

FINDINGS
2016 SUMMER NEWSLETTER

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Nebraska Coalition
FOR LIFESAVING CURES

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2016 SUMMER NEWSLETTER



Jim and Diny Landen
honored at 14th annual
tribute luncheon

The Landens have been active in the local business and non-profit communities for more than 25 years. They both graduated from Southern Methodist University with business degrees, and returned to Omaha in 1987 to continue their business activities and raise their three sons.

Mr. Landen serves as chairman and CEO of Security National Bank, a local community bank, founded by his parents Clarence “Mickey” and Mary Landen.

Diny Landen has also been active in the business community primarily in broadcast and communications.

Through the years, they have served on the boards of many civic, social service, arts and health organizations. Jim Landen is currently on the boards of the Greater Omaha Chamber of Commerce, Clarkson Regional Healthcare Services, the Nature Conservancy and the Salvation Army. He is also serving on the Comprehensive

Cancer Center Building Committee. Diny Landen sits on the UNMC Board of Counselors, the board of directors of Joslyn Art Museum and Project Harmony.

“We all have to believe that there is a cure right around the corner”

At the lunch, the Landens said their support of medical research was very personal to each of them, noting that Jim’s mother suffered from Parkinson’s disease, while Diny’s father died from a rare form of cancer.

“We all have to believe that there is a cure right around the corner,” Jim Landen told the crowd of nearly 200.

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LEFT: Chancellor Emeritus Harold M. Maurer, M.D., Beverly Maurer, Diane Nelson TOP MIDDLE: Beverly Maurer, David Crouse, Ph.D. MIDDLE BOTTOM: Amanda McGill Johnson RIGHT: Wally Weitz, Barbara Weitz, Richard “Dick” Holland



In May, the Nebraska Coalition for Lifesaving Cures asked OBI Creative to produce a video to assist the organization for the Omaha Gives campaign. Visit our new website at **nebraskacures.com** to view the video. You'll be glad you did.

UCSF scientists find molecular link between brain stem cells and Zika infection

By Karen Ring | California Institute for Regenerative Medicine | March, 2016

The Zika virus scare came to a head in 2015, prompting the World Health Organization to declare the outbreak a global health emergency earlier this year. From a research standpoint, much of the effort has centered on understanding whether the Zika infection is actually a cause of birth defects like microcephaly and how the virus infects mothers and their unborn children.

Scientists from UC San Francisco (UCSF) are tackling this question and have unraveled one more piece to the Zika infection puzzle. UCSF professor Dr. Arnold Kriegstein and his team reported that they've identified a protein receptor on the surface of brain stem cells that could be the culprit for Zika virus infection.

Based on previous studies that showed that the Zika virus specifically infects brain stem cells, Kriegstein and his colleagues hypothesized that these cells expressed specific proteins that made them vulnerable to Zika infection. They

looked to see which genes were turned on and off in brain stem cells derived from donated fetal tissue as well as other cell types in the developing brain to identify proteins that would mediate Zika virus entry.

They found a protein receptor called AXL that was heavily expressed in a type of brain stem cell called the radial glial cell, which gives rise to the outer layer of the brain called the cerebral cortex. AXL piqued their interest because it was identified in other studies as an entry point for Zika and other similar viruses like dengue in human skin cells. Furthermore, the team confirmed that radial glial cells produce a lot of AXL protein during development and it appears during a specific window of time – the second trimester of pregnancy.

Diabetes’ demise? Master switch identified for turning stem cells into functional insulin-producing cells

By Todd Dubnicoff | California Institute for Regenerative Medicine | April, 2016

April was a good month for diabetes researchers and the over one million Americans with type 1 diabetes who are hoping for an eventual stem cell-based treatment for this incurable disease. Published a day apart, two studies reported on achieving an elusive goal for the field: creating functional insulin-producing cells in a lab dish from induced pluripotent stem cells (iPS).

One of the studies used cells from human fat tissue (aka “love handles”) to devise a novel, consistent and efficient method for generating iPS-derived insulin-producing cells.

The other study is a CIRM-funded project by Salk Institute scientists. Reporting in Cell Metabolism, the team compared fetal and adult insulin-

producing cells in mice and uncovered a protein “switch” that stimulates human iPS cells to fully mature into insulin-producing cells in a petri dish.

Because a very specific cell type is affected, the pancreatic beta cells, developing a cell therapy for diabetes would seem pretty straight-forward. Simply transplant stem cell-derived pancreatic beta-like cells that naturally release insulin in response to glucose. But over the years, researchers found that it wasn't so easy to make fully mature stem cell-derived beta-like cells in the lab. The cells often got stuck at an immature stage of development resembling those found in the developing fetus.

To get past this bottleneck, the Salk team studied fetal and adult beta cells in mice in hopes that a comparison would reveal key missing ingredients for making fully functional beta-like cells. In particular, they compared the levels of transcription factors, proteins that turn genes on and off and are known to play important roles in determining the cell fate of stem cells. This analysis identified a transcription factor called ERR-gamma present in higher levels in adult cells compared to the fetal cells.

If this transcription factor is really important, removing it should have a very noticeable impact on maintaining blood glucose level. To test this idea, the team genetically engineered mice that lacked ERR-gamma. Sure enough, they showed that the beta cells of these mice did not release insulin in response to a large injection of glucose.

Which methods will work? Are “love handle” beta cells better than ERR-gamma ones? Ultimately, only clinical testing will be able to answer these questions. It's exciting to see so many research teams making progress toward cell therapies for diabetes. As we often say here, the more shots the field takes, the more likely someone will score the game-changing goal of curing diabetes.

Stem Cell Guidelines Released

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



On May 12, 2016, the International Society for Stem Cell Research (ISSCR) released their long-awaited “Guidelines for Stem Cell Research and Clinical Translation.” The society last released their “Guidelines for the Conduct of Embryonic Stem Cell Research” in December of 2006 and “Guidelines for the Clinical Translation of Stem Cells” in December of 2008. This new document fills a gaping void in the necessary guidance for this area considering the rapid pace at which research and translation to the clinic

(FDA) has considerable responsibility in this regard but has been mired in a slow moving, contentious, bureaucratic process to develop the regulatory guidance. Unfortunately, they are still in the “draft document” stage with no nearby end in sight. In addition, their charge only covers clinical applications and not the vast area of basic research.

The new ISSCR Guidelines are wide ranging in scope. They even address issues relevant to some of the most rapidly advancing areas of the field: induced pluripotent stem cells (iPSC); CRISPR-Cas-9 technology; human-animal chimeras; mitochondrial replacement therapy; and banking of stem cells. They provide very relevant and fundamental principles regarding human subject protection in the entire area of stem cell research and translation including the potential application to collection and use of eggs from female donors as well as fetal cells and tissues. As rapidly as

if ever be developed outside of a formal clinical trials process. Nonetheless, the ISSCR acknowledges that in some very limited cases, clinicians may be justified in attempting medically innovative stem cell-based interventions in a small number of seriously ill patients. Such limited attempts at medical innovation contrast with the marketing of unproven stem cell interventions...” This is a clear effort to develop “robust standards for pre-clinical and clinical research” and reduce the large number of bogus or unproven “Stem Cell Therapies” offered to desperate patients and families in the US and around the world. This was the topic of a previous Newsletter article.

Not surprisingly, this section of the Guidelines has seen some push-back from the commercial, for-profit purveyors of stem cell products and stem cell therapy and even from some advocacy groups who are dismayed by the slow pace of FDA action and the stringency of the ISSCR recommendations. Throughout the Guidelines, the ISSCR emphasizes the importance of developing safe and effective therapies that are evidence-based. We are confident that professional stem cell meetings and journals will continue to discuss and debate the details of the document in the coming weeks and months.

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have advanced and the emergence of excessive stem cell hype. The need for new guidance was becoming increasingly obvious. Indeed, the ISSCR is the only international body providing a detailed set of principles and recommendations in this area. Many proposed practices in stem cell research and clinical translation are not covered by the laws or policies of their respective countries (or states) and it has been left to the scientists, clinicians and their professional organizations to step in and fill that void. In the United States, the Food and Drug Administration

this field is moving, the ISSCR has managed to include just about every currently relevant issue. We all hope that they are also willing to issue appendix or supplemental guidance as new topics evolve!

The most commented on and controversial topic in their document addresses “Stem Cell Based Medical Innovation” which they wrap around a side-bar: “WARNING ON THE MARKETING OF UNPROVEN STEM CELL-BASED INTERVENTIONS.” To quote this section directly: “...as a rule, stem cell-based products should rarely

To read the guidelines referred to, visit **isscr.org**

2016 LUNCH AND LEARN

Pioneering stem cell researcher speaks in Omaha

By Tom O'Connor
UNMC public relations



Shoukhrat Mitalipov, Ph.D. and David Crouse, Ph.D.

One of the true pioneers in stem cell research, Shoukhrat Mitalipov, Ph.D., spoke in Omaha Friday, April 22, 2016 at the Thompson Alumni Center at the University of Nebraska at Omaha.

Dr. Mitalipov’s speech, which was sponsored by the Nebraska Coalition for Lifesaving Cures, was attended by more than 50 people. It was held in conjunction with the Nebraska Science Festival.

Those attending heard Dr. Mitalipov detail his groundbreaking research with mitochondria, the energy producers inside every human cell.

“Dr. Mitalipov is an elite scientist in the field of stem cell and genetic research,” said David Crouse, president of the Nebraska Coalition for Lifesaving Cures. “It was great having him come to Omaha and share his cutting-edge research.”

Dr. Mitalipov is a senior scientist in the division of reproductive & developmental sciences at Oregon Health and Science University and the director of the Center for Embryonic Cell and Gene Therapy.

Born in Russia in what is now Kazakhstan, Dr. Mitalipov came to Utah State University in 1995 to conduct his postdoctoral research in stem cell and developmental biology. He moved to Oregon in 1998, and has since become an American citizen.

Dr. Mitalipov’s lab investigates novel gene therapy approaches designed to prevent transmission of gene defects from parents to their children. Mutations in mitochondria contribute to a diverse range of still incurable human diseases that are maternally inherited through the egg’s cytoplasm.

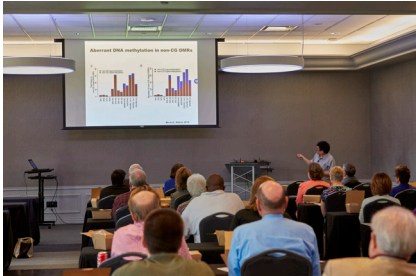
It is estimated that at least one in 200 children inherit mitochondria mutations that may lead to disease and one in 4,000 babies in the U.S. is born with an inherited mitochondrial disease for which there is no treatment. Few of these children will reach adulthood.



In 2009, Dr. Mitalipov’s lab produced twin male rhesus monkeys who were born with replaced mitochondria. A University of Nebraska Medical Center geneticist, Warren Sanger, Ph.D., played an important role in this first-ever accomplishment by doing the genetic testing involved in the research. Dr. Sanger, who was director of the Human Genetics Laboratory and director of clinical genetics at the Munroe-Meyer Institute, died in 2015 at the age of 69.

With some adjustments, Dr. Mitalipov has been able to replicate the procedure he did with the monkeys using human eggs. Because of federal rules against gene manipulation, however, these eggs were not allowed to mature.

Currently, the U.S. and other countries are weighing mitochondrial replacement. Britain has developed regulations to govern clinical trials in people.



2016 MAURER SCIENTIFIC ACHIEVEMENT AWARD RECIPIENT

Dr. Kielian gets 2016 Maurer Scientific Achievement Award

By Tom O'Connor
UNMC public relations



Tammy Kielian, Ph.D., accepts the 2016 Maurer Scientific Achievement Award

Tammy Kielian, Ph.D., professor of pathology and microbiology, received the Harold M. Maurer, M.D. & Beverly Maurer Scientific Achievement Award at the 14th Annual Tribute Spring Luncheon sponsored by the Nebraska Coalition for Lifesaving Cures.

Dr. Kielian was recognized for her research on juvenile Batten disease, a neurodegenerative condition that first presents with blindness around 5-10 years of age, then progresses to seizures, cognitive and motor loss, dementia and premature death.

In 2012, Dr. Kielian shifted her research work to study juvenile Batten disease because her niece in Colorado was diagnosed with the disease. She hopes to begin a Phase I clinical trial in the near future to evaluate her use of gene therapy in treating juvenile Batten disease.

The award, which pays a \$10,000 stipend, is named after Dr. Maurer, who served as chancellor of UNMC from 1999-2014, and his wife. It was created by the Nebraska Coalition for Lifesaving Cures to recognize the Maurers for their staunch support of research.

David Crouse, Ph.D., president of the coalition, introduced Dr. Kielian. He said, “She’s more than a rising star. She’s already there. She’s a triple threat — she excels in research, teaching and service.”

Dr. Crouse retired from UNMC in 2012 after 35 years with the medical center. He held several key administrative roles including associate vice chancellor for academic affairs.

“She’s more than a rising star. She’s already there. She’s a triple threat — she excels in research, teaching and service.”

Each year at the Tribute Spring Luncheon, the Nebraska Coalition for Lifesaving Cures honors individuals from Nebraska who have made a difference in the world through their passionate support of medical research.



Dr. Harold & Beverly Maurer, Drs. Tammy and Mark Kielian