



Major News Summary Friday, September 24, 2010

Stem Cell Policy and Politics

Parties in Stem Cell Lawsuit Want to Keep University of California Out Science AAAS, 09/23/2010

Today, the two sides in the court battle over whether federally funded research on human embryonic stem cells (hESCs) is legal both registered their opposition to the University of California's (UC's) request this week to become a party to the suit, the first university to do so. In briefs submitted to the U.S. Court of Appeals to the D.C. Circuit, the plaintiffs, two researchers who study adult stem cells, argue that UC hasn't justified why it should be allowed to join at this late stage, more than a year after the plaintiffs originally sued. The Justice Department, which is defending the National Institutes of Health (NIH) and the Department of Health and Human Services, says that although UC "has a valuable and significant perspective to offer," making it a party to the case would invite more universities to weigh in and would slow the appeal down.

Stem Cell Research (CA)

New Signaling Pathway That Controls Cell Development And Cancer

Medical News Today, 09/24/2010

Full Text Below

Researchers at UCLA's Jonsson Comprehensive Cancer Center have discovered a new cell signaling pathway that controls cell growth and development, a pathway that, when defective, helps promote the formation of several major forms of human cancer, including lymphoma and leukemia. The new pathway, part of a global DNA damage response, turns off 136 genes, including some that have are known to cause cancer because, unchecked, they can promote aberrant cell division. "It's important to make sure this pathway works correctly, because it prevents cells from dividing excessively" said Dr. Michael Teitell, a professor of pathology and laboratory medicine, a Jonsson Cancer Center researcher and senior author of the study. "When this pathway is defective, cancers can happen."

Stem Cell Research (US)

Stem Cells That Save Big Pharma a Bundle

Bloomberg Businessweek, 09/23/2010

Full Text Below

It's a frustrating and expensive pitfall for pharmaceutical companies: discovering late in the game that a promising new drug has side effects in humans that never surfaced in the laboratory or during earlier trials in animals. That kind of setback sends scientists back to the lab—or even prompts a company to shut down a multimillion-dollar drug development program. Researchers at Roche Holding, Pfizer (PFE), and GlaxoSmithKline (GSK) hope to use human tissue created from stem cells to reduce such mishaps.

Yale Women's Ice Hockey Player Completes Stem-Cell Transplant Procedure

Bloomberg, 09/23/2010

Full Text Below

Yale University women's ice hockey player Mandi Schwartz underwent a stem-cell transplant yesterday as doctors attempt to re-grow the infection-fighting white blood cells she needs to survive. Doctors, who eradicated her cancer cells with multiple chemotherapy and radiation treatments Sept. 15 through 20 at the University of Washington Medical Center in Seattle, used stem cells from two anonymous umbilical cord blood donors to re-grow healthy, cancer-free cells.

[Mandi Gets Stem Cell Transplant](#)

NBC Connecticut, 09/23/2010

After months of waiting, Yale hockey player Mandi Schwartz has received the stem cell transplant she needs to survive cancer, Yale's athletic department reported. Schwartz underwent the procedure Wednesday at the Seattle Cancer Care Alliance's inpatient transplant unit at the University of Washington Medical Center. Schwartz, of Wilcox, Sask., Canada was first diagnosed with acute myeloid leukemia during her junior year at Yale in 2008. She went into remission in 2009 after getting chemotherapy, but was diagnosed with cancer again in April 2010.

[Stem Cell Research \(International\)](#)

[Athersys Touts Positive Results for Stem Cell Treatment for Heart Attack Patients](#)

MedCity News, 09/24/2010

Full Text Below

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[Access Pharma Signs \\$30 mn MuGard Supply Agreement with RHEI Pharma](#)

PharmaBiz.com, 09/24/2010

Full Text Below

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part of a global DNA damage response, turns off 136 genes, including some that have are known to cause cancer because, unchecked, they can promote aberrant cell division.

"It's important to make sure this pathway works correctly, because it prevents cells from dividing excessively" said Dr. Michael Teitell, a professor of pathology and laboratory medicine, a Jonsson Cancer Center researcher and senior author of the study. "When this pathway is defective, cancers can happen."

The study appears in the Sept. 24, 2010 issue of the peer-reviewed journal *Molecular Cell*.

A widely used oral diabetes drug, Metformin, is known to activate the identified pathway and could possibly be protective against cancer in certain pathway defects. It's been shown through epidemiological studies, Teitell said, that diabetes patients on Metformin have lower incidences of lymphoma and leukemia, possibly because the drug is regulating pathway operation. Additionally, new therapies that target the pathway could be developed to correct newly identified defects, thereby blocking the formation of cancer.

The study also revealed an unknown DNA damage response outcome. It is generally agreed that one of three things happen to cells in response to DNA damage cells are temporarily arrested from growing so the damage can be repaired, cells go quiet and permanently stop dividing so they don't pass on the DNA damage, or cells simply die, a process known as apoptosis.

Teitell's study uncovered a fourth option - the DNA damage itself drives less mature cells to develop into more mature cells, in this case into antibody-secreting plasma cells, by turning off the 136 genes identified in the study. Defects in the newly discovered cell signaling pathway don't allow cells to progress to their natural end point by blocking normal gene silencing. The less mature cells become stuck where they are, dividing too rapidly and potentially resulting in lymphoma or leukemia.

Usually DNA damage is thought to be associated with environmental factors, such as exposure to too much sun or to toxic chemicals. Chemotherapy also damages cell DNA. However, Teitell and his team discovered that a normal process, the creation of antibodies to battle infection, results in physiologic DNA damage that also activates the identified signaling pathway.

Teitell, in previous studies, discovered that the gene *TCL1* can cause B-cell cancers, including various types of lymphomas, if it is not turned off at the right time in development. Activation of this new signaling pathway, in fact, is the mechanism that shuts the *TCL1* oncogene down at the appropriate time. If a pathway defect develops, *TCL1* and the other 135 genes remain elevated and cancer may arise.

B-cells are lymphocytes that play a large role in immune responses and they make antibodies in response to infection or vaccination. They divide at the highest rate in the human body, faster than skin, hair or cells of the gastrointestinal tract. In making antibodies to fight infection or in response to a vaccine, these rapidly proliferating cells undergo DNA damage in order to make better, more effective antibodies. The body, in effect, is trading off the potential harm caused by added DNA damage in order to effectively ward off a more immediate invader.

The rapid cell cycling process that occurs during antibody assembly and testing by the immune system needs to be halted at the right time, Teitell said. The body naturally turns off that process after about two to three weeks. A defect in the new pathway interrupts that natural stop signal and blocks the production of effective antibody-producing cells, the plasma cells.

Mara Sherman, the first author of the study who worked as a graduate student in Teitell's lab, said the

paper "reflects an exciting and emerging connection between DNA damage response pathways and cell differentiation."

"Our work points to this DNA damage-response pathway as a potential, novel therapeutic target for the treatment of B-cell lymphoma," Sherman said. "Combined with several intriguing recent studies, our work further suggests that pathways with established roles in genome maintenance may also drive the differentiation of stem and progenitor cell populations."

Patients at risk for developing B-cell related cancers could be screened for genes that, when not turned off, are a signature indicating pathway defects. The pathway also could be playing a role in the development of lung, colon and other major cancer types, Teitell said.

Going forward, Teitell and his team will further study the pathway to detail all aspects of its operation so new therapies can be developed to fix it when something goes wrong.

The study is funded by the National Institutes of Health and the Leukemia & Lymphoma Society.

Stem Cells That Save Big Pharma a Bundle **Bloomberg BusinessWeek, 09/23/2010**

It's a frustrating and expensive pitfall for pharmaceutical companies: discovering late in the game that a promising new drug has side effects in humans that never surfaced in the laboratory or during earlier trials in animals. That kind of setback sends scientists back to the lab—or even prompts a company to shut down a multimillion-dollar drug development program. Researchers at Roche Holding, Pfizer, and GlaxoSmithKline hope to use human tissue created from stem cells to reduce such mishaps.

For more than a decade, stem cells (master cells that form all other cells in the body) have been hailed as potential treatments for Parkinson's disease, spinal cord injuries, and diabetes. While those advances are years away, Big Pharma has begun using the cells to help identify potentially dangerous side effects from drugs under development before they undergo expensive human trials.

Earlier this year, Roche scientists used heart tissue made from stem cells to test an antiviral drug it had abandoned two years earlier because it caused irregular heartbeats in rodents and rabbits. The same dangerous effects were seen in the lab using the stem cell-generated heart cells. The finding is important to drug researchers because it showed that human tissue grown from stem cells can mimic the body's reaction to medicines, helping spot side effects early. And that matters greatly in an industry that can spend upward of \$4 billion to produce a new drug. Had stem-cell-derived heart tissue been available two years ago, Roche could have pulled the plug earlier on its antiviral drug, saving millions, says Kyle Kolaja, Roche's global head of predictive toxicology screens and emerging technologies.

"This is a transformative technology that puts human disease in a dish," says Christopher Scott, director of the Stem Cells in Society program at Stanford University School of Medicine. "It can help companies see the drugs that work and also the ones that are toxic."

The savings can be substantial. A drug study in mice alone can cost about \$3 million, says Michael C. Venuti, chief executive officer at iPierian, which is developing drugs using stem cells. A drug that's found to cause cardiac damage only after it has advanced to large, late-stage human studies might cost a company \$1 billion or more, says Jason Gardner, a Glaxo vice-president who heads its stem cell drug performance unit. "There is a real need to more accurately model human physiology," he says.

The stem cells being employed by drugmakers don't come from embryos, thereby avoiding an ethical and political controversy that's dogged the technology. Instead they were created using a method that allows scientists to transform ordinary skin cells into another type of stem cell (known as induced pluripotent stem, or IPS, cells) as versatile as embryonic cells.

Cellular Dynamics International, a company founded in 2004 by James Thomson, the University of Wisconsin scientist who first isolated human embryonic stem cells in 1998, made the heart cells used by Roche and also being tested by Glaxo and Pfizer. The company is now producing more than 7 billion heart cells a month made from skin and blood, says Robert Palay, CDI's chief executive.

Next year, the company plans to start selling liver and nerve cells as well. "Others are talking about the promise of stem cells, we are delivering today," Palay says. Cellular Dynamics is backed by \$70 million from private equity groups including Sam Zell's Equity Group Investments and Palay's Tactics II Stem Cell Partners.

Competitor iPierian is making cells from people with heart disorders, diabetes, and neurological ailments to develop drugs that threaten these disorders. Founded by venture capitalists at Kleiner Perkins Caufield & Byers in Menlo Park, Calif., the company was built on the work of Shinya Yamanaka of Kyoto University in Japan, who turned skin cells into IPS cells back in 2006. It has since raised \$60 million including money most recently from the venture arms of Google, Glaxo, and Biogen Idec.

iPierian has made IPS cells from the skin of children with spinal muscular atrophy, a deadly muscle-wasting condition. Morphing the stem cells into neurons that carry the disease, they've identified drug candidates that may help motor neurons to survive, said Venuti, iPierian's CEO. The company also used the neurons to test 15 drugs that previously failed in clinical trials, said Corey Goodman, iPierian's chairman. The signs of failure were evident in each case, he said. "IPS technology gives you the opportunity to screen out a lot of things that are going to fail," said Goodman, who formerly was head of Pfizer's biotechnology unit. "That saves money, emotion, and testing."

The bottom line: Drugmakers hope to save big by using stem cells to test drugs for dangerous side effects long before costly human trials are needed.

Yale Women's Ice Hockey Player Completes Stem-Cell Transplant Procedure **Bloomberg, 09/23/2010**

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Doctors, who eradicated her cancer cells with multiple chemotherapy and radiation treatments Sept. 15 through 20 at the University of Washington Medical Center in Seattle, used stem cells from two anonymous umbilical cord blood donors to re-grow healthy, cancer-free cells.

Dean I. Forbes, a spokesman for the Seattle Cancer Care Alliance, said there were no complications during the 30-minute procedure. Schwartz will remain in the hospital for three to four weeks while the donor cells grow, he said.

"She can be one very aggressive girl," Mandi's mother, Carol, wrote on her website. "She will win!"

Yale's athletic department held drives each of the past two springs, registering more than 1,600 people with the National Marrow Donor Program's "Be The Match" registry. Drives held in Canada added 2,600 to the Canadian version of the registry.

Schwartz, 22, an economics major from Wilcox, Saskatchewan, was diagnosed with acute myeloid leukemia in December 2008. The cancer starts inside the bone marrow and grows from cells that were supposed to become white blood cells.

When doctors couldn't find a bone marrow donor, they turned to umbilical cord blood.

Mandi's parents, Carol and Rick, and her fiance, Kaylem Prefontaine, traveled to Seattle for the operation. Her younger brothers, Jaden and Rylan, both ice hockey players at Colorado College, visited. Jaden was selected in the first round (No. 14 overall) of the National Hockey League draft by the St. Louis Blues in June.

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The new data show that Athersys' MultiStem treatment was well-tolerated at all dose levels and also suggest improvement in heart function in treated patients. The newly announced results are based on four months of data on patients who were treated with MultiStem after suffering acute myocardial infarctions, or heart attacks, according to the company.

The results show that MultiStem has a "favorable safety profile" and that adverse events that occurred after patients received the treatment were generally "mild-to-moderate in nature," according to Athersys.

"We are continuing to see strong findings from this Phase 1 study that suggest that MultiStem is well-tolerated and that administration following a heart attack could provide a meaningful improvement in functional heart measures, said project researcher and director of Cardiovascular Cell Therapy at the Cleveland Clinic Dr. Marc Penn in prepared remarks.

Last month, Athersys revealed similar results from the ongoing heart attack trial.

MultiStem is an off-the-shelf stem cell treatment derived from the bone marrow of adults or other non-embryonic sources. The cells have a drug-like effect, reducing inflammation, protecting damaged tissue and forming new blood vessels and then are cleared from the body.

Athersys is partnering with Canada-based Angiotech Pharmaceuticals Inc. to develop MultiStem for cardiovascular applications. The companies are planning another clinical trial that they expect to begin next year, according to Athersys.

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supportive care signed a \$30 million supply agreement for MuGard with RHEI Pharmaceuticals, Inc., a specialty pharmaceutical company focused on bringing proprietary medicines to the China market. Access will ensure manufacturing capacity of up to a minimum of \$30 million of product in the licensed territories. Coinciding with the signing of the above agreement, Access also approved a sub-license agreement between RHEI Pharmaceuticals and Jian An Pharmaceuticals (Jian An) Limited in Shenzhen, China in an effort to leverage Jian An's extensive sales, marketing and regulatory infrastructure for the launch of MuGard in China and Taiwan.

Jian An is headquartered in Shenzhen, China and has a 25-year history of selling pharmaceutical and other medical products in the China market. Jian An has 1400 sales representatives covering all major centres in China through 169 sales offices. With Jian An's sales and marketing infrastructure and the supply agreement which will provide up to \$30 million of MuGard to the territory, Access Pharmaceuticals' commercialization efforts remain on track in China and its other South East Asian territories. Access retains its existing milestone and royalty structure for the territory. In addition, Access and RHEI have also filed a new patent application in China covering MuGard for the relief and reduction of erythema. This new application is expected to provide additional IP protection as well as the potential for a new indication for MuGard.

"We are excited about the new relationship with Jian An in China, as it greatly expands our reach throughout the region with significant sales representative presence," said Sven de Backer, CFO of RHEI Pharmaceuticals. He continued, "We believe Jian An's local expertise will expedite the ongoing marketing approval process allowing us to begin providing patients with an effective treatment for oral mucositis. We are thankful to Access for ensuring adequate MuGard supply for the commercial launch."

"We look forward to working with Access and RHEI and bringing MuGard to market in China," said Zhan Zhangyi, CEO of Jian An Pharmaceuticals. He continued, "We believe MuGard is the right product to help us continue increasing our pharmaceutical market penetration in China. MuGard is an important addition to our growing product portfolio and we look forward to its commercial launch."

"Oral mucositis is a growing problem in the greater China region and we are confident that RHEI's marketing capabilities, with the addition of Jian An's established product-promotion experience, will greatly enhance our effort to bring MuGard to the many patients that may otherwise suffer from the debilitating side effect of anticancer treatments," said Jeffrey Davis, CEO of Access Pharmaceuticals, Inc. He continued, "The recent news surrounding MuGard, including this agreement and the initial product purchase order received in the US, underscores the significant revenue potential we believe MuGard will provide our company."

MuGard is a novel; ready-to-use mucoadhesive oral wound rinse and coating for the management of oral mucositis, a debilitating side effect of many anticancer treatments. Up to 40% of all patients receiving chemotherapy and radiotherapy develop moderate to severe mucositis, and almost all patients receiving radiotherapy for head and neck cancer and those undergoing stem cell transplantation develop mucositis. Updated clinical practice guidelines for the prevention and treatment of mucositis recommend the use of a preventive oral care regimen as part of routine supportive care along with a therapeutic oral care regimen if mucositis develops. The market for the treatment of oral mucositis is estimated to be in excess of \$1 billion world-wide.