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For Stem Cells, a Role on the Battlefield

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When people envision using human embryonic stem cells for "regenerative medicine," they often talk about making neurons to treat Parkinson's disease, cardiac cells to repair the damage caused by a heart attack, or pancreatic islet cells to replace those destroyed by diabetes.

But some scientists say an early therapeutic use of such cells might be more prosaic: making red blood cells for transfusions.

Such blood cells, perhaps made in huge vats, might one day supplement blood donations, which are often in short supply. And the blood might be free of the infectious diseases that can be found in donated blood.

The military is especially interested because it can be hard to find and store red cells for use on the battlefield. The Defense Advanced Research Projects Agency, known as Darpa, is starting a "blood pharming" program aimed at developing a system that can make red blood cells from progenitor cells on the battlefield.

Making red cells is "one of the easiest things one might do starting with embryonic stem cells," said Eric E. Bouhassira, a professor of cell biology and hematology at Albert Einstein College of Medicine, who is doing research in the field.

The reason, he said, is that to treat Parkinson's disease, heart attacks or diabetes, scientists have to figure out not only how to make the proper cells, but also how to get them functioning in the body. But once scientists learn how to make red blood cells — or platelets, the cells that allow blood to clot — they already know how to use them.

In addition, matching a blood type is easier than matching other types of tissue to avoid rejection of a transplant.

Still, those advantages are offset by the huge volume of cells required for transfusions, far more than might be needed to treat Parkinson's or other diseases.

That is why a paper published online in August by the journal Blood drew some attention. Scientists at Advanced Cell Technology reported making 10 billion to 100 billion red cells starting from a plate of human embryonic stem cells.

"It's the first time to my knowledge that anyone has been able to produce these on a sufficient scale to talk of using them for transfusion purposes," said a co-author of the paper, Dr. George Honig, an emeritus professor and pediatric hematologist at the University of Illinois at Chicago.

But even that amount is less than needed for one transfusion. A unit of blood, about a pint, contains more than one trillion cells, said Dr. Dan S. Kaufman, associate professor at the University of Minnesota.

Advanced Cell Technology, which is struggling to raise money to stay in business, is not the only company pursuing blood cells.

James A. Thomson of the University of Wisconsin, the first person to derive human embryonic stem cells, was a founder of Stem Cell Products, a company formed to pursue making blood products from stem cells. The company has since merged with another he helped found, Cellular Dynamics, which is working on making cells to be used in pharmaceutical research.

The idea faces other challenges beyond the huge volume of cells needed. The red cells produced from embryonic stem cells so far tend to resemble embryonic or fetal red cells more than adult ones. They tend to be larger and often contain nuclei, which could impede their passage through the body. And they have a different form of the globin molecule, which carries oxygen.

How well the cells would work in the body is still unknown. The red cells produced by Advanced Cell Technology carried as much oxygen as adult red cells in laboratory tests. But they have not yet been tried in animals or people.

"The real test is in vivo," said Dr. Thalia Papayannopoulou, a professor of medicine at the University of Washington, adding that the manufactured cells might not last as long in the body as donated red cells because of differences in their membranes.

Safety is another issue. Blood substitutes made other ways have harmed patients in some circumstances.

Finally, there is the issue of cost. "People donate for free, and free is a difficult price point to compete with," said Nick Seay, chief technology officer of Cellular Dynamics. Even after the donated blood is processed, hospitals can buy a unit for about $200.

But with the expensive growth factors needed to develop red cells from embryonic cells, the costs could be thousands of dollars per unit, said Dr. Michael P. Busch, director of the research institute at Blood Systems, a large nonprofit blood center.

Red cells might conceivably be one of the first therapies derived from so-called induced pluripotent stem cells, which are made from adult skin cells. These cells are becoming popular for research because they avoid the ethically controversial destruction of embryos needed to create embryonic stem cells.

But a big barrier to using induced cells for therapy is that they are created by adding genes to the skin cell using a virus. One of the genes that has been used can cause cancer, as can the use of the virus. But red cells made this way would presumably not carry the cancer risk because the cells have no nuclei, Dr. Kaufman said.

Other cells, like those from bone marrow or cord blood, can also be used to make red blood cells. But those cells cannot reproduce indefinitely in culture like embryonic stem cells. Researchers like Cornelis Murre at the University of California, San Diego, are working on ways around this.

Darpa's initial "blood pharming" contracts will not involve human embryonic stem cells, said Mr. Seay of Cellular Dynamics. Under Bush administration policy, federal money can be spent for research on only a

small number of approved embryonic stem cell lines. None of those lines is Type O negative, the universal donor that Darpa wants.