



Growth Industry

Local stem cell researchers offer hope for patients—and a boon to Maryland's economy.

By Ron Cassie

Nancy Rusk's toddler, Bryan, had just turned three when his stomach began to harden. On the next trip to his pediatrician, she pointed it out to the doctor.

"The only odd thing I'd noticed up to that point was that when Bryan would watch TV, he wouldn't sit—he'd lie down," Rusk says.

The pediatrician ordered a sonogram, but wouldn't reveal the results.

"He made an appointment at Johns Hopkins two days later and I knew it wasn't good," she says.

Bryan presented with a soccer ball-sized tumor, recalls Dr. Curt Civin, then a Hopkins cancer researcher. Bryan's surgeon could not immediately remove all the cancer cells, which had spread widely, including to his bone marrow, where the body produces blood cells.

"He needed higher doses of chemo or he wouldn't make it," Civin says. "But such high doses would wipe out his bone marrow."

With no other options, Bryan was entered into a Phase I clinical trial Civin had begun, testing purified stem cells, which would be transplanted and, hopefully, grow into new bone marrow and blood cells, replacing those killed by chemo.

Seventeen years later, Bryan Rusk is a junior computer science student at the University of Maryland. Coincidentally, it's the same institution where Civin, who keeps a photo of Bryan at 12 playing soccer in his lab, works today. He left Hopkins a year ago to become the founding director of the University of Maryland School of Medicine Center for Stem Cell Biology and Regenerative Medicine.

"There are incredible possibilities," Civin says, listing sickle cell anemia, Parkinson's Disease, and spinal cord injury among the ailments where stem cell research could help develop breakthrough therapies. "We are going to understand how every cell develops and how every disease develops," Civin adds. "And I really believe it's going to become an engine driving the Maryland economy."

Embryonic stem cells—building block cells with the ability to develop into different types of human tissue—may potentially be used to repair or replace any part of the body. First isolated in mice in 1981, it wasn't until 1998 that Hopkins and University of Wisconsin researchers derived stem cells from human embryos, launching an ethical debate and political controversy that persists to this day.

In 2001, the Bush administration limited research funding to 21 lines of embryonic stem cells already in existence at that time—few of which proved suitable for research, according to Dan Gincel, Ph.D., director of the Maryland Stem Cell Research Fund (MSCRF). Although embryonic stem cells are typically culled from fertility clinic embryos destined to be discarded, Bush maintained he was defending human life because 4- to 5-day-old embryos are destroyed in the process.

When federal support dried up, several states took measures to fund their own embryonic stem cell research, including Maryland. In 2006, the General Assembly passed legislation, signed by then-Gov. Robert Ehrlich despite Republican and Catholic opposition, creating the MSCRF, which, to date, has awarded \$56 million in research grants.

"I was aware, as a non-scientist, of the extraordinary potential of stem cell research," says Democratic Baltimore City Delegate Samuel "Sandy" Rosenberg, a lead sponsor of the legislation. "This funding was an opportunity for Maryland."

With the National Institutes of Health, two world-renowned research institutions in Hopkins and



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 Cell man: University of Maryland's Dr. Curt Civin helps to drive the state's boom in stem cell research.

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the University of Maryland, and the bioscience companies in the I-270 corridor, Maryland—already possessing the country's second-largest cluster of bioscience companies per capita—was in excellent position to reap economic benefits from building a stem cell research industry.

MSCRF has awarded 140 grants over the last three years. According to Gincel, each grant creates about seven new positions.

"These are not just researchers, but physicians who see patients," says Gincel. "Otherwise, we lose the top health care people in the state, who are being courted all the time."

At Hopkins's Institute for Cell Engineering, Ted Dawson, M.D., Ph.D., agrees. He says competition for the best stem cell researchers is fierce among leading bioscience states such as California, Connecticut, and New York.

"When California voters passed a referendum for \$3 billion in research over 10 years [in 2004], it was very encouraging from a national standpoint, but it also meant there could be a substantial brain drain from Maryland to California," Dawson says. "We had some scientists who left and it was a very significant concern."

Maryland's 2006 legislation signaled its commitment to stem cell research, and two years later, Governor Martin O'Malley cemented it with his BIO 2020 initiative, a plan to invest \$1.3 billion in Maryland's overall bioscience industry over the next decade.

The same year, Entrepreneur magazine named the Maryland Technology Development Corporation (TEDCO)—which oversees MSCRF—the top seed organization, public or private, for starting new businesses.

Now, MSCRF, whose funding peaked in 2008 when it awarded \$23 million in grants, is dealing with cutbacks—like everyone in the state—and hoping not to lose momentum. The Fund's awards were reduced to \$18 million last year. They could face a further 30 percent cut this year, according to Gincel.

But so far, the local industry is steady.

In September, Baltimore hosted the fifth annual World Stem Cell Summit, a three-day conference attracting 1,200 public and private bioscience leaders from around the globe, the largest such gathering to date.

Civin, Gincel, and O'Malley were featured presenters. On the first day of the summit, Maryland announced a first-of-its-kind collaboration with the California Institute of Regenerative Medicine. Following the summit, Gincel met with a South Korean-based company that intends to open a Maryland office.

This statewide effort has also kept Maryland in position to benefit from President Barack Obama's decision last spring to rescind the federal ban on embryonic stem cell research, although, for now, Congressional funding restrictions remain in place.

Currently, Maryland bioscience companies generate approximately \$2 billion in revenue and employ about 27,000 people statewide, according to the Maryland Biotechnology Center. Federal and academic institutions, such as the N.I.H., Hopkins, and the University of Maryland system employ a similar number. Those numbers are likely to grow, says Chuck Montague, of the Maryland Biotechnology Center. He estimates 20 or so companies are developing stem cell research sites in the state. He names Columbia's Osciris Therapeutics, and Lonza, a Swiss life sciences company in Frederick, as two of the larger life science companies in stem cell research.

Gincel, an energetic, detail-oriented former Israeli armed services officer who has over 12 years of experience in biochemistry, cell biology, and stem cell research, takes a hands-on approach as director of the Maryland Stem Cell Research Fund.

"Everything we do is open and online," he says. "We don't hide anything, and we don't hold on to the funding—we invest it right away, giving grants. Ninety-eight percent of the grants go to research, a very small percentage toward administrative costs. In that way, we are much more responsible than any other state or similar agency."

This research cannot come soon enough for Civin, a cancer and pediatrics specialist. Mothers have been giving him sick babies for 30 years, wanting him to return them cured.

Frustrated by the "caterpillar pace" of research after the Bush ban, Civin became politically active in 2002, meeting with U.S. senators considering legislation to override Bush's executive order and twice testifying on Capitol Hill. Not only did the ban block the creation of needed embryonic cell lines and federal funding—it also interfered directly in his own lab as colleagues whose salaries were drawn from the N.I.H. were unable to participate in aspects of his research team's project.

Later, in Annapolis, Civin faced grilling from conservative state delegates. Motivated by his ethical values and Jewish faith, as well as a commitment to those mothers—"My job is to leave no stone unturned," he says—Civin testified on many occasions, patiently responding to delegates questioning the morality of embryonic stem cell research. While many patients with blood cancers have been cured through stem cell bone marrow transplants, patients with kidney, pancreas, and brain issues are not getting effective treatment, Civin told legislators, and many do not survive.

Today he believes stem cell research has turned a corner, with the state funding and President Obama's repeal of Bush's order.

"Now, we have eight years of science to make up," he says, adding that it's important to manage expectations. "It's only ten or eleven years since we knew how to isolate stem cells," he says. "It's still not routine. It's very specific labs, doing very sensitive work. We're facing years of long effort."

While he acknowledges the challenging nature of the science, John Kellermann III, 55, a Roman Catholic Republican and a patient advocate on the Maryland Stem Cell Commission, hopes stem cell research will bear fruit in his lifetime. Diagnosed with Parkinson's at 38, he was frustrated with the political process that blocked research and testified frequently in Annapolis in favor of the 2006 legislation.

A husband, father of three, and president of Maryland Families for Stem Cell Research, Kellermann stopped working at 47. He's had two brain surgeries for Parkinson's and now has an electrode in his brain to stimulate motor activity and help him walk.

Parkinson's disease, Civin noted, is an area with a lot of promise because it appears to be caused by a single mutated gene. Researchers believe it will eventually be treated effectively with cell replacement therapy.

"I'm happy to see Maryland as one of a handful of states leading the way with programs and still funding research," Kellerman says. "I can wait. I am a patient guy."

Others, like Josh Basile, a classmate of Bryan Rusk's at Maryland, are concerned about funding cuts and lack of federal research dollars. Basile, 24, was hit by a wave while standing at the shore at Bethany Beach five years ago, breaking his neck and leaving him paralyzed from the neck down. He started a College Park chapter of The Student Society for Stem Cell Research, which today includes about 50 members, nearly all biology students.

"The opposition has done a good job delaying and restricting research, and it hurts," he says. "Restricted funding, the morality debate of 50-cell blastocysts [the embryos where stem cells are derived], means it's going to be slow going forward when it takes so much to get a clinical trial through the system."

A large problem facing researchers adept at creating different cells in a Petri dish is engineering those discoveries into therapies. With stem cell bone marrow transplants, the process was relatively easy, Civin says. New bone marrow cells knew where to go and filled a void left by those destroyed by cancer. Directing cells into the brain or the spinal cord, to name two examples, is trickier.

"Right now, in stem cell research we study nature artificially in the lab, but we don't have the whole sentences to solve the problem," Civin says. "There may be 10 mutations that cause a certain cancer—maybe 100 for all we know. It is as if we understand some of the key words, but we need to put all the key words in and fix the sentences. Once we do that, we can write new paragraphs and change the whole story."

Much attention, Civin says, is directed at the economic benefits of promoting stem cell research in Maryland—and rightly so. But, he's quick to add, it's important to keep the focus on research and the tremendous hope it offers.

"Developing therapies to treat pancreatitis, liver, and kidney disease—you can name every organ—to rebuilding a part of a limb or face or eye," Civin says, "that's really what biomedical research is all about."

He recalls a young woman in a lab coat who knocked on his door last year, shortly after he arrived at the University of Maryland School of Medicine. She looked familiar and Civin asked if she was a former student.

"She was the sister of a patient of mine, who was 17 when she died a decade ago after the bone marrow transplant hadn't worked," Civin says, adding that the young woman is studying the application of cell engineering toward orthopedics. "She's highly motivated because of her sister," he says. "It's through people like her who are inspired—and have today's computer power and the mapping of the human genome at their fingertips—that we are going to make the next breakthroughs."

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