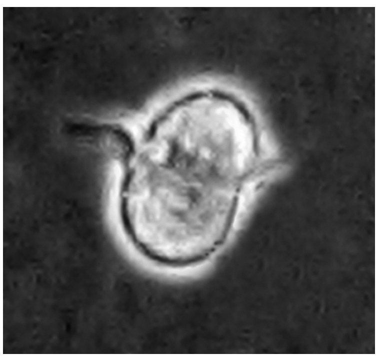
Executive Summary

Stem cells have two defining characteristics: 1) they "self-renew," or make copies of themselves; and 2) they can become any of many specialized (differentiated) cell types. Pluripotent stem cells (embryonic stem [ES] cells, induced pluripotent stem [iPS] cells, and certain cells of the early embryo) can become any cell type of the body. Other stem cells are more restricted in their fates. These multipotent stem cells are popularly called "adult" stem cells because they are found in adult bodies (but also in prenatal ones).

Stem Cell Dividing



A stem cell doing what defines it: self-renewal. These are human neural stem cells.

Source: Brent Reynolds, PhD, McKnight Brain Institute, University of Florida

The language used to describe stem cells is a metaphor for how we can harness them in drug development and regenerative medicine. Stem cells have developmental potential in that they can become many things; so, too, can their commercialization potentially help to treat an astounding variety of medical conditions. Stem cells in the body are sequestered in niches; so, too, will stem cell-based therapeutics find their niches in health care. And perhaps it is fate that we learn to use the instructions in our genomes to direct stem cells to help us heal.

Stem cells burst into public consciousness in 1998, with the derivation of human ES cells. But the roots of the field go much deeper, back to the pioneering nuclear transfer work in amphibians and the advent of bone marrow transplants more than half a century ago, to the mid-1990s cloning of mammals and gene knockout technology, which first used ES cells. But the potential power of stem cell-based therapies was slow to catch on with the public. Perhaps people were sated with news of cloned sheep and mice, or with failed gene therapy experiments. Objections to use of human embryos to derive ES cells slowed progress in some nations, but interest continued, as did research using other sources and types of stem cells.

Today, factors are converging to catapult stem cell technology into the medical mainstream:

- Aging human populations are confronting the ravages of degenerative diseases.
- Human genome information, gene expression profiling, and genome-wide association studies are providing the tools to dissect the intricate signaling that directs stem cells.
- Medicine is becoming much more personalized.
- Stem cell R&D is experiencing an unprecedented degree of international collaboration and cooperation.

Government support, private investment, the interest of the pharmaceutical industry, funding from patient advocacy groups and other eclectic sources, and formation of companies to commercialize new ways to isolate stem cells and apply their powers, are all on the rise. In 2004, the annual meeting of the International Society for Stem Cell Research (ISSCR) in Boston drew only a few hundred people. Four years later, in Philadelphia, the meeting had several thousand.

After a slow start, the stem cell age is finally poised to begin.

Applications range from treating both orphan and common diseases in people, to healing injured horses and dogs with their own fat cells, to banking stem cells as insurance against future disease. Many vendors supply the reagents and materials that support stem cell research, while regulations may need revamping to accommodate delivery of personalized, self-perpetuating cell implants or signaling molecules that activate endogenous stem cells. Yet at the same time, untested treatments are being foisted on a public not always educated in the basic biology. Along with the evolution of the technology must come regulations, standardization of protocols, and oversight.

Roadmap for this Report

Stem cell science and technology feature three general varieties of cells that will have three types of applications. The three cell types are ES cells, iPS cells, and adult stem cells. The three applications are in drug discovery and development, recapitulation of disease, and therapeutics. Matching cell type to research or clinical goal is part of the excitement of the field.

Chapter 1 introduces the current state of stem cell science and technology, against a backdrop of the roles of these cells in normal development. The chapter traces the experiments that set the stage for today's stem cell technology, as well as examination of the state of "stemness" and factors outside the genome that affect cell fate. Human ES and iPS cells are contrasted—each has its own niche.

Chapter 2 considers the technological landscape, continuing Chapter 1's look at ES and iPS cells with a description of many types of adult stem cells and how we might use them. The chapter then covers the care and feeding of stem cells—their isolation, derivation, culture, and characterization, with a closer look at two compelling applications, one using ES cells and one using adult stem cells. The chapter explores how stem cells fit into tissue engineering, and then considers suppliers of reagents, devices, and materials.

Chapter 3 highlights three major applications of stem cell science. In drug discovery and development, stem cells are being used to identify novel drug targets, describe the earliest inklings of disease, and reveal disease subtypes. The first applications will likely be in toxicology testing. ES and iPS cells will be particularly valuable in the second major arena for stem cell science, recapitulating pathogenesis *in vitro*. In the third area, therapeutics, stem cells are being tested as treatments in implants and transplants, and as *in vivo* targets that can be activated with introduced factors. The chapter concludes with a closer look at three therapeutic goals: treating the failing heart, cancer, and eye diseases.

Chapter 4 presents a commercial outlook, looking at a mix of areas that are critical to the translation of stem cell science from bench to bedside. Pharma is just beginning to fund stem cell research at academic centers and biotech companies, and venture capitalists are on the lookout for researchers who can succinctly pitch a stem cell-based product or service.

Interesting intellectual property challenges for ES, iPS, and neurospheres are discussed. The chapter also considers public perception of stem cell technology, the origins of the hype that fuels medical tourism, bioethical concerns, and the policy patchwork that currently underlies the field.

Chapter 5 offers the voices of those in the field of stem cell research, with roundtables. Taken from news conferences and panel discussions at the ISSCR annual meeting in June 2008, these conversations reveal how the people who invented the enabling technologies and have done groundbreaking experiments think and share ideas. The two roundtables in this report address iPS cells and the bench-to-bedside trajectory of stem cell research.

Three other interviews follow.

Chapter 6 was very difficult to write, for selecting just a handful of companies to profile, out of many hundreds, was nearly impossible. The goal in the choice was diversity. Companies dealing with ES cells, iPS cells, and adult stem cells are represented.