CIRM: get a little closer

By Michael J. Haas, Senior Writer

In its latest batch of grants the **California Institute for Regenerative Medicine** divided a smaller pool of funding among fewer research teams than it did in 2009, reflecting the institute's interest in funding projects that are close to entering the clinic.

Last month, CIRM announced awards totaling \$151 million to teams from 7 academic institutions and 1 company—**StemCells Inc.**—that are expected to submit INDs or complete Phase I or Phase II testing when work on the 4-year grants is complete (*see Table 1, “2012 CIRM grants”*).

StemCells will use its \$20 million grant to develop HuCNS-SC, purified human neural stem cells, to treat spinal cord injury (SCI) in the neck. The company already has the technology in Phase I/II testing to treat SCI in the back.

Two of CIRM's partners will contribute additional funding to specific projects. The **Andalusian Initiative for Advanced Therapies** will provide \$1.6 million to the Spanish collaborators of a team at the **University of California, Davis** that is developing an intramuscular injection of VEGF-producing mesenchymal stem cells (MSCs) to treat critical limb ischemia.

The U.S. **NIH** will provide undisclosed funds and resources to a team at **University of California, Los Angeles** that is developing stem cells engineered to express melanoma-specific T cell receptors (TCRs) to treat melanoma.

“NIH's dollar commitment is difficult to quantify because the project will involve the time of staff scientists already on the NIH payroll, along with the use of existing equipment” at the agency, said CIRM spokesperson Don Gibbons.

Gibbons said CIRM selected the 8 projects from a total of 21 applications, including 6 from industry. Of the 13 projects that did not receive grants, 2—including 1 from **OncoMed Pharmaceuticals Inc.**—have been sent back to CIRM's panel for re-review in light of new data submitted by the applicants. Those data address the reasons the review panel originally decided those projects did not meet CIRM's criteria, he said.

Gibbons noted that, compared with in 2009, the pool of applicants and number of awards were smaller this year because “the call for applications was more specific about how close to clinical trials the teams needed to be for funding.”

In 2009, CIRM awarded a total of \$229.8 million to 14 projects that were expected to result in IND submissions during the 4-year grant period.¹ CIRM has reviewed the progress of each of those projects annually in conjunction with the Clinical Development Advisory Panel (CDAP), which is composed of industry and other experts outside CIRM, Gibbons said.

According to a CDAP report issued by CIRM in March, 12 of the projects from 2009 are on track to meet their original goals with no changes in funding levels (*see Table 2, “Update on 2009 CIRM grants”*). Moreover, 2 of those 12 projects have spawned new companies: in 2011 the **City of Hope** brain cancer project leader founded **TheraBiologics Inc.**, and also in 2011 the **University of**

Table 1. 2012 CIRM grants. Research grants awarded by the California Institute for Regenerative Medicine (CIRM) to develop stem cell-based therapies.

Source: CIRM

Lead Institution	Lead principal investigator	CIRM funding (\$M)	Proposal summary
Cedars-Sinai Medical Center	Clive Svendsen	17.8	Treat amyotrophic lateral sclerosis (ALS) using progenitor cells secreting glial cell-derived neurotrophic factor (GDNF)
Stanford University	Robert Robbins	20.0	Treat end-stage heart failure using embryonic stem cell (ESC)-derived cardiomyocytes
Stanford University	Judith Shizuru	20.0	Develop a method for chemotherapy-free bone marrow transplants (BMTs) in severe combined immunodeficient (SCID) patients using an antibody that targets blood cell-forming stem cells
StemCells Inc.	Nobuko Uchida	20.0	Treat cervical spinal cord injury (SCI) using neural stem cells
University of California, Davis	John Laird	14.2	Treat critical limb ischemia using intramuscular injection of VEGF-producing mesenchymal stem cells (MSCs)
UC Davis	Nancy Lane	20.0	Treat osteoporosis using endogenous MSCs
UC Davis	Vicki Wheelock	19.0	Treat Huntington's disease (HD) using bone marrow-derived MSCs engineered to produce brain-derived neurotrophic factor (BDNF)
University of California, Los Angeles	Antoni Ribas	20.0	Treat melanoma using stem cells engineered to express melanoma-specific T cell receptors (TCRs)
Total		151.0	

Table 2. Update on 2009 CIRM grants. Status of research grants awarded in 2009 by the California Institute for Regenerative Medicine (CIRM) to develop stem cell-based therapies.

Source: CIRM

Lead institution	Lead principal investigator	CIRM funding (\$M)	Proposal summary	Status
Cedars-Sinai Medical Center	Eduardo Marbán	5.6	Treat advanced heart failure using autologous cardiac-derived cardiospheres or cardiosphere-derived cells	Team is developing allogeneic cardiac-derived cells and on track to submit an IND within four-year award period
City of Hope	Karen Aboody	18.0	Treat recurrent glioblastoma using neural stem cells modified to carry a tumor-killing drug	Team is on track to complete preclinical proof of concept by end of 2012
City of Hope	John Zaia	14.6	Treat HIV using genetically modified autologous hematopoietic stem cells that give rise to HIV-resistant T cells	Team is progressing toward IND-enabling studies
Stanford University	Alfred Lane	11.7	Treat epidermolysis bullosa using genetically modified induced pluripotent stem (iPS) cells derived from patient's skin cells	Team has generated iPS cell lines from several patients
Stanford University	Gary Steinberg	20.0	Treat stroke using implanted neural stem cells derived from human embryonic stem cells (hESCs)	Team has shown functional recovery in three preclinical models of stroke
Stanford University	Irving Weissman	20.0	Develop a mAb that targets leukemia stem cells	Team is conducting preclinical studies of a humanized anti-CD47 mAb
University of California, Los Angeles	Irvin Chen ^A	20.0	Treat HIV using RNAi-modified autologous hematopoietic stem cells that give rise to HIV-resistant T cells	Team has identified small hairpin RNAs that prevent HIV cell entry and replication
UCLA	Donald Kohn	9.2	Treat sickle cell disease using genetically modified hematopoietic stem cells that become normal red blood cells	Team has identified a lead therapeutic and had a pre-IND meeting with FDA
UCLA	Dennis Slamon	20.0	Develop compounds that target cancer stem cells in glioma, colon and ovarian tumors	Team is conducting IND-enabling studies of a lead inhibitor targeting an undisclosed kinase
University of California, San Diego	Dennis Carson	20.0	Develop mAbs and small molecules that destroy leukemia stem cells to treat acute myelogenous leukemia (AML), chronic lymphocytic leukemia (CLL) and three other hematological malignancies	Grant revised in 2012 to focus on two mAbs to treat AML and CLL; budgets and timelines being reassessed
UCSD	Larry Goldstein ^B	15.6	Treat amyotrophic lateral sclerosis (ALS) by implanting precursor astrocyte cells derived from hESCs	Team anticipates selecting a single cell line by mid-2012
University of California, San Francisco	Mitchel Berger	19.2	Treat brain tumors using neural stem cells modified to carry a tumor-killing drug	Grant discontinued in March 2012 for failure to meet an undisclosed milestone
University of Southern California	Mark Humayun	15.9	Treat age-related macular degeneration (AMD) using transplanted retinal pigment epithelium (RPE) cells derived from hESCs	Team on track to file IND within four-year award period
ViaCyte Inc. ^C	Allan Robins ^D	20.0	Treat type 1 diabetes by implanting islet stem cells generated from hESCs	Team is preparing for IND-enabling studies
Total		229.8		

^AGeoff Symonds at biotech company **Calimmune Inc.** is also a principal investigator. ^BThe original principal investigator was Samuel Pfaff of the **Salk Institute for Biological Studies**. ^CFormerly Novocell Inc.; the company changed its name to ViaCyte in 2010. ^DThe original principal investigator was Emmanuel Baetge of Novocell (now ViaCyte).

Southern California (USC) age-related macular degeneration (AMD) project team spun out **Regenerative Patch Technologies Inc.**

Also according to the CDAP report, CIRM recommended that the **University of California, San Diego**–led leukemia project team focus its efforts on developing two potential antibody therapeutics targeting leukemia stem cells to treat acute myelogenous leukemia (AML) and chronic lymphocytic leukemia (CLL). The team's project originally aimed to identify up to three antibodies and three small molecules to treat AML, CLL and three other hematological malignancies.

The CDAP report also noted that CIRM discontinued the grant to

a **University of California, San Francisco**–led brain tumor project because it failed to reach an undisclosed milestone.

Gibbons declined to say which of the 2009 projects might reach the clinic first but added that CIRM president Alan Trounson “has indicated he thinks the HIV team at City of Hope and the macular degeneration team of USC are pretty close.”

Haas, M.J. *SciBX* 5(32); doi:10.1038/scibx.2012.833
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REFERENCES

1. Fulmer, T. *SciBX* 2(44); doi:10.1038/scibx.2009.1621

COMPANIES AND INSTITUTIONS MENTIONED

Andalusian Initiative for Advanced Therapies, Seville, Spain
California Institute for Regenerative Medicine, San Francisco, Calif.
City of Hope, Duarte, Calif.
National Institutes of Health, Bethesda, Md.
OncoMed Pharmaceuticals Inc., Redwood City, Calif.
Regenerative Patch Technologies Inc., Glendale, Calif.

StemCells Inc. (NASDAQ:STEM), Newark, Calif.
TheraBiologics Inc., Los Angeles, Calif.
University of California, Davis, Calif.
University of California, Los Angeles, Calif.
University of California, San Diego, La Jolla, Calif.
University of California, San Francisco, Calif.
University of Southern California, Los Angeles, Calif.