Can Public Policy Keep Pace with Stem Cell Science?

Stem Cell Century: Law and Policy for a Breakthrough Technology

Russell Korobkin with Stephen R. Munzer
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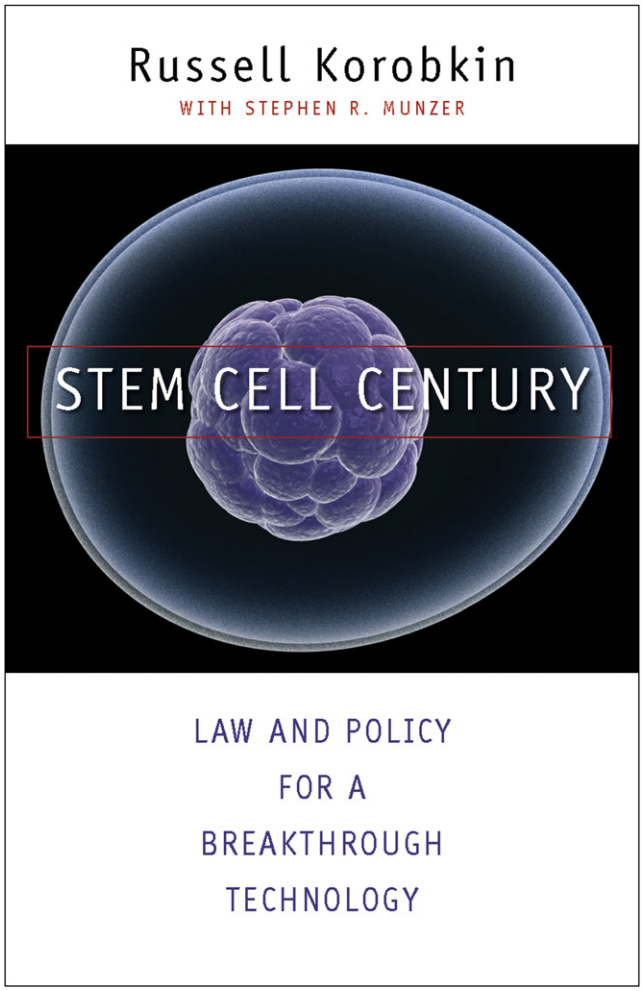

Stem cell policy needs to keep pace with the torrid progress of stem cell science. Since the November 2007 announcement that induced pluripotential cells could be derived from human somatic cells, many scientists have shifted their focus from attempting human somatic cell nuclear transfer (SCNT) to deriving pluripotential cells whose nuclear DNA matches that of a specific donor. Correspondingly, many contentious policy debates may now be moot, including debates over payment for fresh oocytes donated specifically for research, the safety of hormonal manipulation and oocyte retrieval, the use of SCNT as a research tool, and the creation of human-animal cytoplasmic hybrids. Although additional embryonic stem cell lines are still needed, it is likely that they will be derived from frozen embryos remaining after a woman or couple has competed infertility treatment. Research use of frozen embryos still evokes controversy, but less intensely than creating embryos specifically for research.

The Stem Cell Century, by UCLA law professor Russell Korobkin, is a clear, well-reasoned analysis of important issues in stem cell policy. Over one-half of the book primarily concerns embryonic stem cell research and SCNT, and therefore, in the eyes of this reviewer, is now of primarily historical interest. In addition, the book's analysis of payment for materials used in research is less salient with regard to research with somatic cells and frozen embryos. The additional procedures required to obtain these materials are far less invasive or risky than oocyte retrieval, and payment to donors beyond expenses is either not offered or at a de minimus level.

A number of chapters address ongoing public policy issues, such as patents, profits from publicly funded research, and compensation to donors. While enlightening, these chapters focus narrowly on legal scholarship, particularly on close analysis of court rulings and the reasoning behind policy alternatives. However, in the real world, policies will also be driven by negotiation, compromise, and timing, and many other factors need to be considered.

Patent reform is heatedly debated, not just for biotechnology but also for other new forms of knowledge. The broad scope of Wisconsin Alumni Research Foundation (WARF) human embryonic stem cell patents has been challenged, and a preliminary ruling invalidated three patents in April 2007. The author does not discuss a number of reports addressing patent reform in biotechnology, which raise issues and offer options beyond those his book considers. The National Academy of Sciences issued a consensus-based, peer-reviewed report entitled *A Patent System for the 21st Century* (ed. S.A. Merrill, R.C. Levin, and M.B. Myers [Washington, D.C.: National Academies Press, 2004]). This report recommended that inconsistencies among US, European, and Japanese patent systems be reduced. The report also recommended reinvigorating the nonobviousness standard by instituting an Open Review procedure in which third parties can challenge patents before an administrative law judge. These procedures would include expert testimony. As regards the WARF patents, a key issue is whether other scientists would have found the innovation to be obvious at that time. Resolving this issue requires expert scientific testimony. Certainly, a full policy analysis would consider a wider range of issues and options, which traditional legal scholarship might not identify.

The taxpayers' stake in profits from publicly funded research is the topic of another chapter. Current NIH policy allows grantees to patent discoveries and to retain royalty and licensing payments, with no return to the federal treasury even for blockbuster patents. The author carries out a careful policy analysis of sharing of licensing revenues, articulating the options and pointing out inconsistencies in various positions and arguments. Although such analysis is helpful, public policy is shaped in the political arena. The revenue-sharing policy of the California Institute for Regenerative Medicine (CIRM), which will award 3 billion dollars in state funding for stem cell research, is an important case study (see http://www.cirm.ca.gov/policy/policy.asp).

CIRM is proposing an innovative, tiered revenue-sharing agreement that depends on the amount of licensing revenue generated by a patent based on CIRM-funded research. A number of issues had to be decided, including a distinction between for-profit and not-for-profit grantees, policies for licensing of patents and for profits from commercial products, a threshold level that triggers higher payments in the case of blockbuster patents, a cap on payments relative to the size of the original CIRM grant, and access to treatments for patients who are uninsured or who receive care through public funding. Each of these issues deserves further analysis. The author suggests that a proposed return to the state of 25% of company-held licensing revenues exceeding $500,000 is too low, and suggests that 50% is probably more appropriate, without explaining why this is the case. Based on presentations at public meetings, however, a 50% level of sharing would likely lead for-profit companies to eschew CIRM funding, leading to possible delays at early stages of the development of cellular-based therapies. In turn, patient advocates would have rejected such a revenue-sharing policy, fearing that it might delay the development of therapies. Thus different interest groups, policy objectives, and incentives needed to be balanced. Negotiations involved a variety of interest groups, including research institutions, public interest groups, disease advocacy groups, venture capitalists, and for-profit biotechnology firms. The CIRM revenue-sharing policies (which are still not yet final) resulted from 15 public meetings and formal public comments on proposed policies. The process involved give-and-take over the entire set of issues. Whether the top level of revenue sharing should be 25%, 50%, or some other percentage needs to be viewed in the context of the other issues.

A chapter on default rules for tissue donations takes as a starting point the decision in the landmark Moore case, which raised the issue of property rights with regard to human tissues. The author analyzes the nature of property rights and suggests default rules that should apply when the researcher and tissue donor have not made a clear agreement regarding compensation for donated tissue. However, this analysis has little implication for research using somatic cells or frozen embryos. Unlike oocyte donation, there is little need for high compensation to attract donors. Standard practice now is to include in the consent form for donation explicit statements that the researcher may patent discoveries using the tissue and that the donor will not share in any financial benefits. Thus, the author's proposed solution has already been adopted and accepted. His careful analysis yields no new policy recommendations.

The book's analysis of compensation focuses on individual donors. However, an important issue is potential benefit to a class of patients with a specific disease, whose tissues are of particular value to researchers. The case of Greenberg versus Miami Children's Hospital Research Institute is an illustrative example. Parents of children with Canavan disease helped a researcher obtain tissue and funding. Their understanding was that any diagnostic tests would be affordable and accessible. When the researcher patented the genomic sequence for the Canavan disease and charged licensing fees for a Canavan diagnostic test that made the test unaffordable, the parents sued. The plaintiffs lost in the appellate courts, but an out-of-court settlement was reached and sealed. The author analyzes the legal reasoning behind the appellate ruling and points out its logical inconsistency. However, the author does not follow up on the concerns of disease advocacy groups for affordable and accessible tests and treatment resulting from donated tissues, particularly when their cooperation in obtaining such tissue greatly facilitates the research. These issues will likely be settled through negotiations between advocacy groups and researchers; advocacy groups are becoming savvier at making these arrangements explicit at the beginning of a research project. It is likely that other disease advocacy groups will also become better negotiators and narrow the balance of power between researchers and patient groups.

A number of important policy issues will likely emerge regarding stem cell science. Clinical trials of stem cell interventions have been carried out using cord blood stem cells and autologous adult stem cells. The safety of these interventions has been well established. However, interventions using cells derived from embryonic stem cells and fetal tissue are carried out in multiple countries where there are few to no requirements for oversight or for evaluation of clinical outcomes and safety. The International Society for Stem Cell Research (ISSCR) has convened a task force working on guidelines for stem cell clinical trials. One issue is whether stem cell scientists as a professional group should affirm their commitment to valid and generalizable knowledge and to well-designed clinical trials of innovative stem cell interventions. Another issue is how to help potential participants make informed decisions about participating in these clinical trials, while allowing them to maintain hope. Other stakeholders in clinical trials, particularly regulatory agencies, scientific review bodies, and institutional review boards, should start to develop policies and regulations for such clinical trials. Insightful scholars such as Prof. Korobkin could contribute to the development of such policies. One challenge will be for them to disseminate their work in a way that has greater impact on real-time policy development. Publishing books or articles in law and policy journals may not, in a timely manner, reach scientists who are helping to develop public and institutional policies.

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