is potentially immortal. Of course, these cells could die. Hit one with a hammer and it's dead. But they're not programmed to age. Aging is, as far as we know, a unique property of somatic cells. Our goal is to extract all the knowledge we can about how germ-line cells achieve

immortality and find a way to translate that into making young cells for old people—in essence, to find a way to make old people young.

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LE: *Let's consider the merits of telomerase therapy vs. stem cell therapy. After capturing telomerase technology for Geron, you left Geron and went full tilt into stem cell research. Explain why.*

MW: If we age because our cells have a built-in clock that controls how many times our cells can divide, and if we are right that the telomere is the clock that triggers this aging, then telomerase would be a key to rewinding that clock, potentially making old cells young. Telomerase could be introduced into the body, essentially making old tissues young, and maybe old people young. There are multiple assumptions involved in each step of this approach but, in the best of all scenarios, if all these things went our way, we would still need one more piece of the puzzle, a means of introducing telomerase into the cells of a human being. I knew by the mid-1990s that this means—gene therapy—a problematic technology. I wasn't convinced that we were going to be able in the near term to deliver telomerase into the body effectively.

We knew that we could potentially perform telomerase therapy on cells in a cell culture dish, so I began thinking about how we could introduce these cultured cells into the body. Stem cells turn into multiple cell types, and I thought that perhaps we can find very primitive stem cells that could be introduced into the human body where they would spread and interweave themselves into the tissues as rejuvenated cells. As I thought about this tree of cellular life, I came to realize that there must be a human cell at the base of the tree of cellular life that leads to all the cells in the body. It then occurred to me that perhaps we don't need telomerase at all because the base of the tree of cellular life can also become a sperm or egg cell. Perhaps the embryonic stem cell is a naturally immortal and young cell, the reason that babies are born young, and therefore it might be able to make young cells in a lab dish. That was the genesis of my efforts to isolate the embryonic stem cell.



LE: *In the human body, there are cells that divide and cells that don't divide. Gerontologists usually think the non-dividing cells suffer the most from aging. But, since those cells don't turn over, how are embryonic stem cells going to be able to replace them?*

MW: I believe a telomerase-type therapy may rejuvenate only the proliferative capacity of cells that divide in the body and therefore prevent age-related changes in just those cells. For cells that don't divide, we believe we can make any desired replacement cell in the body—such as a heart muscle cell or a neuron found in the brain—from embryonic stem cells. The resulting cells should be, as far as we know, truly young. Through transplantation, through various routes of entry, these cells could be introduced back into the body to provide physiological support to the aging person.

I don't mean to make it sound overly simple, but we can now imagine, through therapeutic cloning, a means of repairing or replacing any cell or tissue in the human body. Perhaps it's not unlike the early 1960s when engineers and scientists believed we had the technology to carry a man to the moon. When we will be able to deliver new therapies to extend the human life span and improve the quality of human life entirely depends on how many hands are put to work on this project and how many hours of research we can do every year. At this point, I'm sorry to report that we're moving forward at a snail's pace. But the good news is, momentum is increasing every month, and I'm hopeful that some of the fruits of this technology will be available in our lifetime.

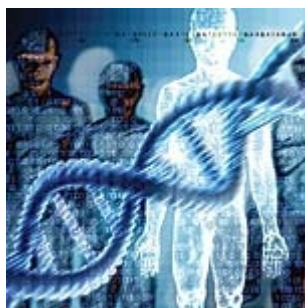
LE: *Do you have human embryonic stem cells? You published a scientific paper* showing that you could grow cloned human embryos to a certain stage, but not far enough to obtain human embryonic stem cells. Where do you stand today?*

MW: I have presented, in meetings, some progress toward making stem cells from egg cells alone, through a related technology called “parthenogenesis.” We’ve made continual progress in embryonic stem cell technology and feel more optimistic than ever about the relative ease of turning back the clock of aged cells. We think the cellular time machine is a practical means of making young cells available to individuals. I don’t have any doubt of its ability to work. But, again, I would emphasize that to turn this little cellular time machine into a therapy to actually rebuild the aging heart or immune system will require many years of hard work.



LE: *Have you had any religious or ethical feedback about using parthenogenesis as an alternative to therapeutic cloning?*

MW: Shortly after we published our work on cloned human embryos, we were planning to publish a paper in the journal Science, showing that we had successfully made “parthenotes,” or embryos made by parthenogenesis (a word whose roots parthenos and genesis mean “virgin birth” to reflect that only the DNA from the egg cell is involved). My belief was that if religious groups were upset about us cloning human embryos, they would see it as the most flagrant of all insults that scientists had created a “virgin birth” in the laboratory. True, we did it with monkey cells, but the implications for humans were clear.



To my surprise, some of our opponents argued that because parthenotes do not lead to a live birth when they occur naturally in the body, they could not be human beings. They had no objection to the procedure, and actually thought it was a good idea. It goes to show you that religious positions are not as predictable as one would think. Some have even argued that because parthenogenesis is a solution to the problem of making autologous cells—that is, cells identical to the patient’s cells (at least for women)—that we should use parthenogenesis and ban therapeutic cloning. I’ve tried to make the case that, first, we should let all flowers bloom, and second, some of us are men, and we get sick and grow old, too.

LE: *Near the end of your book you mention some very exciting coming applications of therapeutic cloning that could rapidly and profoundly modify human aging and even human lifespan. These involve the use of therapeutic cloning to produce primitive bone marrow and endothelial stem cells.*

MW: This, I hope, is how we will make some dramatic changes in how we age in our lifetime. Imagine taking a cell from you or me, transporting it back in time to young embryonic stem cells, differentiating them into primitive blood stem cells, and releasing them into the bloodstream to repopulate the blood with young immune cells. Another very promising new possibility is to introduce into the bone marrow cloned young endothelial precursor cells that can then spread throughout our vascular tree to “re-plumb” the cardiovascular system with brand new cells. There’s an old saying, “We’re as old as our arteries,” and some of the most serious complications of aging are related to the cardiovascular system. Even more recent and promising is the possibility that these same cells introduced into the bone marrow could leave the vascular system to actually regenerate damaged heart muscle and skeletal muscle.

Those are the areas we’re now targeting. Our hope is that we may be able, at least to a limited extent, to apply these cellular technologies to create the first substantial intervention in clinical geriatrics, a profound new technology to help people in a meaningful way to combat the ravages of aging.

LE: *Since cardiovascular disease is the leading cause of mortality in the aging population, these approaches alone might actually be able to add five or ten years to the human life span, and might eliminate vascular dementias and many strokes on top of that. But you also mention that this same approach might be turned into a way to combat the other major killer disease of aging, cancer.*

MW: I believe that if we extend the human life span, we will expand the problem of cancer. Cancer represents chaos at work, and the longer human cells are around, the more prone they are to becoming damaged in a way that leads to the runaway process of cell proliferation we call cancer. One promising application of these technologies in cancer would be to engineer these vascular precursor cells in the bone marrow in such a way that when they are recruited to a growing tumor mass, they carry with them certain genetic modifications that allow us to target them for destruction. This would, in effect, “give a tumor a stroke.”

LE: *In the preface of your book, you say, “I believe this book is, in itself, a mere preface to a much larger story still in the making.” What do you see as the next chapter in this story?*

MW: I believe that the evolution of human life is proof that life has evolved in the struggle against entropy to form an immortal machine called the immortal cell, the cell that led to you and me, which scientists call the germ-line. What I believe the future holds for medical research is a nearly infinite pipeline of young cells extracted from the immortal, regenerative power of the human germ-line, countless numbers of cells of any kind that could be used to repair the human body from the ravages of age.



Equally profound is that with our understanding of DNA, the blue-print of human life, we can now combine the power of these immortal cells with our knowledge of the genome. Meaning that we will be able to turn back the clock of old human cells, and then genetically engineer them in any way desired. Because the immortal cell lasts indefinitely, there is no limit to the number of genetic changes that might be made. These technologies, when all assembled together, present an awesome prospect.

This also could lead to use of the technology that I do not advocate, germ-line genetic engineering. Here I'm making the distinction between somatic cell engineering, which is engineering cells within the body for the benefit of the existing individual, and the cloning of people with genetically engineered cells to make brand-new people with genes designed to enhance those people. This is going beyond trying to help people who are sick, to the engineering of human beings for the purpose of making "super people." To prove such a technology is safe would take a lifetime of study and become very costly. We'll be debating such new issues of medical ethics, science, religion and public policy for the next century.

LE: Is there a final message you would like to leave with our readers?

MW: I would encourage readers to think through and study these issues, and if, after due consideration, they believe these discoveries can be used to advance medical therapies, to take the time and trouble to write their members of Congress to lend their support to therapeutic cloning and to oppose any ban. There are many people in Congress who would like to vote on our side in this important debate but need to know they have the support of their constituents.

To find your Senators, call the U.S. Capitol switchboard at 1-202-225-3121. To discuss these issues with your Senators, you can be connected to their offices directly. You can also find out how to contact your Senators by logging on to www.senate.gov.

Dr. Michael D. West is CEO of Advanced Cell Technology. In 1990 he founded Geron, the first prominent biotechnology company to focus on human aging, where he served as a director and vice president until 1998.

Dr. Gregory M. Fahy received his Ph.D. in pharmacology from the Medical College of Georgia in 1977 and has worked as a research scientist and research director in the life extension sciences ever since. He is now the Chief Scientific Officer of 21st Century Medicine, a member of the Board of Directors of the American Aging Association, and a member of the Editorial Board of the Journal of Anti-Aging Medicine.

** Cibelli JB, Kiessling AA, Cunniff K, Richards C, Lanza R, West MD. Somatic cell nuclear transfer in humans: pronuclear and early embryonic development. e-biomed: The Journal of Regenerative Medicine 2001 Nov 26; 2: 25-31.*

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