

Researchers Turn To Adult Stem Cells

Biotech Firms See Potential for Medical Use

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Friday, August 20, 2004

Biotech executive C. Randal Mills flies a lot, and he's learned what to expect. Almost as likely as getting those tiny bags of peanuts or pretzels, someone in a neighboring seat will ask, "So what do you do for a living?"

Mills says his answer -- that he's chief executive of a stem-cell research company -- is met with comebacks that fluctuate between "you must be having a really hard time" to "you must really hate President Bush."

Mills's company, Osiris Therapeutics Inc. of Baltimore, is one of about a dozen firms developing therapies using adult cells, not cells from embryos. That puts Osiris both outside and inside the national debate over stem-cell research.

It isn't directly affected by the limits placed on federal funding of embryonic-cell research by the Bush administration. But in another sense it is in the thick of the scientific and political controversy: If life-saving treatments can be developed with adult cells, it would probably ease pressure on the administration to reverse its stand.

Three years ago, Bush limited federal spending for research using embryonic stem cells to a number of cell "lines" already derived from 5-day-old human embryos. Some conservatives liken research on embryos to abortion, while critics of Bush's policy say he has hobbled studies that could lead to cures of a broad range of diseases.

Stem cells differ from other cells because they can divide and regenerate. Embryonic stem cells, which were first isolated in 1998, are prized by scientists for their "plasticity," the potential to grow into many other cells or tissues. Scientists have for many years theorized that adult stem cells can regenerate only as cells of the tissue from which they are drawn.

But many of the companies working with adult stem cells are staking their efforts on a series of provocative and controversial scientific studies they claim show that adult stem cells can convert into other cell types -- that cells drawn from bone marrow can grow into cardiac muscle cells, for example.

None of the companies working with adult stem cells has yet brought a drug to market, but several have treatments in clinical trials. Some struggle for funding; a few are publicly traded. Others keep going with investments from biotech giants such as Amgen Inc. and Boston Scientific Corp. Like other biotech start-ups, all face skepticism as they try to show that their research can work as medicine and as a business.

The debate over adult stem cells, including among patients and investors, concerns whether they will ever approach the potential of embryonic stem cells, whose proponents predict revolutionary therapies to cure diseases such as Parkinson's. That question prompts impassioned disagreements between those who favor and those who oppose expanded research on embryonic cells.

"Adult stem cells are really where the real progress is being made," said Jay P. Lefkowitz, a former adviser to Bush on stem-cell policy.

"This is voodoo science," said Steve Brozak, a New York biotechnology investment banker who is running for Congress in New Jersey as a Democrat. "This is only a political sidestep. Adult-stem-cell research holds no real promise that I can see. It's not usable."

Executives and academics who work with adult stem cells note that last year the National Institutes of Health spent \$190 million on adult-stem-cell research and that there are hundreds of clinical trials in progress that are using such cells. In comparison, the NIH spent \$24.8 million on embryonic-stem-cell research last year, though that may be in part a gauge of the political challenges to doing such research. There are no clinical trials in progress using embryonic stem cells, according to the NIH.

Adult stem cells are used in bone-marrow transplants and to treat certain cases of blood disorders and leukemia. Companies say they are in the very early stages of devising treatments for heart attacks, liver disease, bone and cartilage diseases and brain disorders.

"It is mind-blowing stuff," said Johns Hopkins University professor Saul J. Sharkis, who recently published a study maintaining that his lab converted bone-marrow stem cells from animal donors into healthy liver cells. "I never would have thought this would be possible," Sharkis said. "Preposterous. Not possible. No way."

Osiris, which grew out of research by scientists at Case Western University in Cleveland, is using stem cells from bone-marrow donors to target, among other maladies, heart disease, specifically heart attacks. It is in early-stage human testing of a therapy in which heart-attack patients are intravenously injected with stem cells that are said to migrate to the heart and replace damaged cells.

Mills said the company, which has a stem-cell factory at its waterfront Fells Point headquarters, has patented technology that allows it to take a small amount of bone marrow, extract the stem cells, and grow them into thousands of stem-cell doses. "We've developed a process to find the needle in the haystack and grow it thousands and thousands of times over," he said.

But even some advocates of adult-stem-cell research are skeptical that technology has yet been developed to isolate enough adult stem cells from donor samples for therapeutic use, let alone reproduce them in large quantities.

The other obstacle for adult-stem-cell companies is funding. Only a few are publicly held -- StemCells Inc. in California, Aastrom Biosciences Inc. in Michigan, Curis Inc. in Massachusetts among them -- and investors haven't showed much enthusiasm for them lately. From a high of \$17.12 in 1995, StemCells' stock closed yesterday at \$1.42 a share, down 3 cents. Aastrom's stock, which climbed to \$7.69 in 1997, closed yesterday at 74 cents a share, unchanged.

Most others, like Osiris, are privately held and only now are changing from university spinoffs to profit-conscious companies, using a combination of grants and the capital markets. Mills declined to disclose who has invested in the company, which has 50 employees, though he said it has received several multimillion-dollar grants from the Defense Department and the National Institute of Standards and Technology.

Landing investors is tricky for companies that are early in the clinical process, particularly with unproven adult stem cells.

"I believe that as we continue to make clinical progress that the data will be there to support individual investment of equity capital," said R. Douglas Armstrong, Aastrom's chief executive and chairman. For now, the company can afford to run only a limited number of clinical trials.

The key, said Mills and other executives, is corporate partnerships. Osiris is partnering, under undisclosed financial terms, with Boston Scientific in developing cardiac treatments. Mills said he hopes to take Osiris public, perhaps by the end of 2005.

ViaCell Inc., a Boston company, has sold a \$20 million equity stake to Amgen. Under the deal, the two companies would split any eventual profits from stem-cell therapies. ViaCell filed for an initial public offering of stock this year after canceling a previous bid to go public.

The partnerships provide not only cash but also validation, the message that a well-financed, established firm thinks that the research might lead to useful, profitable medicines.

"While I can't tell you how medicine will be revolutionized or which stem cells will do it, I think it's a safe bet that a revolution will take place," said James F. Battey Jr., the head of the NIH's stem-cell task force.

Sharkis said: "The world needs to know that we're not there yet, but we will be there and that we will make a difference."

For now, though, ViaCell said of potential products in its most recent IPO filing : "If we are not able to successfully develop and commercialize them, we may not generate sufficient revenues to continue our business operations."