CIRM's expanding reach

By Tim Fulmer, Senior Writer

The **California Institute for Regenerative Medicine**'s newest batch of grants differs from previous stem cell research awards in two key ways—they are later stage and reflect CIRM's collaboration with agencies outside of California.

CIRM has awarded about $1 billion to support a total of 321 grants since it was founded in November 2004. But the most recent set of awards—a total of $229.8 million to 14 teams—is the first expected to result in IND submissions when work under the four-year grants is completed.

Canada's **Cancer Stem Cell Consortium** (CSCC) and the U.K.'s **Medical Research Council** (MRC) will provide an additional $35 million and $8 million, respectively, to fund portions of research carried out in labs located in those countries.

Unlike the Early Translational Research grants that CIRM issued in April, the latest round is highly disease oriented, with each research proposal focused on a single area such as cancer, HIV, type 1 diabetes, macular degeneration and stroke (*see* **Table 1, "CIRM grants"**).

Only two biotech companies received grants: **Novocell Inc.** and **Calimmune Inc.** CIRM spokesperson Don Gibbons did not disclose if other biotechs applied for funding and were turned down or if this round of applicants was dominated by university researchers simply by chance. Nor did he disclose how the institute determined the amount of funding extended to the companies.

A $20 million grant to a Novocell-led group will support the development of encapsulated insulin-producing cells derived from human embryonic stem cells (hESCs) to treat type 1 diabetes.

Novocell SVP and CSO Emmanuel Baetge told *SciBX* that encapsulating the insulin-producing cells in a semipermeable polyethylene glycol (PEG)-based coating ensures ample transport of nutrients and oxygen into the cells while protecting them from a potential host immune response and thus reducing the need for long-term immunosuppression. Moreover, the cells will be implanted subcutaneously to allow for monitoring and retrieval if necessary.

In nonhuman primates, Novocell has shown that encapsulated islet cells derived from same-species donors required immunosuppression for 30 days following implantation, after which the islets functioned for 20 months without the need for additional immunosuppression.

Meanwhile, Novocell has developed a method to generate functional islets from hESCs. Last year, company researchers reported

Table 1. CIRM grants. Below is a list of 14 research grants awarded by the California Institute for Regenerative Medicine (CIRM) to develop stem cell–based therapies.

Lead institution	Lead principal investigator	CIRM funding ($M)	Proposal summary
Cedars-Sinai Medical Center	Eduardo Marbán	5.6	Repair heart tissue damaged by heart attack using autologous heart stem cells
City of Hope	Karen Aboody	18.0	Treat brain tumors using neural stem cells modified to carry a tumor-killing drug
City of Hope	John Zaia	14.6	Treat HIV using genetically modified autologous hematopoietic stem cells that give rise to HIV-resistant T cells
Novocell Inc.	Emmanuel Baetge	20.0	Treat type 1 diabetes by implanting islet cells generated from human embryonic stem cells (hESCs)
Salk Institute for Biological Studies	Samuel Pfaff	15.6	Treat amyotrophic lateral sclerosis (ALS) by implanting precursor astrocyte cells derived from hESCs
Stanford University	Alfred Lane	11.7	Treat epidermolysis bullosa using genetically modified induced pluripotent stem cells derived from the patient's skin cells
Stanford	Gary Steinberg	20.0	Treat stroke using implanted neural stem cells derived from hESCs
Stanford	Irving Weissman	20.0	Develop a mAb that targets leukemia stem cells
University of California, Los Angeles (UCLA)	Irvin Chen[A]	20.0	Treat HIV using RNAi-modified autologous hematopoietic stem cells that give rise to HIV-resistant T cells
UCLA	Donald Kohn	9.2	Treat sickle cell disease using genetically modified hematopoietic stem cells that become normal red blood cells
UCLA	Dennis Slamon	20.0	Develop compounds that target cancer stem cells in solid tumors
University of California, San Diego	Dennis Carson	20.0	Develop mAbs and small molecules that destroy leukemia stem cells
University of California, San Francisco	Mitchel Berger	19.2	Treat brain tumors using neural stem cells modified to carry a tumor-killing drug
University of Southern California	Mark Humayun	15.9	Treat macular degeneration using transplanted retinal cells derived from hESCs
Total		***229.8***	

[A]Geoff Symonds at biotech company **Calimmune Inc.** is also a principal investigator.

that pancreatic endoderm derived from hESCs generated glucose-responsive, insulin-secreting cells in mice.[1]

The next step is to encapsulate those hESC-derived islet cells.

Baetge told *SciBX* that the company's approach potentially solves a key difficulty facing all encapsulation technologies: balancing accessibility to serum nutrients with the need for disguise from the host immune system.

The coating's semipermeability ensures glucose and insulin can freely diffuse into and out of the islets, whereas the PEG molecules provide a biocompatible barrier that prevents the islets from contacting host immune cells and triggering an immune response, he said.

Calimmune and the **University of California, Los Angeles** (UCLA) received a $20 million grant to develop RNAi-modified hematopoietic stem cells that differentiate into HIV-resistant T cells.

Irvin Chen, co-principal investigator on the grant, told *SciBX* that his lab and the biotech will split research responsibilities. Calimmune will shoulder late preclinical development, including "clinical assay development and validation, therapeutic gene vector production and management of regulatory issues," he said. Chen is professor of microbiology and immunology at UCLA and director of the UCLA AIDS Institute.

In 2007, Chen and colleagues at UCLA, the **California Institute of Technology** and **NIH**'s **National Heart, Lung, and Blood Institute** reported that RNAi-based stem cell transplants developed into lymphocytes. The lymphocytes were less susceptible to infection in nonhuman primate models of HIV than lymphocytes not expressing the RNAi.[2]

Next year, CIRM expects to award two sets of grants supporting early preclinical research, Gibbons told *SciBX*.

"One of those sets will focus on basic stem cell biology and will include some funding from Japanese sources to support researchers in that country," he said. "A second set of grants, which will focus on immunology and stem cells, will involve Australian researchers and include funding from Australian sources."

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2. An, D.S. *et al. Proc. Natl. Acad. Sci. USA* **104**, 13110–13115 (2007)

COMPANIES AND INSTITUTIONS MENTIONED

California Institute for Regenerative Medicine, San Francisco, Calif.
California Institute of Technology, Pasadena, Calif.
Cancer Stem Cell Consortium, Toronto, Ontario, Canada
Calimmune Inc., Tucson, Ariz.
Medical Research Council, London, U.K.
National Heart, Lung, and Blood Institute, Rockville, Md.
National Institutes of Health, Bethesda, Md.
Novocell Inc., San Diego, Calif.
University of California, Los Angeles, Calif.