Nearly 30 Percent of New CIRM Awards go to UC San Diego Stem Cell Researchers

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UC San Diego scientist garnered 8 of the total 27 of Basic Biology III awards announced today by the Independent Citizens' Oversight Committee (ICOC) of the California Institute for Regenerative Medicine, the state agency created by California voters to pursue the promise of stem cells in science and medicine.

"Basic science has been our strength at UC San Diego because we have dedicated time and energy to developing our expertise in stem cells," said Larry Goldstein, PhD, director of the UC San Diego Stem Cell Program. "Through our excellence in scientific research fundamentals, UCSD stem cell researchers are creating the basis for future advances in this exciting field."

Of the 27 Basic Biology III awards given to researchers at nine institutions throughout California, UC San Diego researchers received eight, for a total of $10.891 million. The awards are designed to fund investigations into basic mechanisms underlying stem cell biology, cellular plasticity and cellular differentiation, or the ability of stem cells to be programmed into different types of cells in the body. According to CIRM, "Studies supported by these awards will form the foundation for future translational and clinical advances, enabling the realization of the full potential of human stem cells and reprogrammed cells for therapies and as tools for biomedical innovation."

UCSD researchers, projects and their awards are:

David Cheresh, PhD, professor of pathology, UC San Diego Moores Cancer Center, has been awarded $1,361,448 to study neuronal cells called autonomic neurons, which are part of the peripheral nervous system, are responsible for the "fight or flight" response and control breathing and heart rate. The researchers discovered that these neurons align and pattern along with blood vessels, and their work aims to understand how blood vessels help the differentiation of autonomic neurons. Understanding gained from these studies will not only benefit patients with autonomic nervous system disorders, but may also facilitate development of functional blood vessels using hESCs for tissue engineering applications.

Anirvan Ghosh, PhD, professor and chair of the Neurobiology Section of the Division of Biological Sciences, has been awarded $1,391,400 to investigate synaptic defects in autism using patient-

derived induced pluripotent stem cells (iPSCs.) Studies will use neurons derived from iPSCs from patients with autism who have known mutations in the genes involved in synaptic function. As part of the research, expression of these genes will be modified to model changes that occur in the disorder. The research also aims to identify proteins that may be targets for the development of new therapeutics.

Charles C. King, PhD, associate research scientist in the Department of Pediatrics, has been awarded $1,313,649 for work to better understand, describe and ultimately optimize human embryonic stem cells (hESCs) for use in the treatment of type 1 diabetes. Of the several genetic factors that contribute to stem cell differentiation, microRNAs (miRs) are emerging as important determinants. King's team is working to identify and validate temporal expression of miRs at various stages of hESC differentiation to insulin-producing cells. This work will help create a population of cells of significant therapeutic impact in the treatment of diabetes.

Farah Sheikh, PhD, assistant professor, Division of Cardiology, Department of Medicine, has been awarded $1,341,955 to study the molecular mechanisms underlying human cardiac cell junction maturation and disease using induced pluripotent stem cells (iPSCs) of patients with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC). The goal is to study the basic biology of these heart muscle junctions, as mistakes in their genetic code can lead to ARVC, an inherited form of heart disease associated with sudden cardiac death in young people, including athletes. Using iPSCs from those carrying ARVC genetic mistakes to generate new heart muscle cells in the lab, the researchers will provide a true human model of the disease to identify early disease markers and drug targets to control this fatal cardiac disease.

Deborah Spector, PhD, professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, was awarded $1,372,660 to study viral-host interactions in cases where human cytomegalovirus (HCMV), a major cause of birth defects, affects neural differentiation of progenitor cells. The goal of this research is to understand how HCMV affects the normal development of neurons, to serve as the basis for therapeutic strategies to fight HCMV infection in newborns as well as immunocompromised individuals.

Gene Yeo, PhD, assistant professor, Department of Cellular and Molecular Medicine, was awarded $1,372,660 for research focusing on a class of proteins that bind directly to RNA – called splicing factors – that act in combination to control the process of alternative splicing. Alternative splicing can result in human genetic diseases such as ALS, Parkinson's, Alzheimer's and other neurodegenerative disorders when mis-regulated. By producing a regulatory map of RNA binding sites of these proteins, the researchers will evaluate the importance of alternative splicing in neurological disease modeling and stem cell biology– ultimately leading to advances in drug discovery and toxicology testing.

Binhai Zheng, PhD, associate professor, Department of Neurosciences, was awarded $1,355,063 for his work to generate and characterize corticospinal neurons from hESCs, which are damaged or severely compromised in patients of spinal cord injury and ALS. To aid in this process, he and his colleagues have engineered a fluorescent reporter that literally illuminates how hESCs differentiate into corticospinal motor neurons, which are essential in controlling skilled, voluntary movement in humans. Using mouse models, the scientists will study whether neurons developed in culture can be introduced back into an organism and then grow neuronal projections to the spinal cord, as they would during normal development.

Kun Zhang, PhD, assistant professor, Department of Bioengineering, Jacobs School of Engineering and the UCSD Institute for Genomic Medicine, was awarded $1,382,140 to study mutations associated with stem cell reprogramming and differentiation. By understanding the functional consequences of mutations that can arise during the course of reprogramming a patient's own stem cells into pluripotent stem cells, the researchers hope to clear one of the biggest hurdles in the field of hIPS cells – the risk of cancer. The scientists will comprehensively identify genetic changes in protein coding sequences, or exomes, through large-scale DNA sequencing, with the goal of better understanding of how such mutations occur and propagate.

The May 4 awards bring UC San Diego's total to nearly $94 million since the first CIRM awards in 2006.

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