

## Man Who Helped Start Stem Cell War May End It

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If the stem cell wars are indeed nearly over, no one will savor the peace more than James A. Thomson.

Dr. Thomson's laboratory at the University of Wisconsin was one of two that in 1998 plucked stem cells from human embryos for the first time, destroying the embryos in the process and touching off a divisive national debate.

And on Tuesday, his laboratory was one of two that reported a new way to turn ordinary human skin cells into what appear to be embryonic stem cells without ever using a human embryo.

The fact is, Dr. Thomson said in an interview, he had ethical concerns about embryonic research from the outset, even though he knew that such research offered insights into human development and the potential for powerful new treatments for disease.

"If human embryonic stem cell research does not make you at least a little bit uncomfortable, you have not thought about it enough," he said. "I thought long and hard about whether I would do it."

He decided in the end to go ahead, reasoning that the work was important and that he was using embryos from fertility clinics that would have been destroyed otherwise. The couples whose sperm and eggs were used to create the embryos had said they no longer wanted them. Nonetheless, Dr. Thomson said, announcing that he had obtained human embryonic stem cells was "scary," adding, "It

was not known how it would be received.”

But he never anticipated the extent and rancor of the stem cell debate. For nearly a decade now, the issue has bitterly divided patients and politicians, religious groups and researchers.

Now with the new technique, which involves adding just four genes to ordinary adult skin cells, it will not be long, he says, before the stem cell wars are a distant memory. “A decade from now, this will be just a funny historical footnote,” Dr. Thomson said in the interview.

As for the science behind it, the thrill of discovery, he said, “Surprisingly, there is no ‘Wow’ moment,” either from 1998 or now. Both times, the discovery came after he had spent months rigorously testing the cells to be sure they really were stem cells, worrying all the while that they could die or be lost to contamination. When he knew he had succeeded, the suspense was gone.

“Imagine holding your breath for a few months,” Dr. Thomson said. When he was done, he said, “I felt mostly a sense of relief.”

But he knows what he wrought. Stem cells, universal cells that can turn into any of the body’s 220 cell types, normally emerge only fleetingly after a few days of embryo development. Scientists want to use them to study complex human diseases like Alzheimer’s or Parkinson’s in a petri dish, finding causes and treatments. And, they say, it may be possible to use the cells to grow replacement tissues for patients.

The problem until now had been the source of the cells — human embryos.

The topic, says R. Alta Charo, a University of Wisconsin ethicist,

“took on an almost iconic quality the same way Roe v. Wade has.”

In the meantime, many leading scientists decided not to get into the stem cell field. There was a stigma attached, Dr. Thomson says. And, he adds, “Most scientists don’t like controversial things.”

A native of Oak Park, Ill., James Alexander Thomson, 48, did not set out to throw bioethical bombs. All he wanted, he said, was to answer the most basic scientific questions about cellular development.

First there was a degree in biophysics from the University of Illinois. As a graduate student, Dr. Thomson began working with mouse embryonic stem cells and then, with federal support, he extracted stem cells from monkey embryos. After earning two doctorates from the University of Pennsylvania, one in veterinary medicine and one in molecular biology, he continued research at his own laboratory at the University of Wisconsin.

Eventually he realized, though, that studying mice and monkeys could take him only so far. If he wanted to understand how human embryos develop and why their development sometimes goes awry, he needed human stem cells. But, he says, he hesitated.

In 1995, he began consulting with two ethicists at his university, Dr. Norman Fost, a physician, and Ms. Charo, a law professor. He wanted to anticipate what the ethical problems might be and what the criticisms might be.

Dr. Fost was impressed.

“It is unusual in the history of science for a scientist to really want to think carefully about the ethical implications of his work before he sets out to do it,” Dr. Fost said. “The biggest problem in ethics

is not anticipating problems.”

But Dr. Fost and Dr. Thomson guessed wrong about what would bother people most. They thought it would be what Dr. Fost termed “the technological power” of stem cells. What if someone put human stem cells into the brain of a rat, for example?

“I thought at the time that this was possibly the biggest issue,” Dr. Fost said. “It was unprecedented in the history of biology. It’s the ‘Help, get me out of here’ scenario. Let’s say the rat brain turns out to be entirely human cells. What’s going on in there? Is it a human brain? And how would you study it — you can’t ask the rat.”

Meanwhile, as Dr. Thomson was planning his effort to obtain human embryonic stem cells, another discovery changed his entire view of development. In 1997, Ian Wilmut, a scientist in Scotland, announced the creation of the first cloned mammal, Dolly, cloned from frozen udder cells from a long-dead sheep.

Dr. Wilmut had slipped an udder cell — a cell that normally would never be anything but an udder cell — into an egg whose genetic material had been removed. The egg somehow brought the udder cell’s chromosomes back to the state they had been in when embryo development first began.

“Dolly changed the way I thought about developmental biology,” Dr. Thomson says. “Development was reversible.”

Four years ago he and, independently, Shinya Yamanaka of Kyoto University set out to figure out a way to mimic what an egg can do. Both succeeded and both discovered that all they had to do was add four genes to the cells and the cells would turn into what look, so far, just like stem cells.

“It is actually fairly straightforward to repeat what we have done,”  
Dr. Thomson said.

More work remains, but he is confident that the path ahead is  
clear.

“Isn’t it great to start a field and then to end it,” he said.