FINDINGS

Nebraska Coalition for Lifesaving Cures
900 S. 74th Plaza, Ste. 301
Omaha, Ne 68114

402-390-2461
nebraskacures.com

Cures Save Lives

PRSRT STD
U.S. POSTAGE
PAID
OMAHA, NE
PERMIT #446

Board of Directors

FINDINGS

Nebraska Coalition *for Lifesaving Cures*

The Newsletter of the Nebraska Coalition for Lifesaving Cures

Summer 2015

UNMC announces Richard Holland Future Scientist Award winners

Pictured left to right: Alexis Page; Riley Jones; Kari Heck; Christina Miller and Austin Sanford.

Undergraduate students from five Nebraska colleges and universities recently received the 2015 Richard Holland Future Scientist Award from the Nebraska Coalition for Lifesaving Cures. The first place winner was Christina Miller of Creighton University, second place was Riley Jones of Doane College, third place was Kari Heck of University of Nebraska-Lincoln, honorable mention was Alexis Page of University of Nebraska Kearney and Austin Stanford of University of Nebraska Omaha.

The students received cash prizes totaling $2,500 at the annual INBRE (Institutional Development Award (IDeA) Networks of Biomedical Research Excellence Program) conference on Aug. 4 in Lincoln.

The awards are named in honor of Richard Holland, an Omaha philanthropist, longtime supporter of research and chairman of the board for the Nebraska Coalition for Lifesaving Cures.

The students were judged on their oral presentations of the research work they conducted this summer as part of the INBRE program.

The INBRE program is overseen by James Turpen, Ph.D., associate vice chancellor for academic affairs and a professor in the UNMC Department of Genetics, Cell Biology and Anatomy at the University of Nebraska Medical Center. Dr. Turpen is the principal investigator of the $16.2 million National Institutes of Health (NIH) grant that funds the program.

Established in 2001, the INBRE Scholars program was created to expose students to serious biomedical research and build a statewide biomedical research infrastructure between undergraduate and graduate institutions.

The students, referred to as INBRE scholars, enter the program after completing their sophomore year of college upon recommendation of their college professors.

FROM THE PRESIDENT

Human embryo editing as a path to genomic engineering

by Dr. David Crouse
President, Nebraska Coalition for Lifesaving Cures

One must be impressed by the phenomenal rate at which advances in medicine and the life sciences take place. It was only a few years ago that "gene therapy" was a very hot topic for advancing treatment of some difficult human diseases, particularly those with a simple genetic origin (cystic fibrosis, severe combined immunodeficiency disease, hemophilia, etc.). In each of those diseases, the objective was to treat or cure a particular patient by replacing or modifying a defective gene present in their cells, causing the disease. After many years of effort, a few of those therapies have been successful, but many have still been plagued by harmful side effects. Throughout the study of genetically based diseases, many physicians and scientists have desired to find a way to treat the gene defect at the earliest possible time – in the sperm, egg, or very early embryo (in IVF) – before the disease is expressed in an affected offspring. Very recently the technological approach that would allow such early treatment has been described – and even applied.

You know that such a report is truly unique and has a substantial impact when it is described in media ranging from the BBC, Forbes, Wired Magazine and National Geographic to the leading science and medical journals: Science, Nature, Scientific American and the Journal of the American Medical Association (JAMA). The scientific and clinical significance of this finding cannot be underestimated and the associated ethical complexity it raises is very substantial. First, let us review the science. A process known as the CRISPR/Cas9 technique, has been described and applied successfully in which a defective gene of the early embryo can be molecularly detected, "snipped out" and replaced with a normal copy of the same gene. This has been described as a genetic "find and replace" process like in a word processor and though scientifically complex it is technologically simple and relatively inexpensive. It has scientific/clinical impact because it means that a genetically based disease can be eliminated from the early embryo (just a few cells – like those used to establish embryonic stem cells) before significant development occurs, thus eliminating the disease. What is even more significant is that the deletion/replacement will occur in every cell of the developing embryo and thus eliminate the faulty gene from showing up in all tissues including sperm and eggs. This eliminates the disease from subsequent generations – this is truly genomic engineering.

The second major point is an ethical quandary and is straight forward. Parallel to the great possible health benefits, this process could be used for nearly any gene or genes thus allowing a change in eye color, stature, intelligence, or nearly any other trait that has a genetic basis, as most do. Some claim that this kind of "embryo editing" opens the door to the real possibility of "designer babies" and should be outlawed while others see it as a path to eliminating some diseases that have plagued humankind for all of history. Obviously, there should be a middle path and most major scientific groups have urged moving forward slowly.

For example, the National Institutes of Health (NIH) has declared that it will not fund gene editing in human embryos. Indeed, this decision is covered by guidelines for stem cells and the Recombinant DNA Advisory committee. In addition, the International Society for Stem Cell Research (ISSCR), the Society for Developmental Biology, the Alliance for Regenerative Medicine and a panel of interested stakeholders (see Science, vol 348, pg 36-39, 3 April 2015) have recommended a world-wide moratorium be set for germline genomic engineering and that a global group with representation from law, bioethics, genetic engineering, the public and government agencies be established as soon as possible to recommend policies.

All of this activity was precipitated by a surprise paper published in April by a Chinese group. They demonstrated the utility of the CRISPR/Cas9 technique in gene editing for beta thalassemia in human embryos that were not destined for implantation. They also showed that the approach had problems in that it sometimes was incomplete resulting in mosaic embryos or leading to "untoward mutations." Clearly the procedure is not ready for prime-time application but shows huge promise for future importance.

Another area that points to the impact that the CRISPR/Cas9 system is expected to have is in the world of high-tech investments. Just last week it was announced the "Bill Gates and 13 other investors…" were pouring $120 million dollars into a company that has hitched its intellectual property engine to the patents on the process. The Forbes article also describes the investments of a number of other prominent investment groups into similar biotech startups. It is recognized by both scientists and investors that the system could also be applied to the pharmaceutical industry where it would allow the rapid development of "microbial farms" to produce custom drugs. Indeed, if the old adage of "putting your money where your mouth is…" means anything, we will hear much more about the CRISPR/Cas9 approach to embryo engineering in the future.

FOR MORE INFORMATION VISIT nebraskacures.com/news-and-resources/

Landmark IPSC clinical study on hold due to genomic issue

Knoepfler Lab Stem Cell Blog

The pioneering induced pluripotent stem cell (IPSC) clinical study in Japan led by top stem cell clinical researcher Dr. Masayo Takahashi has been stopped according to the Wall Street Journal. One patient was transplanted in September 2014 with their own IPSC-derived retinal pigment epithelial cells (using an innovative RPE sheet, see image) for treatment of macular degeneration.

The study then moved on to a possible second patient, whose IPSC did not pass a genomic validation step. Reportedly, these IPSC contained a mutation, potentially in a known oncogene, which is a serious concern. Thus, the team decided to at least temporarily suspend the trial pending a possible redesign. The new plan could involve a change in how the IPSC are produced.

It remains unclear at this time whether the mutation in the second patient's IPSC was pre-existing in the patient's skin cells or if it occurred during the reprogramming process itself.

Overall, this situation is of course a concern, but it also reflects the very rigorous and appropriate degree of caution that this team was using in validation studies. Notably, the first transplanted patient is apparently doing well.

Researchers test shingles virus treatments using embryonic stem cells

Vaccine News Daily Reports

A team of scientists from Bar-Ilan University (BIU) in Israel recently discovered that human embryonic stem cells are useful for testing drug treatments against varicella-zoster virus (VZV), also known as the chickenpox virus.

The researchers recently created a novel experimental model that uses neurons from human embryonic stem cells to test potential treatments and therapies to prevent shingles. This new model may also help scientists discover preventions for other illness that invade the human nervous system, like polio and herpes.

"We hope to use this model to develop a therapeutic method, based on gene editing, which would prevent the virus from waking up and causing shingles," BIU Mina and Everard Goodman Faculty of Life Sciences Member Ronald Goldstein said. "Such a method could be used in the treatment of patients with elevated shingles risk, such as people whose immunity has been compromised due to trauma, disease or immunosuppressant therapies."

Embryonic stem cells found to repair damaged lung tissue in animal models

by Patricia Silva, PHD
Lung Disease News

A new study recently published in the journal Nature, embryonic stem cells are able to repair damaged lung tissue in mice models. The study was led by researchers at Weizmann Institute of Science in Israel and is entitled "Preconditioning allows engraftment of mouse and human embryonic lung cells, enabling lung repair in mice."

Restoration of the injured lungs is a long-standing, therapeutic challenge. The research team concluded that embryonic stem cells are able to successfully heal and reconstitute damaged lung tissue in mice models. The team's next goal is to determine the optimal dose of drugs required to avoid rejection of the transplanted cells, and "to create a bank of lung tissue that will be a resource for embryonic lung stem cells," concluded the study's senior author, Dr. Yair Reisner.

Building a bridge to therapies: Stem cell-derived neurons restore feeling to injured limbs

by Todd Dubnicoff
The STEM CELLAR: The official blog of CIRM

In a study in Nature's Scientific Reports, researchers at Uppsala University in Sweden made significant progress toward understanding and treating a related but different sort of injury that disrupts nerve signals coming into and out of the spinal cord. Although the ruptured nerve fibers from the limbs have the ability to extend back toward the spinal cord, inflammation from the site of injury makes the spinal cord impenetrable and blocks any restoration of normal sensory function.

To explore the potential of overcoming this spinal cord barrier, the research team transplanted human embryonic stem cell-derived neurons into mice mimicking human avulsion injury. Five months after the transplant, growth of nerve fibers into the spinal cord was seen, but these nerve fibers that had reconnected with the spinal cord were host animal cells and not the transplanted human stem cell-derived neurons.

Because stem cells have the ability for unlimited growth, any future therapy based on these findings must show that the transplant doesn't lead to excessive cell growth. In an encouraging sign, no tumor formation or extreme growth of human neurons in the animals were observed.