

CIRM Awards More Than \$2.5 Million in Transplantation Immunology Grants to Two UC San Diego Researchers

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A pair of University of California San Diego researchers - Martin Marsala, a specialist in spinal cord trauma and disorders, and Yang Xu, an immunologist - have been awarded more than \$2.5 million in new grants from the California Institute for Regenerative Medicine (CIRM).

The grants are two of 19 Stem Cell Transplantation Immunology awards totaling \$25 million that were approved at the June 23 meeting of CIRM's Independent Citizens' Oversight Committee to fund work that translates basic research into clinical cures.

Marsala, MD, professor of anesthesiology in the UC San Diego School of Medicine, was awarded a grant worth more than \$1.3 million to develop methods that would promote and prolong the survival of therapeutic stem cells grafted into the central nervous system, using few or no immunosuppressive drugs.

"Immunosuppressive drugs have many negative side effects," said Marsala. "If we can improve immune tolerance to specific cell lines, we may be able to develop therapies that are well-tolerated; which would have a significant impact for patients."

There are multiple prongs to Marsala's project. Researchers will test engraftment of three different neuronal precursor cell lines of human origin using an animal model. They will study the comparative survival of cells grafted into healthy and into injured spinal cord tissue. And they will test the engraftment success of genetically reprogrammed neuronal cells generated from pig skin cells.

Xu, PhD, a professor of biology at UC San Diego, and colleagues received a \$1.2 million CIRM grant to exploring improving the human immune system's tolerance to grafted tissues derived from human embryonic stem cells (hESCs). Xu's project involves developing an appropriate animal model for testing the idea of inducing tolerance by transplanting hESC-derived hematopoietic stem cells (multipotent stem cells that give rise to all blood cell types) into recipients prior to grafting other tissues derived from hESCs.

"Right now, rejection of grafted tissues expressing antigens from the donor can be delayed for a time if the immune system is persistently suppressed," said Xu. "But eventually, most grafts are rejected. And persistent immune suppression increases the risk for cancer and infection."

"By learning how to effectively generate and graft hESC-derived hematopoietic stem cells before other tissues are grafted, we hope to induce immune tolerance that would allow other transplanted hESC-derived cells to survive long-term and accomplish their missions."

The latest round of CIRM funding brings the total grants to the UC San Diego Stem Cell Program to more than \$72 million since grants were first awarded in 2006.

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