CHEST

Ethics and Policy Issues for Stem Cell Research and Pulmonary Medicine

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Stem cell research and related initiatives in regenerative medicine, cell-based therapy, and tissue engineering have generated considerable scientific and public interest. Researchers are applying stem cell technologies to chest medicine in a variety of ways: using stem cells as models for drug discovery, testing stem cell-based therapies for conditions as diverse as COPD and cystic fibrosis, and producing functional lung and tracheal tissue for physiologic modeling and potential transplantation. Although significant scientific obstacles remain, it is likely that stem cell-based regenerative medicine will have a significant clinical impact in chest medicine. However, stem cell research has also generated substantial controversy, posing a variety of ethical and regulatory challenges for research and clinical practice. Some of the most prominent ethical questions related to the use of stem cell technologies in chest medicine include (1) implications for donors, (2) scientific prerequisites for clinical testing and use, (3) stem cell tourism, (4) innovation and clinical use of emerging stem cell-based interventions, (5) responsible translation of stem cell-based therapies to clinical use, and (6) appropriate and equitable access to emerging therapies. Having a sense of these issues should help to put emerging scientific advances into appropriate context and to ensure the responsible clinical translation of promising therapeutics. CHEST 2015; 147(3):824-834

ABBREVIATIONS: FDA = US Food and Drug Administration; iPS = induced pluripotent stem; SCNT = somatic cell nuclear transfer

Stem cell research and regenerative medicine have stimulated considerable scientific and popular excitement.[1] Since 1998, when embryonic stem cells were first derived from human embryos, efforts have focused on unlocking the potential of stem cells in a variety of different applications, from disease modeling and drug discovery to tissue regeneration and stem cell-based therapies.[2] By combining stem cells with novel tissue engineering strategies and biomaterials, scientists are exploring the possibility that whole tissues and organs can be engineered for replacement of damaged or diseased ones.

Stem cells and related technologies can be used to screen new drugs for efficacy and toxicity in cells from affected patients and for transplantation using patient-matched sources of cells to minimize rejection. As

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such, stem cells offer hope for those affected by an array of intractable diseases and conditions. However, stem cell research has also been surrounded by public controversy. Most prominent have been concerns about human cloning and debates about the moral status of embryos that must be destroyed to derive embryonic stem cells, including questions concerning potential moral distinctions of using donated surplus embryos from in vitro fertilization compared with embryos created specifically for stem cell research.

As research involving stem cells and regenerative medicine has progressed, new ethical and policy questions have emerged. In this article, after reviewing some of the major potential applications of stem cell science and tissue engineering in pulmonary medicine, we describe some of these ethical and policy issues that will need to be addressed as stem cell research advances further toward the possibility of translation into clinical use, both in general and specifically in chest medicine. Although the primary intent of this article is to describe the ethical issues involved, where there is consensus concerning particular issues, we offer prescriptive recommendations.

Regenerative Medicine in Chest Medicine

The term "stem cells" refers broadly to cells that have the capability of differentiating into diverse cell types. These include pluripotent stem cells (eg, embryonic stem cells, induced pluripotent stem [iPS] cells, and those derived by somatic cell nuclear transfer [SCNT]), which are capable of self-renewal and can become any cell type, as well as "adult" stem cells (eg, hematopoietic stem cells, mesenchymal stem cells, adipose-derived stem cells, and umbilical cord blood stem cells) that have a more limited ability in terms of cell types that they can become.[3]

Of special interest to regenerative medicine are pluripotent stem cells that can be a "match" for a patient with a disease, which include SCNT-derived cells and iPS cells. SCNT-derived cells are created when the nucleus from an adult cell is transferred into a donor egg whose nucleus has been removed, creating an embryo through a process known as "therapeutic cloning." Of note, this process is distinct from "reproductive" cloning, which many find to be ethically problematic; however, SCNT involves the creation and subsequent destruction of an embryonic blastocyst.

iPS cells are derived from virtually any human cell that is reprogrammed to a naive state where it can become any other cell type. A variation is the direct conversion of one cell type to another without reverting to a stem cell state as an intermediate (but using similar laboratory techniques), known as direct reprogramming or "transdifferentiation."[4] Deriving these cells does not require the destruction of human embryos, thus obviating some religious, moral, and political concerns. Table 1 describes different types of stem cells and some of the ethical issues related to them.

Although regenerative medicine has focused considerable attention on the spinal cord, the eye, and the heart, remarkable progress has been made regarding the respiratory tract.[5-10] For example, stem cells and regenerative medicine may offer solutions for disorders as diverse as acute lung injury, ARDS, idiopathic pulmonary fibrosis, COPD, genetic disorders (eg, cystic fibrosis and sickle cell disease), and reactive airway disease.[11-14] Translating stem cell-based therapies for the respiratory tract faces a number of hurdles, including ensuring safety and optimizing routes of delivery and dosage, but excitement abounds.[15]

The clinical use of stem cell-based therapies is not just theoretical.[16] In fact, clinical trials involving both embryonic stem cells and iPS cells aimed at retinal diseases have started, and trials for cardiovascular disease are planned in the near future. Applications especially relevant for chest medicine include Prochymal (Osiris), a mesenchymal stem cell-based intervention that is currently in phase II trials for COPD[17]; and AdipoCell (Bioheart, Inc), a stem cell-based intervention derived from autologous adult stem cells from adipose tissue that is slated for clinical testing in patients with ischemic cardiomyopathy.[18] Selected recent and current trials of stem cell therapies in chest medicine are listed in Table 2. Of note, at present these are early-stage trials using adult stem cell sources.

Although a comprehensive review of the scientific bases for stem cell and regenerative medicine-based therapies in chest medicine is beyond the scope of this article, it is helpful to understand that related research is currently progressing along several distinct paths:

1. Exploring endogenous "adult" stem and progenitor cell populations in the lung, with the hope of activating regeneration pathways that are otherwise overwhelmed in disease.[19-21]
2. Harvesting adult stem/progenitor cells that can be expanded and manipulated to promote regeneration.[11,22]
3. Producing pluripotent stem cells from skin, blood, and/or lung tissue harvested from patients with lung disease to model these diseases and test drug candidates in vitro.