ed into the hip bone, could be manipulated in culture and perhaps used to replace neurons in the brain or damaged heart muscle.

Such applications, however, face the same hurdles as other potential stem cell treatments. More immediately exciting, say many scientists in this area, is the chance to study what it is about a cell that allows it to remain malleable and able to change its fate in response to environmental cues.

Indeed, the efforts to harness stem cells' potential for biomedical applications is a boon for cell and developmental biologists. With cultured stem cells, cellular changes "that have only occurred in the complex context of the early embryo are now happening before your eyes in a dish," says Washington University's Gottlieb. And those changes seem to be very similar to the ones that happen in the developing embryo, producing normal-looking neurons that make synapses and heart cells that set up rhythms. "What we're looking forward to is a much greater level of understanding and control," he says. "It's a field in which chapter one has been written. I'm looking forward to chapter two."

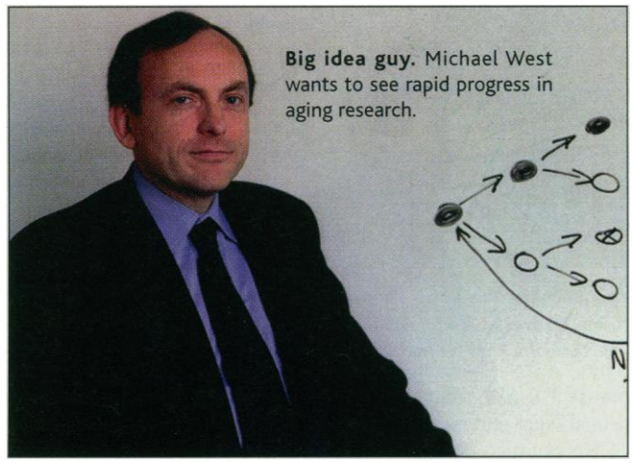
–GRETCHEN VOGEL

STEM CELLS
PROFILE

A Man in a Hurry

While pushing research on stem cells and other areas that might help an aging population, Michael West has also sparked controversy

For Michael West, the man whose support of stem cell research led to three dramatic announcements last fall, aging is a driving force. But it's not so much his own aging that worries him. Instead, it's the fact that the population as a whole is growing older, placing an increasing demand on the nation's health care system. "Addressing the medical problems associated with aging has got to become our number-one priority for research in this country," says West, who is president and chief executive officer of Advanced Cell Technology (ACT) in Worcester, Massachusetts.



Big idea guy. Michael West wants to see rapid progress in aging research.

And because aging is relentless, West himself has been relentless in funding and promoting cell technologies that could rejuvenate diseased tissues. In so doing, he has earned praise for his vision and energy as well as criticism for his bulldog approach. Although he's now heading up ACT, West is the founder of Geron Corp. of Menlo Park, California, a biotechnology firm that funded the two groups that last November reported isolating human embryonic stem (ES) cells (*Science*, 6 November 1998, pp. 1014 and 1145). These cells might have wide application in the clinic because they can be maintained in lab culture and, theoretically at least, can differentiate into all types of tissues (see p. 1432).

"Mike is a big idea guy," says Jerry Shay, a cell biologist who worked with West at the University of Texas Southwestern Medical Center in Dallas, "but he is also a guy willing to do what needs to be done to make sure that important ideas actually get translated into action." To West, that sometimes means courting controversy.

The ES cell work had already stirred debate because one group extracted the cells from aborted fetal tissue and the other from embryos discarded by a fertility clinic. Barely a week later, West added more fuel to the fire. He announced that ACT cofounder James Robl of the University of Massachusetts, and his then graduate student José Cibelli, had produced what appeared to be ES cells by first fusing human nuclei with cow oocytes whose own nuclei had been removed and then allowing these hybrid cells to divide. (See *Science*, 20 November 1998, p. 1390.) West announced this, he says, because he was leery of the legality of the work, and wanted to gauge the reaction of both the public and the U.S. government before he committed company funds to continue this research.

And react they did. President Clinton asked the National Bioethics Advisory Committee (NBAC) to review the medical and ethical aspects of the work. And much of the scientific community slammed him for publicly discussing data that had not yet been published in a peer-reviewed journal—stirring public debate about results that were not even documented. "I argued at length with Mike about going public with this," says John Gearhart at Johns Hopkins University School of Medicine, one of the two researchers whose work on stem cells West supported while at Geron. "First, you don't publish scientific work in *The New York Times*, and second, I think this approach of doing interspecies research is inappropriate."

But West shrugs off the criticism. "NBAC's immediate review found that there were no totally new ethical issues raised by this research as long as it is not intended to produce an embryo with the potential to develop into a child," which West says the hybrid cells could not do in any case. "As a result, we're now free to pursue this avenue of research aggressively, and we do intend to publish our results in the scientific literature. "

West wasn't always driven to cure the ills of aging. In fact, he got a slow start on a scientific career. After graduating from Rensselaer Polytechnic Institute in 1975, West went to work in the family business selling trucks, which he eventually parlayed into a truck-leasing business. He soon became interested in gerontology, especially the question of why the ordinary somatic cells of the body have a finite lifetime. When he sold the truck business, he was free to turn to science. "I made a fair amount of money on that transaction, which has given me the freedom to do what I've wanted to do in science without having to worry about making a living," says West.

A false start in graduate school at the University of Arkansas for Medical Sciences—he showed that one of his Ph.D. adviser's papers was incorrect—further delayed his research career. But he obtained his Ph.D. at Baylor College of Medicine in 1988, then decided to go to medical school there. He never finished, however, because his interests took a new turn.

At Baylor, he met Jerry Shay and longtime colleague Woodring Wright, who were among those who had linked shortening of the telomeres, specialized DNA sequences capping the ends of the chromosome, to cellular aging. The idea is that when the telo-

CREDIT: RICK FRIEDMAN

meres hit a certain length, cells go into senescence and die. Cancer cells have a way of restoring their telomeres, however, and thus can continue dividing when normal cells would stop.

West became fascinated by the telomere research and its potential to short-circuit the aging process and possibly cancer as well. "Mike sought us out when he arrived here for medical school, and we were smart enough to let him work in our lab at night and on the weekends, when he wasn't in class," says Shay with a laugh. West was so taken with the potential of the work that he quit school in 1991 and started Geron to explore ways of exploiting it in the clinic. "He didn't want to waste time finishing the last year of medical school. He wanted to start work on this immediately and see what telomere biology could do for human medicine," Shay says.

West also got the firm to branch into the field of stem cell research, which led to last fall's developments. By then, however, he had left because of differences in corporate philosophy. Although neither Geron nor West would comment on his leaving, others involved with Geron who know West speculate that he pushed the firm too hard into areas of research that other executives felt were peripheral to its main mission. "Mike was the founder, and I'm sure he was frustrated with the fact that the people running the company weren't pushing certain research projects forward," says one academic researcher who receives funding from Geron. Says another, "I think it was a huge mistake for Geron to get rid of Mike, even though there were certainly clashes going on over research direction."

Since that departure, West has founded another business, Origen Therapeutics in South San Francisco, which is attempting to use avian stem cells to develop improved chicken varieties. That led him to his current job with ACT. During a meeting with officials from Avian Farms, the nation's largest poultry producer and ACT's financial backer, West learned that Avian Farms was looking for someone to run ACT. In short order, he had won the job, reportedly investing in the company, too.

As president, West is pushing ACT in two directions. The company's original goal was to use cloning and gene transfer technologies to engineer cows that produce pharmaceutical proteins in their milk. Two cloned cows born last year testify to the firm's success in this area; under West, ACT will continue to focus most of its efforts on this relatively noncontroversial research.

But West is also determined to move forward with the cow-human embryo work. Cibelli, who is now a senior scientist at the company, is currently repeating his earlier work on a large number of cells. West believes that if this approach succeeds, it will solve both ethical and practical problems. "First, we wouldn't be using [human] fetal tissue or frozen embryos," he says, "and second, should we eventually be able to turn stem cells into human organs for transplantation, we would be able to use a patient's own somatic cells to make the fusion and avoid any issues of rejection."

But a few critics say that in his enthusiasm, West slights the ethical dimensions of the work. "Michael West is a man who sincerely believes that what he is doing is right because it will ultimately benefit human health," says Richard Doerflinger, a theologian who works on pro-life issues for the U.S. Catholic Conference in Washington, D.C., and (like West) has testified before Congress on this issue. "But he really doesn't acknowledge the moral issues involved in what he's doing."

West disagrees. "First, I disagree that this is a moral issue, because these cells cannot become human beings. If they could, I would not be promoting this research. So then, where's the morality in blocking studies that can benefit millions and millions of people?"

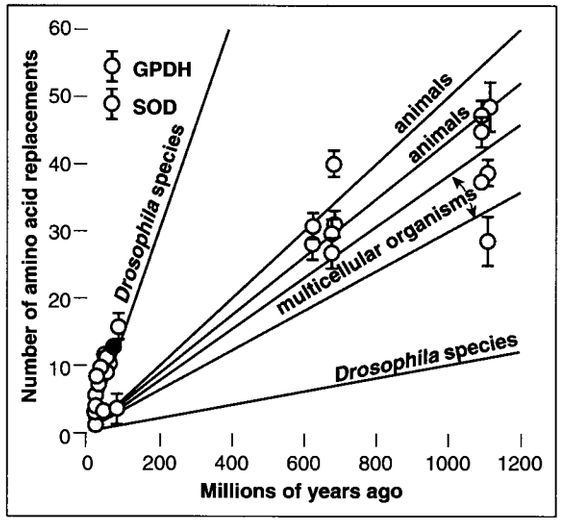
—JOSEPH ALPER

EVOLUTIONARY BIOLOGY

Can Mitochondrial Clocks Keep Time?

New data fuel fundamental challenges to the accuracy of molecular clocks, although researchers say they are tackling the problems

Put a scientist on the analyst's couch, say the word "mitochondria," and she's likely to blurt out "powerhouse of the cell" in response. But if she happens to be an evolutionary biologist, she might instead connect this organelle with a different type of power: the ability to illuminate evolutionary events deep in the past. For over two decades, biologists have been using mitochondrial DNA (mtDNA) to time the divergences of organisms from each other and to map human migrations. Such "molecular clock" studies have suggested that modern types of mammals and birds shared the Earth with the dinosaurs, that animals evolved hundreds of millions of years before their first fossils, and that "mitochondrial Eve," our common female ancestor, lived about 200,000 years ago in Africa.



Rate spread. Not only do the enzymes GPDH and SOD have different rates of evolution, the rates vary in different groups of organisms.

CREDIT: F. J. AYALA/PNAS

The DNA sequences pouring in from sequencing projects have fueled the effort and extended the clock approach to many genes in the cell nucleus. But the wash of data has uncovered some troubling facts. It's now clear that in many cases, the main assumption underlying molecular clocks doesn't hold up: Clocks tick at different rates in different lineages and at different times. And new work on the biology of mitochondria suggests that their evolution may be more complicated than researchers had suspected (see special issue beginning on page 1475).

"There's an emerging consensus that there are significant rate heterogeneities across different lineages," says John Avise, an evolutionary geneticist at the University of Georgia in Athens. "How big they are and how to deal with them is very much a matter of concern." Even those who once embraced the clocks are now somewhat skeptical. "Sure, there are mitochondrial clocks. A lot of them," says Wesley Brown of the University of Michigan, Ann Arbor, who no longer uses mtDNA sequences to time ancient divergences.