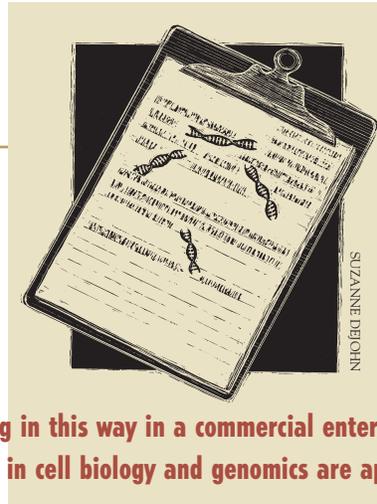


Under advisement

By Ronald M. Green, Ph.D.



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Five years ago, Michael West, the president of a small, privately funded biotech company called Advanced Cell Technology (ACT), asked me to help form an ethics advisory board to provide oversight for the company's planned research on human embryonic stem cells. Dartmouth faculty often get asked to participate in this way in commercial enterprises; it allows us to stay on the cutting edge of our fields, and it also ensures that scientific advances are applied appropriately and ethically.

Cells: West showed me a presentation he had prepared. Its point was simple but surprising: although we all die, at least some of our cells are immortal. Sperm and egg cells, in particular, are part of a continuous line of organic life reaching back to the remote past. If we could unlock the secrets of this kind of cellular immortality and reverse cell death, said West, we might be able to apply that to developing new approaches to medical therapies. Cell death and degeneration cause some of the most serious diseases still facing us—diabetes, Parkinson's, and a host of diseases of aging. In West's vision, cell regenerative medicine could open the way to dramatic new therapies and cures.

The presentation must have been effective. I volunteered to help ACT's scientists pursue their research ambitions. From an ethical standpoint, my position as advisor has presented one challenge after another. Many Americans oppose human embryonic stem cell research because it involves the destruction of embryos, which they regard as morally equivalent to you and me. But West and his colleagues are also attempting therapeutic cloning. This combines nuclear transfer technology (cloning) with stem cell science to produce patient-specific cell lines not subject to rejection. But because of the widespread concern that human cloning technology might one day be used for reproduction, some people reject therapeutic cloning, too.

Halted: In August 2001, shortly after ACT's research began, President Bush announced a policy permitting federal funding for research on only a limited number of embryonic stem cell lines created before that date. He stated his strong opposition to therapeutic cloning and supported bills to ban it. Although these bills have not yet been passed, they have had a chilling effect on the field. Some leading U.S. stem cell researchers moved to other countries. And venture capital for such work, which small firms like ACT relied on, dried up. By late 2002, when ACT's therapeutic cloning program was experiencing its first successes, its funding ran out and the work was halted.

President Bush had promised the availability of more than 60 stem

cell lines, but by 2004 it was clear that many fewer were eligible. There are now only 22, and they not only lack the genetic diversity needed to create a library of stem cell types but are contaminated by mouse proteins and viruses, so are unsuitable for transplants. Newer technologies for cell derivation

have overcome these problems, but federally funded researchers can't use them since they were created after August 2001.

In 2004, a little-known team of Korean researchers announced that they had created a cloned human embryo and used it to derive a line of stem cells. This seemed to be dramatic proof of principle for therapeutic cloning. About a year later, this team announced the creation of 11 new cell lines using procedures that increased the efficiency of the cloning process tenfold. Stimulated by this research, state legislatures around the U.S. began considering funding stem cell research to fill the gap left by federal abandonment. California led the field with a 10-year, \$3-billion initiative, and other states followed suit. With renewed investor interest, ACT restarted its program.

Controversial: The recent news that almost all of the Korean work was fraudulent, however, has cast a pall over stem cell research and given ammunition to those who oppose it on ethical and religious grounds. The critics say we should concentrate on less controversial adult stem cells. They are unmoved by the fact that substantial federal funding for adult stem cell research (10 times the amount allocated for embryonic stem cell research) has not yet demonstrated that adult stem cells have the power of their embryonic counterparts.

On the other hand, the Korean team's ethical and scientific failures have opened new opportunities. Researchers who had felt hopelessly behind the Koreans now see a chance to do that work properly. A further lesson is that ethical oversight is crucial—to protect human subjects (egg or embryo donors) and to make sure the science is pursued with utmost integrity.

So, once again, I find myself on the telephone and attending meetings regarding research at the forefront of an ethically controversial field. There are no material rewards for this work; if I'm asked why I do it, my thoughts return to Mike West's vision. Thanks to advances in cell biology and genomics, our understanding of how cells develop, grow, age, and die is increasing enormously. By learning how to control these processes through stem cell and cloning research, we may someday be able to produce replacement tissues for those suffering from a wide variety of serious diseases. We may also be able to produce immunologically compatible organs for transplantation, helping the thousands of people who die every year because of a scarcity of donor organs. I continue to believe that if we support our best scientists—and help them avoid ethical pitfalls—then cell regeneration technologies will transform medicine in this century. ■

"Grand Rounds" covers a topic of interest to the Dartmouth medical faculty. Green is the director of Dartmouth's Ethics Institute, the Eunice and Julian Cohen Professor for the Study of Ethics and Human Values, and an adjunct professor of community and family medicine at DMS. He is the author of The Human Embryo Research Debates: Bioethics in the Vortex of Controversy, published by Oxford University Press in 2001.