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Breakthroughs 1999

Floyd E. Bloom

Rarely do we have an opportunity to enjoy bounties of discovery that promise such great benefits to the scientific community as we have enjoyed recently. This editor always reaches the end of the year wondering how researchers can top their past achievements. But the sheer momentum of discovery has again provided a solution. The ability to isolate and maintain human pluripotent stem cells in culture offers humanity incredibly exciting possibilities for replacing diseased organs and repairing selected cellular defects. These achievements and others are recognized as *Science*'s Breakthroughs of the Year.

"[H]uman pluripotent stem cells... offer...incredibly exciting possibilities..."

For nearly 20 years, scientists have been able to isolate mouse embryonic stem cells, and these have been a critical tool in the creation of transgenic mice containing mutations that have yielded rich insights into gene function. Study of embryonic stem cells apart from this important application has shown that they are able to proliferate in vitro seemingly without limit and to remain undifferentiated. The new promise now comes from the beginnings of a technology by which growth conditions and factors can be used to guide such cells to form organ-specific tissues. Such partially differentiated cells have been shown to integrate and replace cells in diseased tissues, chiefly of mice for now, but perhaps of humans in the future. And although embryonic stem cells may have maximum potential, researchers are also learning to manipulate stem cells from adults, which are much more accessible and can develop into a surprisingly broad repertoire of cell types. Ultimately, perhaps, stem cells can form whole complex organs such as a kidney or liver, reducing the need to await organ donations. Not only have scientists already been able to form neurons, glia, muscle, and bone, but to partially overcome missing cellular components underlying abnormal myelination, weakened bones, or dystrophic muscle. Most recently, embryonic neural stem cells appeared to provide partial repair of a traumatized spinal cord more than a week after injury.

However, like all unanticipated powerful steps forward, this technology causes a great deal of concern because of ethical considerations. What rules should govern the donation of unneeded and unimplanted embryos from in vitro fertilization for use as sources of embryonic stem cells? The National Institutes of Health's recently released guidelines on this critical issue prohibit federal funding for acquiring and isolating embryonic stem cells, while creating a new body (the Human Pluripotent Stem Cell Review Group) to oversee compliance with their proposed guidelines. Clearly, the more utility to be gleaned from adult stem cells, the less these concerns about embryonic cells will matter. Although much remains to be done to convert today's results into tomorrow's treatments and tools, the likelihood of success seems high.

This is the 11th year-end recognition by *Science* of the top developments in scientific research, assessed by our editors for their effects on society and the advancement of science (see the special section coordinated by Deputy News Editor Elizabeth Culotta, beginning on p. 2238). Without question, the potential of embryonic stem cells again fulfills our definition of a breakthrough [see *Science* **274**, 1987 (1996)] as a rare discovery that profoundly changes the practice or interpretation of science or its implications for society. Our 1999 runners-up include the three-dimensional resolution of the ribosome's proteins interacting with messenger RNA and transfer RNAs. We also recognize important new developments in collisions between fermionic potassium atoms in different quantum states, new extrasolar planets, and a new major player in the molecular mechanisms of memory.

As in previous years, we have again attempted to look into the near future to anticipate which paths of today's research are likely to become superhighways in 2000. We also score ourselves on last year's predictions. *Science* reaffirms the importance of recognizing such major achievements as provisionally established advances, fully realizing that more data will be sought and convinced that some of the new data will surprise us. This is the last of the Breakthroughs to which this editor will be privy in advance. Sincere thanks for what we have learned. Let's share the joys of what remains to be discovered.