“Living Drug” Stem Cells to Fight Cancer, Blindness, HIV—and Infertility?

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JStone [1] / Shutterstock.com [2]' src="/sites/biosciencetechnology.com/files/legacyimages/shutterstock_177267131.jpg" width="250">Led by PBS’s Charlie Rose, top US stem cell experts this month hailed new clinic-bound techniques designed to persuade “aspects of the body to cure itself,” as New York Stem Cell Foundation head Susan Solomon put it.

The main technique hailed involves making stem cells from adult cells, then forging those into armies of robust, proliferating, specialized cells that may let people essentially cure their own blindness; kill their own tumors; and, as Cornell Center for Reproductive Medicine chief Zev Rosenwaks noted, “obliterate” their own infertility.

“Clearly there is enormous hope,” Rose told the standing-room-only crowd at the Ansary Stem Cell Symposium in New York City. “The people in this room” shoulder “enormous responsibility for the future of medicine.”

The meeting’s “topic du jour” was the “induced pluripotent stem cell” (iPSC) technique, in which researchers create replicating, multi-potent stem cells out of limited adult cells. Harvard University hematologist George Daley noted the first IPSC trial was launched last year--fittingly, in Japan. IPSCs were first created there, in the Osaka University lab of developmental biologist Shinya Yamanaka. In 2007, Yamanaka showed [3] he created human iPSCs by genetically tweaking only four genes. Ever since, researchers have been creating iPSCs, studying them, and trying to turn them into armies of rejuvenated adult cells.

It has not been easy. The cells often don’t dedifferentiate fully, and can go tumorous. But enough finessing has apprently occurred that some researchers are comfortable launching the world’s first iPSC clinical trial, which began enrollment in Japan last year [4]. The aim is to help heal damaged retinal pigment epithelium (RPE) cells in macular degeneration patients. In that trial [5], RPE cells made from iPSCs will be transplanted.

Another reason the first IPSC trial is occurring in Japan, said Solomon: “Japan’s equivalent of the NIH” is so excited about iPSCs that it is “streamlining” some regulations to fast-track progress to the clinic.

Daley noted there is reason to be optimistic about that trial. The same RPE transplantation approach earlier hit the clinic using human embryonic stem cells (ES cells) with “encouraging [6] results.”

“Drugs and surgery don’t treat degenerative diseases,” he said. But stem cells—both native and created—can. “It is a paradigm shift. The notion that cells are

stable entities has changed.”

Game Changer

MIT geneticist Rudy Jaenisch discussed how new, precise gene-editing techniques called Crispr and Cas9 [7] are letting him correct genetic mutations in all kinds of cells--including iPSCs. These techniques induce a double-stranded DNA break, which prompts meticulous DNA repair mechanisms to swing into gear “without leaving a genetic footprint…This makes for very precise gene editing. You can target many genes at the same time.” He thinks genetically engineered iPSCs may correct patients’ polygenic disorders in the not-too-distant future.

Recently, genetic engineering [8] of iPSCs from Rett Syndrome patients led to discoveries about the initiation of the disease—and a potential drug target that is now being tested in a clinical trial, he said.

“This system represents a game-changer,” he said. “It has transformed the field for disease modeling.”

Sloan Kettering oncologist Michel Sadelain presented his latest clinical trial data showing that patients’ T cells can be engineered to go after their own tumors—by creating hybrid T cell/antibodies that zoom in on particular antigens on B Cell Lymphoma cells. The approach is so clinically successful that last year, *Science* made it--and like cancer immunology procedures-- “breakthroughs of the year.”

Sadelain said his next step was to create iPSCs out of ordinary blood cells, and shape *them* into hybrid T/antibody cells. By creating iPSCs first, he can create larger armies of cells, he noted.

Later he told *Bioscience Technology* that stem cells are among the most permanent residents of the body. They don’t turn over as quickly as T cells can. So theoretically, his iPSC-turned-killer-Ts could become long-lived guardians of cancer patients, protecting them from cancer for years.

Longer Lasting, Living Drugs

Rosenwaks reported that some groups [9] are creating eggs and/or sperm from iPSCs. So far the only published work has been in animals. But those animals have even procreated using germ cells made by turning back the clock on older cells via the iPSC approach. Many have noted it will be revolutionary if/when that feat is repeated in older women.

And several speakers pointed out that cloning’s recent comeback should speed things up. Last year, Oregon Health and Science University researcher Shoukhrat Mitalipov cloned human cells for the first time. He took the nuclei of adult human cells, popped them into enucleated eggs, and let the eggs turn back the clock on the older cells—the way they do sperm—to create “young” ES cells genetically identical to their donors.

This year, more groups [10] pulled off the feat, one group in cells from patients as old as 75. [11] Cloning, at this juncture, appears to more reliably create physiologic ES cells than the iPSC approach. It “will help us identify all the factors letting the egg transform the nucleus,” said Alan Trounson, former head of the $3 billion California Institute of Regenerative Medicine (CIRM).

Cautionary notes were sounded. Mitalopov said iPSCs are “stem cells that don’t exist in the body.” They must be understood before being widely used, he said. And Trounson noted iPSCs are many years behind ES cells.

But there was an indisputable air of excitement. Trounson said progress is being made with genetically engineered stem cells and HIV. CIRM-funded scientists are mutating a receptor gene on patient blood stem and CD4 T cells. That mutation blocks HIV from entering. Replacing immune systems via these cells may bring ever closer “the possibility of curing HIV AIDS,” he said. Clinical trials [12] are ongoing. One patient—the “Berlin Patient [13]” – has been cured.

Concluded Sadelain: “We are finding the keys to longer lasting, living drugs.”

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