Yan Shi and Sheng Ding, Scripps Research Institute

Discovered a way to significantly improve upon the revolutionary technique that uses genes to turn skin cells from an adult state back into pluripotent stem cells. They identified and used small, drug-like chemicals to introduce genes that help coax mouse brain cells back into pluripotent stem cells. Using the chemicals reduced the need to use viruses to carry the genes, one of the major drawbacks of the technique developed two years ago by Japanese researcher Shinya Yamanaka to produce pluripotent stem cells. The new findings provide a safer, more efficient method to reprogram cells, moving us closer to finding a way for clinical testing of reprogrammed stem cells. The study was published in the June 5 issue of Cell Stem Cell. Read more about this research here: http://www.scripps.edu/news/press/060408.html. (While CIRM does fund research in Dr. Ding's lab, it did not fund this particular work.)

Hong Wu and Wei Guo, University of California, Los Angeles

Discovered a series of mutations that can convert normal blood stem cells into cancer stem cells. It is believed that many types of cancer result from cancer stem cells created by such mutations. In this case the first mutation converted normal stem cells and then caused over expression of an oncogene, a cancer gene, resulting in a proliferation of leukemia stem cells and acute T-cell lymphoblastic leukemia in a mouse model. The team hopes that by studying these pathways they will find ways to block them with small molecule drugs and cure the often fatal disease. The study was published in the May 22 issue of Nature. Read more about this research here. http://www.cirm.ca.gov/press/pdf/2008/05-22-08.pdf

Jeanne Loring and Louise Laurent, Scripps Research Institute

Discovered that human embryonic stem cells have a very specific signature when it comes to the regulators of their genes. Micro RNA's are very small, naturally occurring bits of genetic material. They don't code for specific proteins like genes do, but they regulate the activity of genes and turn on and off their protein production . In embryonic stem cells microRNAs are actively preventing the production of proteins that tell cells to differentiate into specific heart or bone tissue, for example, but are pushing hard on genes that result in self renewal—those for pluripotency. The team hopes to use these microRNAs to reprogram any type of cell to become as pluripotent as embryonic stem cells and to do it more safely than current reprogramming called iPS. The study was published in the April 10, 2008 issue of the journal Stem Cells. Read more about this research here. http://www.scripps.edu/news/press/041008.html

Weiwei Fan and Doug Wallace, University of California, Irvine

Used mouse embryonic stem cells to demonstrate that a specific mutation can cause cardiomyopathy, with a thickened heart wall, in the mouse. The team looked at the small DNA molecule located outside of the nucleus, so-called mitochondrial DNA, which we all inherit exclusively from our mothers. They also discovered that severe mutations in this mitochondrial DNA are readily eliminated from the mouse germ line in just four generations. They expect the method they used to become a robust research tool to study the impact of mutations on stem cells. The study was published in *Science* on February 15.

Hong Wu and Wei Guo, University of California, Los Angeles

Discovered a series of mutations that can convert normal blood stem cells into cancer stem cells. It is believed that many cancers result from such mutations that create cancer stem cells. In this case the first mutation resulted in the conversion of normal stem cells and then over expression of an oncogene, a cancer gene, resulted in proliferation of leukemia stem cells and acute T-cell lymphoblastic leukemia in a mouse model. The team hopes that by studying these pathways it will find ways to block the pathways with small molecule drugs and cure the often fatal disease. The study was published in the May 22 issue of Nature. Read more about this research here. http://www.cirm.ca.gov/press/pdf/2008/05-22-08.pdf

First Clinical Trial Begins for a Therapy Enabled By CIRM Funding

Researchers at the University of California, San Diego, used a training grant and a SEED grant from the California Institute for Regenerative Medicine to conduct stem-cell research that verified a suspect gene mutation was by itself necessary and sufficient to cause a class of severe blood diseases called myeloproliferative disorders. They then worked with a team of researchers from other academic institutions and from the San Diego pharmaceutical company TargeGen to conduct animal tests of a compound TargeGen had already isolated and shown to inhibit that same genetic pathway. As a result of this broad collaboration, human clinical trials for this potential therapy began in February. Read more about this research here: http://ucsdnews.ucsd.edu/newsrel/health/04-08rarebloodd isorder.asp

Laura Elias & Arnold Kriegstein, University of California, San Francisco

Discovered that membrane proteins that form cell to cell connections also have an important role in controlling how neurons migrate in the brain. Understanding neuronal migration is a critical aspect of cell therapy in the nervous system, as replacement cells will need to be directed to their appropriate site of action. This research project is also an example of how funding work in one field moves along work in another. The membrane proteins highlighted in this report had previously been identified in some cancers, and these new observations in neurons provide rationale for targeting them in cancer therapy. The finding was featured as a Nature cover story on August 23, 2007. Read more about this research here: http://pub.ucsf.edu/newsservices/releases/200709042/

Hanna Mikkola, University of California, Los Angeles

Discovered that blood stem cells originate and are multiplied in the placenta.Knowing this will help researchers to create the right environment for growing an individuals blood stem cells until there are enough for transplantation, something that has not been possible to date and forced many cancer patients to accept mismatched cells that have a high chance of producing significant and often deadly complications. The study is published March 6, 2008 in the journal *Cell Stem Cell*. Read more about this research here: http://www.stemcell.ucla.edu/documents/MikkolaCellStemCell080305nr.pdf

Deepak Srivastava & Kathy Ivey, Gladstone Institute

Discovered how two specific tiny genetic factors called microRNAs influence the differentiation of stem cells into heart muscle. They found that the factors not only drive the versatile cells to become heart, but also actively prevent them from becoming other tissue such as bone adding to their potential to make therapy more specific and targeted for patients. The study is published March 6, 2008 in the journal *Cell Stem Cell.* Read more about this research here: *http://www.gladstone.ucsf.edu/gladstone/php/content.php?sitename=publicaffairs&type=1&id=585*

William Lowry & Rupa Sridharan, University of California, Los Angeles

Succeeded in inducing skin cells to become pluripotent cells with genetic featured very much like embryonic stem cells. They verified work published during the completion of their project which showed that the introduction of four specific genetic factors is sufficient to induce differentiated adult cells into reverting to an embryonic stem cell-like state. This was critical validation of a procedure that could lead to a new way of developing personalized cell lines for therapy. The findings were published in the February 26, 2008 issue of the Proceedings of the National Academy of Sciences. Read more about this research here: http://www.stemcell.ucla.edu/documents/PlathPNAS080211PR.doc

Cynthia Kosinski, University of California, San Francisco

Found nearly a thousand genes that are expressed differently in different parts of the colon. The colon is constantly renewed via its own stem cells and understanding how these genes are expressed differently as the cells specialize will help understand what happens when this goes wrong as in colon cancer. The Findings were published in the September 25, 2007 Proceedings of the National Academy of Sciences. Read more about this research here: http://www.pnas.org/cgi/content/full/104/39/15418

Miguel Ramalho-Santos, University of California, San Francisco

Identified a group of genes that are active in embryonic stem cells but not in more differentiated cells. Also developed a technique to find DNA regions that could be important for activating these genes, and identified a factor that directs the production of proteins from genes that contain these regulatory DNA regions. These studies will greatly inform research efforts that rely on maintaining a stem cell's ability to proliferate and to generate the many different cell types in a human body. Findings were published in the August 2007 PLoS Genetics. Read more about this research here: http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.0030145

Youngjun Kim, University of California, San Diego

Found the function of a key protein involved in the cell cycle, the process by which a cell duplicates all its genes and divides. The protein is critical to the assembly of the membrane around the cell's nucleus. A fundamental understanding of the cell cycle is integral to advancing all cell-based therapies. The findings were published in the April 17, 2007 Proceedings of the National Academy of Sciences. Read more about this research here: http://www.pnas.org/cgi/content/full/104/16/6596

Chay Kuo, University of California, San Francisco

Found that proteins involved in the generation of neurons early in development also help neural stem cells produce neurons after birth. Furthermore, the researchers identified a self-repair mechanism in the brain that relies on these neural stem cells. Understanding how endogenous neural stem cells repair and remodel a mature brain is critical to successful stem cell therapy. The findings were published in the December 15, 2006 issue of Cell. Read more about this research here: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WSN-4MK0FFP-P&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=b62557a225338fb36a4fe47936b2f06e