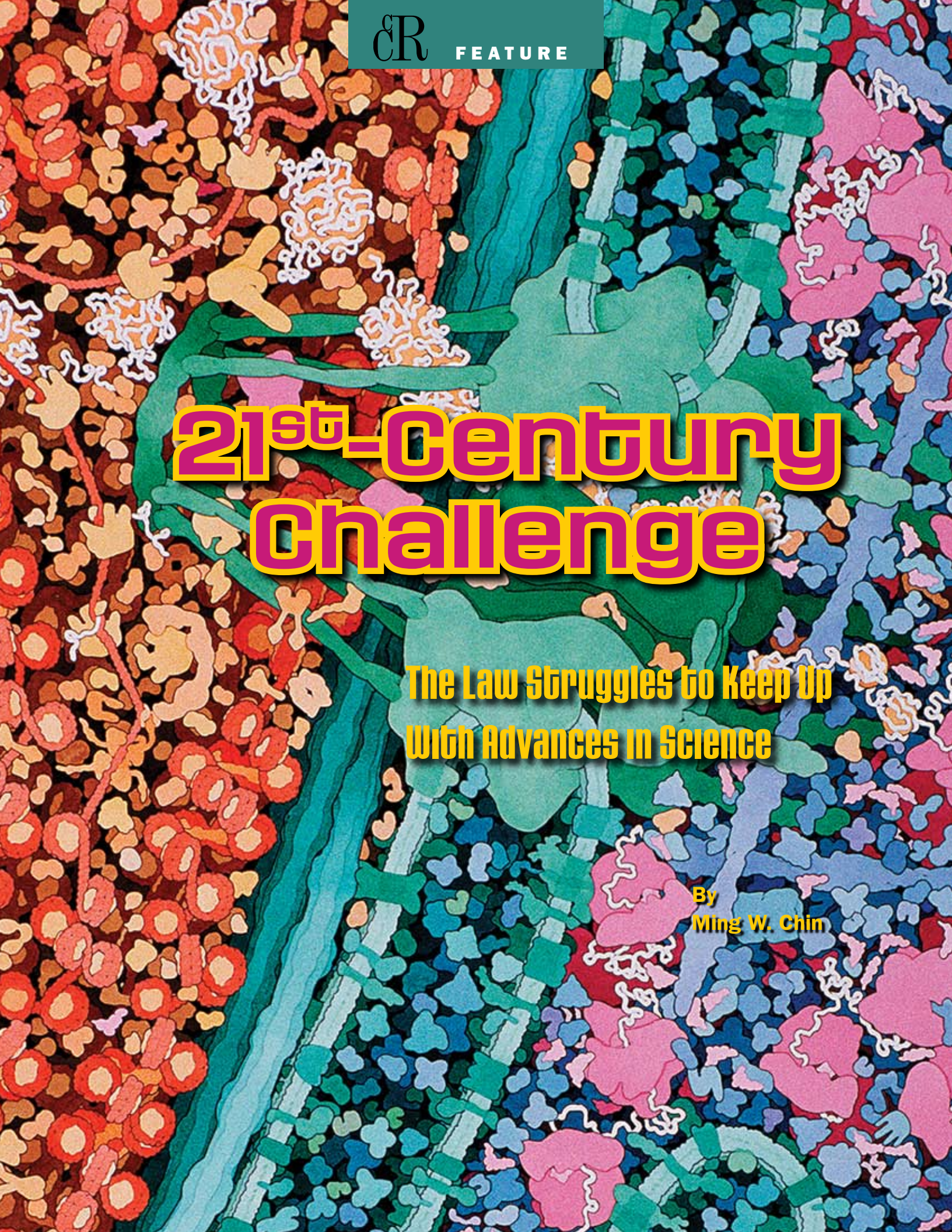


21st-Century Challenge

The Law Struggles to Keep Up With Advances in Science

By
Ming W. Chin

For two centuries, science has been a major force in people's lives. In the 19th century, it was chemistry that yielded great revelations. In the 20th century, physics literally exploded before our eyes. Traditionally, the hard and exact sciences such as chemistry and physics have been the most highly regarded disciplines. However, in the 21st century, biology—and biogenetics in particular—will more than likely dominate advances in science. It is therefore critical to consider the legal and ethical aspects of bioscience and its worldwide impacts on the courts, the law, and society in the 21st century.

Only 50 years ago, Francis Crick and James Watson discovered DNA's double-helix structure. Now it seems that almost every day we hear about a new genetic breakthrough somewhere in the world. First, there was Dolly the sheep. Dolly was followed by Suzie the calf, Dot Com the piglet, Cc the kitten, and Promotea the horse. In 2003 scientists announced the birth of three genetically engineered miniature pig clones, a development hailed as a major step toward transplanting pig organs into humans. Another group of scientists met in 2002 at the New York Academy of Sciences to discuss proposed experiments for using stem cells to create human-mouse hybrids.

With the completion of the decade-long Human Genome Project, essentially all of the 3.1 billion biochemical "letters" of human DNA—the coded instructions for building and operating a fully functional human—have been deciphered. Armed with this genetic code, scientists can begin teasing out the secrets of human health and disease at the molecular level, which at the very least will revolutionize the diagnosis and treatment of everything from Alzheimer's disease and heart disease to cancer. Scientists can also manipulate plants and animals to increase food production and combat environmental hazards.

Modern genetic engineering eliminates the natural barrier between species that limits traditional cross-breeding techniques—that is, it enables the shifting of desirable genetic traits between two species that in nature could not combine their DNA to produce viable offspring. Thus, although modern genetic engineering is still in its infancy, its beneficial possibilities are unprecedented. It is no wonder, then, that each new genetic discovery is announced with tremendous excitement and anticipation.

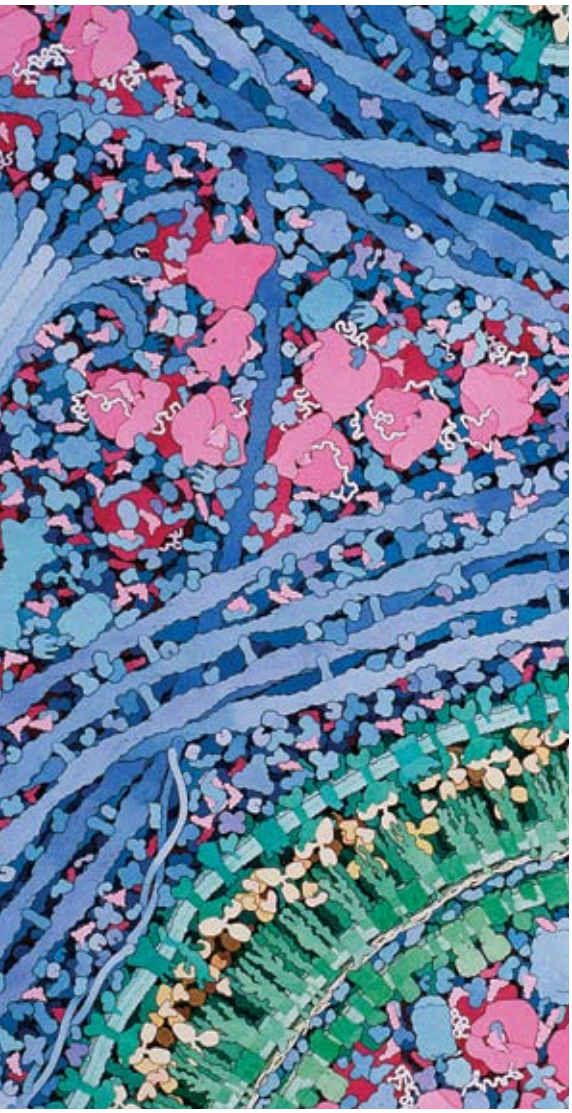
Given the rapid pace of development, it is easy to be dazzled by the science itself and to overlook the ethical and pragmatic considerations. The legal and ethical issues—particularly for lawyers and judges—that have emerged in the wake of these astonishing advances are difficult and complex. Traditionally, the role of bioscience in American law was limited to matters of identity: DNA was used to establish paternity or compare blood samples. Today, however, the legal impacts of bioscience extend well beyond the

Pages 8, 10, and 13: Details from a series of three watercolors on display in the Center for Integrative Molecular Biosciences at the Scripps Research Institute in La Jolla. The paintings depict a macrophage engulfing a bacterium. Macrophages circulate through the blood, searching for bacterial infection. When they find bacteria, they engulf and digest them.

WATERCOLOR BY DAVID S. GOODSELL, THE SCRIPPS RESEARCH INSTITUTE

use of DNA evidence. Genetic testing is now used to help predict life expectancy or determine the likelihood of an individual's having a certain disease. Scientists have developed or are developing more than 900 genetic tests that screen for disorders such as Tay-Sachs, Lou Gehrig's, Huntington's, and Gaucher diseases; cystic fibrosis; inherited breast and ovarian cancers; colon cancer; sickle-cell anemia; muscular dystrophy; Li-Fraumeni syndrome; and multiple forms of Alzheimer's disease. And sophisticated brain testing techniques are beginning to shed light on the truth of what people say and the reasons for what they do.

Genetic and neurological tests will inevitably create tensions and raise new legal questions for society. On the one hand are the great benefits, such as more effective disease prevention and more effective treatment through early detection. On the other hand, advances in bioscience create enormous risks of privacy invasion, discrimination in employment, and denial of health or life insurance. They also give rise to the disturbing prospect of classifying individuals by their DNA or their brain functioning. We must carefully consider and balance these risks and benefits, or litigation involving bioscience will certainly overwhelm us.



As technology advances, science and law will become more deeply entwined. Technological strides have forced people to change and expand their ways of thinking about concepts such as privacy, discrimination, and life itself. To accommodate these changes, our legal system must be prepared. Unfortunately, in many ways, the legal system has already failed to keep pace.

On the medical front, advances in bioscience unquestionably offer enormous benefits. For the last 15 years, scientists and researchers have been trying to develop gene therapy techniques to treat a host of diseases and conditions. We now know that many diseases and abnormalities occur because a particular gene either does not work properly or is completely missing, and we end up with either too much or too little of certain proteins or enzymes. The idea in gene therapy is not merely to treat the symptoms of the disease but to fix the problem at its core by inserting a healthy gene into a person's cells.

To insert a healthy gene into a patient, researchers generally use a virus that has been altered so that it cannot reproduce or cause disease. The virus carries the healthy gene to the targeted cell and unloads it. Once inside the cell, the healthy gene can begin to function so that the body produces the right amounts of the necessary enzymes and proteins. Despite slow progress and numerous setbacks, many scientists still view gene therapy as a medical revolution that will eventually offer a cure—not just a treatment—for a broad range of ailments, including cancer and AIDS.

Two other areas of global importance are cloning and stem cell research:

- In reproductive cloning, a fetus is produced by implanting a cloned embryo into a woman's uterus.
- In therapeutic cloning and embryonic stem cell research, distinct types of tissues are grown from genetic material.

Embryonic stem cells are cells "whose job in the body is not yet determined."[1] They are the precursors to all adult cells in the body, including the cells that make up organs (such as the liver and pancreas). Because these stem cells have the ability to differentiate themselves, they are "good candidates for restoring tissues that have been damaged by injury or disease"; thus, the "goal of any stem cell therapy is to repair a damaged tissue that can't heal itself."[2] In experiments conducted with stem cells derived from adult human bone marrow, researchers have successfully demonstrated that "stem cells can be coaxed to differentiate into airway epithelial cells," which can be genetically altered, potentially to treat cystic fibrosis.[3] Stem cell research advocates believe that stem cells have the potential to treat a wide range of ailments and degenerative diseases, such as Parkinson's disease and spinal cord injuries. Research in this area has taken off since 1998, when scientists first isolated human embryonic stem cells.

In addition, since 2003, when researchers finished decoding human DNA, the search for better, faster, and more effective medications has begun in earnest. Increasingly, scientists armed with our genetic blueprint can identify the individual molecules that make us susceptible to a particular disease. With this information and some high-speed silicon-age machinery, they can build new molecules that home in on their targets like well-aimed arrows. In the new era of genomic medi-

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cine, doctors will treat diseases such as cancer and diabetes before symptoms even begin, and will use medications that, with exquisite precision, boost or counteract the effects of individual proteins by attacking diseased cells while leaving healthy ones alone.

In addition, thanks to the emerging field of pharmocogenetics, patient-specific drugs will play a greater role in our health care, reducing the risks associated with medications. Currently, medications that were properly prescribed make millions of people seriously ill and kill over 100,000 people each year. But the era of one-size-fits-all medication is ending, as physicians are learning to read a patient's unique genetic code and tailor treatments accordingly. Researchers are now looking for the sites in the genetic sequence that differentiate one person from the next, which are called SNPs (single nucleotide polymorphisms), pronounced "snips." Decoding the estimated 10 million SNPs and determining how they affect individuals could lead to the design of drugs matching particular DNA profiles, which would avoid the complications and side effects of many traditional medicines and attack illness at the molecular level.

Already, researchers have identified the most prevalent cell receptors for certain cancers and are developing antibodies to block the normal, destructive activities of those cells. Drug companies are searching for new ways to use existing drugs on the basis of genomic studies. Treatments for AIDS, heart disease, depression, and even obesity may someday be available through pharmacogenetic research.

These advances pose new ethical and legal challenges. Several have already arisen in connection with gene therapy research. In 1999 Jesse Gelsinger, an 18-year-old volunteer for a university's gene therapy study—who was in relatively good health at the time, despite a metabolic condition—died from a reaction to a gene therapy treatment only four days after receiving it. Investigations into Gelsinger's death revealed some troubling information: the university failed to exclude him from the study, as it should have done based on his ammonia levels at the time of treatment; it failed to mention, as part of the informed consent process, that monkeys given a similar treatment had died; and it failed to report immediately that two patients had experienced serious side effects from the gene therapy. More broadly, the investigations revealed that gene therapy researchers in general were substantially underreporting adverse events associated with gene therapy trials, that some scientists were asking that problems not be made public, and that there may have been at least six deaths that were attributed to genetic treatments but went unreported.

Justice Chin pipetting, or loading, an agarose gel that is used to compare DNA.

A recent lawsuit in Massachusetts demonstrates another kind of disclosure issue associated with gene therapy. Roger Darke agreed to participate in an experimental gene therapy treatment for chronic heart disease, which required injection of a healthy gene directly into his heart. Less than 24 hours after undergoing the procedure, he died. A lawsuit was later filed alleging that the doctor performing the procedure and the hospital where it was performed were liable because they had failed to disclose a financial stake in the gene therapy treatment that gave them an incentive to encourage patients to submit to the treatment. The doctor and the hospital argued that this theory was legally invalid because the doctrine of informed consent requires only disclosure of medical information. The Superior Court of Massachusetts disagreed, finding that the informed consent doctrine is "broad enough" to require a doctor to disclose "that he has a financial interest in the treatment that he recommends."[4]

Of course, stem cell research also is very controversial, principally because most techniques for obtaining stem cells involve destroying an embryo. In addition, efforts to create patient-specific embryonic stem cells—stem cells that genetically match a patient's DNA—involve the cloning of human embryos. Thus, both cloning and stem cell research present society with difficult moral choices.

California's Legislature has weighed in on this debate through several laws and resolutions. One of those

Women of Color in the Courts

The emerging role of women of color as leaders and managers in the California courts is featured on a new Web site developed by the Judicial Council's Access and Fairness Advisory Committee. The site contains valuable information for women of color and other interested persons—both women and men.

Visitors to the site can

- Get updates on national issues, such as plans and proposals for regional and national conferences
- Read profiles of women of color who are serving as judges or court executive staff members
- Check a calendar of events, including International Association for Women of Color Day, to be celebrated on March 1, 2006
- Link to dozens of additional organizations, libraries, and other resources

Check out the new Web site at

www.courtinfo.ca.gov/programs/woc

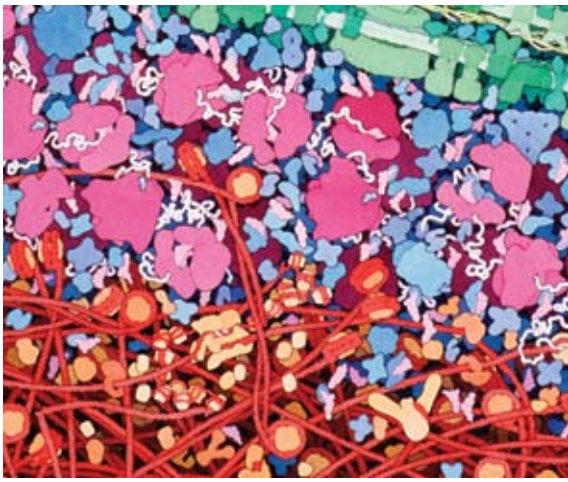
Your only limits are the ones you put on yourself. Don't set your goals too low. Associate with people who make you strive to be better.

— Judge Consuelo Callahan
U.S. Court of Appeals for the Ninth Circuit
(the first woman and first Hispanic appointed to the Superior Court of San Joaquin County)

laws indefinitely extends California's existing ban on human reproductive cloning.[5] Another law expressly declares that stem cell research "shall be permitted" in California and directs health care providers to present to people receiving fertility treatments "the option of storing any unused embryos, donating them to another individual, discarding the embryos, or donating the remaining embryos for research."[6] Under this law, donations of embryos for purposes of research require written consent, and the sale of embryos for research is strictly prohibited.[7]

In passing these laws, the California Legislature made an explicit policy declaration that stem cell research "offers immense promise for developing new medical therapies" for an "estimated 128 million Americans" who "suffer from the crippling economic and psychological burden of chronic, degenerative, and acute diseases."[8] At the same time, the Legislature expressly recognized that stem cell research raises profound ethical, medical, social, and legal concerns that must be carefully considered and balanced in formulating public policy. For this reason, the Legislature established a new panel—made up of representatives from the disciplines of medicine, human biology, cellular microbiology, biotechnology, law, bioethics, and religion—to study these concerns and advise the Legislature on how to pursue stem cell research "responsibly."[9] The Legislature also established a separate new committee—made up of independent bioethicists and representatives from medicine, religion, biotechnology, genetics, law, and the general public—to advise the Legislature and the Governor on human cloning.[10]

The California Legislature did not stop at the California border in trying to guide policy in this area. In 2002 it passed a resolution urging Congress and the President to "reject legislation that inappropriately impedes the progress of medical science by impeding stem cell and therapeutic cloning research, and denies Ameri-



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cans legal access to effective medical therapies."[11]

In 2004 California voters weighed in on the debate by passing Proposition 71. That initiative created the California Institute for Regenerative Medicine to distribute almost $3 billion from the sale of bonds over the next 10 years for research into developing medical therapies that use stem cells. Some have said that Proposition 71 "could make [California] a world leader in one of the most promising, though controversial, fields of biology, perhaps touching off a new biomedical Gold Rush."[12] However, that rush has already been stifled by litigation. Three lawsuits have been filed—two in state court and one in federal court—challenging various aspects of the proposition, including its constitutionality. These lawsuits, which have effectively blocked the bonds from being issued, may substantially delay implementation of Proposition 71.

The controversy over Proposition 71 is a good example of the delicate and sometimes contentious relationship between science and the law. Scientists are primed and ready to develop cures based on stem cell research. However, their progress depends to some extent on how the courts resolve the legal issues related to Proposition 71.

Ultimately, there may be a nonjudicial, scientific light at the end of this tunnel. In August 2005 scientists at Harvard University announced a potential breakthrough that could eventually end the controversy over stem cell research: a technique for turning ordinary skin cells into patient-specific embryonic stem cells without either creating or destroying human embryos. However, in announcing their discovery, the Harvard researchers emphasized that several technical problems remained to be solved.

Of course, because these advances in genetic research use stem cells and human tissue, they pose a host of other new legal questions. As products of human genome research move into the marketplace, how does society address attempts to commercialize products developed from an individual's genetic information? How do the laws of intellectual property apply? Do donors have a right to know that their tissue and cells are being used? Do they have a privacy interest in this material? Do they have an ownership right in this material, or in any discovery or product derived from research on this material? In a famous case 15 years ago, the California Supreme Court held that an individual has no ownership right in his or her cells and tissue after their extraction, and has no right to know of postoperative research involving his or her cells or of their economic value unless the doctor has a direct interest in them that undermines his or her fiduciary duty to the patient.

New genetic technology also is forcing the medical community to address the tension between a physician's duty of confidentiality to the patient and duty of disclosure to others who may have a medical need to know genetic information about the patient. Should doctors inform a patient's relatives of genetic conditions that may affect them, even if the patient objects? What is the ethical answer to this question? What is the medical answer? What is the legal answer? Are the answers different?

This paper has touched on only a few of the issues raised by progress in bioscience—issues that our society must be prepared to confront. As promised, it has identified more questions and problems than answers and solutions. Scientists, lawyers, and judges will be in the forefront of society's attempt to grapple with these issues.

If history teaches us anything, it is that scientific progress is inevitable and unrelenting—and it will certainly overwhelm us if we are not prepared. It is my belief and my hope that if we begin to pose these questions, we will be much better prepared to find reasonable solutions to the complex problems that genetics certainly will bring to our courts. CR

Ming W. Chin is an associate justice of the California Supreme Court. This article is based on his convocation lecture in October 2005 at the California Science and the Law Conference, which was held at the Salk Institute for Biological Studies in La Jolla. The full text of the lecture is available at www.courtinfo.ca.gov/reference/documents/MingChinSpeech.pdf.

Notes

1. Genetic Science Learning Center at the University of Utah, "What Is a Stem Cell?" http://gslc.genetics.utah.edu/units/stemcells/whatissc.

2. Genetic Science Learning Center at the University of Utah, "What Is the Goal of Stem Cell Research?" http://gslc.genetics.utah.edu/units/stemcells/scresearch.

3. *Medical News Today*, "Combined Stem Cell–Gene Therapy Approach Potential Treatment for Cystic Fibrosis" (Dec. 21, 2004), http://www.medicalnewstoday.com/printerfriendlynews.php?newsid=18121.

4. *Darke v. Estate of Eisner* (June 3, 2004) 2004 WL 1325635 (No. 02-2194).

5. Health & Saf. Code, § 24185.

6. Health & Saf. Code, §§ 125300, 125315.

7. Health & Saf. Code, §§ 125300, 125315, 125320.

8. Stats. 2002, ch. 789, § 1(a), (c).

9. Sen. Conc. Res. No. 55, Stats. 2002 (2001–2002 Reg. Sess.), res. ch. 153.

10. Health & Saf. Code, § 24186.

11. Sen. Joint Res. No. 38, Stats. 2002 (2001–2002 Reg. Sess.), res. ch. 163.

12. C. T. Hall, "Proposition 71: State Voters Strongly Backing Cell Research," *San Francisco Chronicle* (Nov. 3, 2004).