Adult Stem Cells: New Therapies, No Cloning

by Wolfgang Lillge, MD

Most people around the world believe that embryonic stem cells offer the greatest promise for developing new medical treatments: In reality, adult stem cells from the body of the patient being treated, have shown a much greater potential for curing severe diseases. One reason for this distorted public opinion is the pattern of media reports about ongoing research with stem cells. Any new result, even if a very minor one, with embryonic stem cells, is blown up in the media as a major breakthrough. But when researchers announce even greater success using adult or alternative sources of stem cells, there are generally only small notes in the remote corners of the science pages.

The same spin has an obvious political purpose, as it has a major influence on the current cloning debate, both in the United States and abroad. There is a powerful lobby, including biotechnology companies and investors, that is pushing hard to completely open up scientific research to the "therapeutic" cloning of human embryos, disregarding moral objections associated with it. While adult stem cell research continues—somehow anonymously, but with remarkable success!—the public focus is clearly on embryonic stem cell research. The current debate in the U.S. Congress on whether to allow cloning of human embryos for research purposes is a reflection of that.

What is needed in the legislative process is a clear perspective about the consequences of such decisions. Scientists cannot achieve progress by overriding basic human values; here, this means developing treatments for diseases by killing human embryos in the process. One must understand there is no qualitative difference between cloning a human embryo for "therapeutic" means (to obtain embryonic stem cells) and for "reproductive" means (to produce a complete human clone).

The Use of Stem Cells

The legislation in the United States is still undecided: The House has passed a strict cloning ban, which the President supports; many Senators are being lobbied and have come out for human embryo cloning for "medical research only." In Germany, such attempts remain banned, but the importation of stem-cell lines produced by this method from other countries, has now been permitted. In Britain, no restrictions exist on attempts at human cloning. What must be brought to bear is the informed moral stand of the citizens, against a further moral decline of society.

Reviewing the research results of the last couple of years, it becomes obvious that embryonic stem cells involve severe problems when scientists try to use them as means of treatment. Largely unmentioned is the high "price" paid for these very uncertain results. To obtain embryonic stem cells, an embryo—a nascent human being—must be killed in the *morula* phase of growth, when one can harvest "pluripotent" cells (i.e., those still able to develop into many different cell types).

The general idea of therapy with stem cells, both embryonic and adult, is to use these cells to regenerate or replace diseased tissue, as in Parkinson's disease or multiple sclerosis patients. One of the major advantages of adult stem cells is that cells from the patient's own body can be used, which removes the risk of immune reaction against reimplanting these cells; whereas, in the case of embryonic stem cells, exogenous cells are used which definitely will provoke a major immune response. The only future way out of this immune dilemma would be to produce embryonic stem cells of the patient, by way of "therapeutic cloning." For that, you take a body cell, extract the nucleus, insert this nucleus into a denucleated egg cell, and stimulate its embryonic development. If it reaches the *morula* phase, you kill the embryo extracting the stem cells, which should be immunologically identical to the patient's cells. After culturing and transforming them into the needed tissue, they will be retransplanted to the patient for treatment.

There has been, so far, no report of successful treatments of humans in this way. These cells seem to be too "unripe"—also reflected by the fact, that embryonic stem cells have a severe tumor risk. Of course, all these approaches are in a very early phase of research; but why pursue a technique where such problems are combined with a major moral handicap?

New Promising Results

The pattern of media twisting was visible recently when several important research results were achieved. Anyone who relies just on television for news, or quickly scans newspapers, would have missed them altogether. Using experimental procedures with adult stem cells, patients with Parkinson's disease and multiple sclerosis have experienced significant medical improvements. Comparable benefits using embryonic stem cell treatments have not yet been demonstrated even in animal experiments.

The most recent case concerns a 57-year-old man, who was diagnosed at the age of 49 with Parkinson's disease, typified by a progressive loss of dopamine-producing cells in the brain. The disease worsened progressively, leading to tremors and rigidity in the patient's right arm. Traditional drug therapy did not help. As reported by neurosurgeon Michel Levesque of Cedars-Sinai Medical Center in Los Angeles, at a conference in Chicago in early April, stem cells were harvested three years ago from the patient's brain using a routine brain biopsy procedure. They were cultured for sev-

eral months in the laboratory, growing to several million cells. About 20% matured into dopamine-secreting neurons. In March 1999, these neurons were injected into the patient's brain. Within three months the man's motor skills had improved by 37%, with an increase in dopamine production of 55.6%. By March 2000, the patient's overall performance had improved by 83%, and as of March 2002, no symptoms of Parkinson's disease can be seen—and that, without taking any other Parkinson's medication.

Even if this is yet only a single case, a treatment program on the basis of adult stem cells could soon outdo other approaches, including recent therapeutic attempts using neural cells of aborted fetuses. Levesque will now expand his program to 12 additional patients.

One can only assume, that had the treatment been conducted with embryonic stem cells, the media would have spread the story all over the place.

There is also a potential new treatment for people with severe cases of multiple sclerosis (MS). Recent research results were presented during the American Academy of Neurology's 54th Annual Meeting in Denver, April 13-20, 2002. The new treatment involves removing stem cells from the patient's blood, killing those cells that are working against the body's immune system, and then returning the healthy stem cells back to the body. Similar treatments have also been tried in advanced stages of cancer, where strong chemotherapy would destroy the blood-producing system in the bone marrow.

"The hope is that these stem cells will eventually reconstitute into healthy immune system cells and the disease process can be stopped," said study author George Kraft of the University of Washington Medical Center in Seattle. There, 26 people with severe MS underwent this treatment, called autologous stem cell transplantation. Their results were followed for an average of 14.2 months. Conventional treatments had previously been unsuccessful for all of the patients, either with no improvement or intolerable side effects. After the stem cell transplant, 20 patients were stable, with no change in their amount of disability. Six showed some degree of mild improvement by some measures. "This is good news," said Kraft. "These patients had all been rapidly deteriorating over the past year, so to get them to a point where they are stabilized is great progress."

Meanwhile in a Canadian study begun in 2000 at the University of Ottawa, younger MS patients, at a less severe stage of the disease, have shown even greater benefit from the same procedure. Six months after the first patient was treated, she was found to have no evidence of the disease on MRI scans. Three other patients have also received successful adult stem cell grafts, with no current evidence of active disease. It is still too early to tell whether the Canadian patients have achieved permanent remission or a cure, but there can be no question that the research is significant.

We may add a short list of other advances made in adult-cell therapies and research in the recent period:

- In Israel, doctors inserted white blood cells of a paraplegic patient into her severed spinal cord, after which she regained bladder control and the ability to wiggle her toes and move her legs.
- Harvard Medical School researchers killed cells producing insulin in mice, inducing diabetes; then, the animals' adult stem cells took over and regenerated missing cells needed to produce insulin and eliminate the disease. This compares to an experiment in which embryonic stem cells, injected into diabetic mice, achieved a 3% insulin production rate, and all the mice died. "The permanent reversal of Type 1 diabetes in mice may end the wrenching debate over harvesting stem cells from the unborn to treat adult diseases," said the *Harvard University Gazette* of July 19, 2001, of this astonishing success. "It should be possible to use the same method to reverse Type 1 diabetes in humans," says Denise Faustman, the associate professor of medicine who leads the research. Set-up has already begun for a trial for human patients at Massachusetts General Hospital in Boston.

Nature Creates Doubts

Against the mounting evidence in favor of adult stem cell treatments, a note was published in *Nature* magazine in March, implying that hopes for this research and practice may be premature. The claim that adult stem cells are just as versatile as embryonic ones may have been misleading, said the British publication's note; they may be just fusing with other cells to form abnormal hybrids, which are mistaken for pristine new tissues.

What seemed a strong argument on first view, soon turned out not to be very convincing. The conditions of the experiment reported were such, that no significant results could be expected, and later the authors themselves admitted that fusion of this type is a very rare event. However, the *Nature* warning was multiplied widely enough in leading non-scientific media, to create a general doubt in public opinion.

In contrast, a small, but highly important note went almost unnoticed: Catherine Verfaillie at the University of Minnesota reported, that she had found stem cells in the bone marrow of adults, that can turn into every single tissue in the body. Until now, only stem cells from early embryos were thought to have such "pluripotent" properties. If further research confirms these findings, there would be no need to resort to "therapeutic cloning" of human embryos in order to get matching stem cells.

Experiments so far seem to confirm that the cells—dubbed multipotent adult progenitor cells, or MAPCs—have the same potential as embryonic stem cells. Verfaillie says that her lab has reliably isolated the cells from about 70% of the 100 or so human volunteers who donated marrow samples. She reports the cells seem to grow indefinitely in culture, like embryonic stem cells; some cell lines have been growing for almost two years and have kept their characteristics, with no signs of aging.