

**Empire State Stem Cell Board
Funding Committee Meeting Minutes
September 17, 2010**

The Empire State Stem Cell Board Funding Committee held a meeting on Thursday, September 17, 2010, at the offices of the Department of Health, 90 Church Street, New York, New York. Commissioner Richard F. Daines, M.D., presided as Chairperson.

Funding Committee Members Present:

Dr. Richard F. Daines, Chairperson

Dr. Bradford Berk*

Mr. Robin Elliott

Dr. Gerald Fischbach

Dr. David Hohn, Vice Chair

*via videoconference

Dr. Hilda Hutcherson

Dr. Mario Loomis

Dr. Allen Spiegel

Dr. Michael Stocker

Ms. Madelyn Wils

Funding Committee Members Absent:

Mr. Kenneth Adams

Dr. Bruce Holm

Department of Health Staff Present:

Dr. David Anders

Ms. Bonnie Brautigam

Ms. Janet Cohn

Mr. Thomas Conway

Ms. Judy Doesschate

Dr. Matthew Kohn

Ms. Beth Roxland

Ms. Lakia Rucker

Dr. Lawrence Sturman

Ms. Carrie Zoubul

Observers Present:

Ms. Stacey Hondropulos

Ms. Michelle Lewis

Mr. Joseph Loomis

Ms. Elizabeth Misa

Mr. Alexandre Marchac

Ms. Caroline Marshall

Mr. David McKeon

Motion to Convene in Executive Session

Dr. Daines advised that the meeting would begin with an executive session to discuss the evaluations of applications for funding pursuant to the “Empire State Institutional Training Program in Stem Cell Research - Predoctoral and Postdoctoral Fellows” Request for Applications (RFA). Dr. Hohn made a motion to move to executive session, which Dr. Stocker seconded. The motion passed and members of the public and non-essential staff left the room.

Executive Session

At Dr. Daines’s request, Dr. Sturman and Ms. Brautigam reviewed the evaluation criteria for the applications and provided members with information about the peer review process. Dr. Sturman reminded members that a total of \$7.5 million had been allocated to fund the best scoring

applications. Members with potential conflicts of interest left the room and the individual applications were discussed.

Motion to Adjourn Executive Session

Dr. Daines then asked for a motion to adjourn the executive session and reconvene in public. Dr. Fischbach so moved and Dr. Stocker seconded the motion. The motion passed.

Public Session - Opening Remarks and Introductions

Dr. Daines called the public portion of the meeting to order and welcomed board members, staff and the public. He then asked members and staff to introduce themselves.

Recommendations for Approval of Empire State Institutional Training Program in Stem Cell Research - Predoctoral and Postdoctoral Fellows

Dr. Daines advised the Committee that it would be voting on awards to applicants who responded to the RFA for funding pursuant to the institutional training programs for stem cell research predoctoral and postdoctoral fellow awards. He noted that the applications had been reviewed and summarized by a panel of independent experts from outside New York State and that the summaries had been discussed in executive session.

Ms. Brautigam provided a brief overview of the evaluation criteria and process. Dr. Daines advised that they would first act on the recommendations for which no member had declared a conflict of interest. Dr. Sturman then provided the Committee with the following information and recommended funding in the following amounts:

App #	Sponsoring Institution	PI	Proposal Title	Recommended Funding
N10I-015	New York University	Ruth Lehmann, Ph.D.	Training Program in Stem Cell Biology	\$1,884,320
N10I-011	Joan and Sanford I. Weill Medical School of Cornell University	Shahin Rafii, M.D.	Weill Cornell Training Program in Stem Cell Biology and Regenerative Medicine	\$1,869,721
N10I-013	Memorial Sloan-Kettering Institute for Cancer Center	Lorenz Studer, M.D.	Research Training in Stem Cell Biology	\$1,863,000

Dr. Hohn moved to recommend approval of the award in the amount recommended by staff and Dr. Stocker seconded the motion. The motion passed unanimously.

Dr. Berk then left the room, having recused himself, and the Committee considered the following application:

App #	Sponsoring Institution	PI	Proposal Title	Recommended Funding
N10I-007	University of Rochester	Mark Noble, Ph.D.	Stem Cell Training Programs at the University of Rochester	\$1,781,977

Mr. Elliott then moved to recommend approval of the award in the amount recommended by staff. Dr. Stocker seconded the motion. The motion passed unanimously and Dr. Berk returned.

Approval of Minutes for the May 21, 2010, Funding Committee Meeting

Dr. Daines then directed members to the draft minutes of the May 21, 2010, meeting of the Funding Committee and asked for a motion to approve the minutes. Dr. Spiegel so moved and Dr. Hohn seconded. The motion passed.

Program Updates

Dr. Daines then asked Dr. Sturman to provide program updates. Dr. Sturman directed members to a chart that showed the current status of awards and existing contracts. He noted the following information:

1. Eight Shared Equipment and Facilities Awards totaling \$32.4 were currently in place and scheduled to run through December 31, 2012. Ten million of the \$32.4 million awarded had been reimbursed.
2. With respect to Targeted induced Pluripotent Stem (iPS) Cells, Innovative Investigator Initiated Research, and Innovative Development or Exploratory Activities Awards (IDEA), totaling \$69.7 million, 94 of the 98 contractors had submitted vouchers totaling \$19 million. Seventy-eight progress reports had been submitted in the current quarter.
3. Contracts for Summer Undergraduate Internships Awards, for just under \$1 million, and Undergraduate Curriculum Development Awards, for just over \$1 million, had been executed with start dates of May 1, 2010 and July 1, 2010, respectively. Three Targeted human Embryonic Stem Cell (hESC) research awards totaling \$2.9 million were in the final stage of the contracting process, with start dates of September 1, 2010.
4. Innovative Investigator Initiated Research and IDEA Awards totaled \$35 million. Fifty-two applications had been recommended for funding in March. Award announcements had been issued in August and the contracting process had been initiated, also with anticipated start dates of September 1, 2010.
5. Fellow-to-Faculty Awards: Three applications were recommended for awards totaling \$3.2 million. Award announcements had not been yet been made.

Status of Other RFAs/Request for Proposals (RFPs)

6. Shared Facilities RFAs totaled \$30 million. Seven applications had been recommended for funding in May. Award announcements had been made and the contracting process had been initiated, with start dates of November 1, 2010.
7. The Institutional Training RFA titled “Empire State Institutional Training Programs in Stem Cell Research for Pre and Post–doctoral Fellows” had been issued on May 13, 2010. Fifteen applications had been received and four had been recommended for funding today.
8. The Short Term Faculty Training Opportunities and Research Training for Medical, Dental and Veterinary Students RFAs awaited DOH approval. Together, these RFAs represent an additional \$2.5 million, earmarked for training.
9. The third round of Innovative Investigator Initiated Research and IDEA applications had been approved by this Committee for \$25 million, to be issued in the coming months.
10. The Consortia to Accelerate Therapeutic Applications of Stem Cells RFA was approved by the Funding Committee for \$80 million. The goal was to release the RFA with sufficient lead time for this Committee to make recommendations for awards at its May 2011 meeting. A related RFP for Scientific Oversight of the Consortia was to follow.

Dr. Sturman advised members that the Annual NYSTEM 2010 Awardees Science Meeting had been held on May 26 and 27, 2010, at the City University of New York (CUNY) Graduate Center and that several board members had attended some sessions. He reported that over 150 scientists had shared the results of their NYSTEM-funded research in plenary and poster sessions and that topics ranged from fundamental stem cell biology to the role of stem cells in the understanding and treating neurological, cardiovascular, hematological and hepatic diseases, and cancer.

Dr. Sturman informed members that a new database would be launched on the NYSTEM website later this month to facilitate information sharing among Shared Facilities awardees. The information would be organized into three categories: Pluripotent Stem Cell Facilities, Specialized Stem Cell Facilities, and Shared Equipment and Imaging Facilities. Dr. Sturman said it was hoped that this resource would increase the sharing of NYSTEM-funded equipment and facilities and lead to new collaborative research opportunities in New York's stem cell science community. He reported that next year's Annual Meeting was scheduled to take place May 24 and 25, 2011, at the CUNY Graduate Center.

Dr. Sturman advised members that the NYSTEM Science team had attended the 9th Annual International Society for Stem Cell Research meeting, where they had heard a discussion on the potential of trans-differentiation, a subject in which the Board had earlier expressed interest. Dr. Anders would be addressing them later in the afternoon on this topic. Dr. Sturman told members that the Education Workgroup had identified the need for increased public education efforts in order to enhance understanding among diverse communities of the ethical, legal and social issues raised by stem cell research. He noted that the Education Workgroup, chaired by Robin Elliott and comprised of board members Brooke Ellison, Samuel Gorovitz and Samuel Packer, and community members Mary Dickerman and Olivia Flatto, have been engaged in ongoing discussions. He then turned the floor over to Robin Elliott.

Mr. Elliott reported that the workgroup had met twice since the last meeting of the Funding Committee via teleconference. He stated that the workgroup was researching both

traditional and non-traditional means of communication and hoped to propose one or more RFAs of a modest scale, totaling approximately \$1.9 million over the next few years. He also suggested enhanced use of NYSTEM's own resources to further disseminate information, such as its web site.

Mr. Elliott advised members that Ms. Dickerman had visited the stem cell program in Maryland to learn more about its education efforts; that Dr. Gorovitz would visit California in October to meet with the California Institution for Regenerative Medicine (CIRM) program and that he himself would soon be going to Newcastle, England, where Susan Solomon of the New York Stem Cell Foundation had been exploring a promising education venture. Mr. Elliott concluded by stating that the next workgroup meeting was scheduled in conjunction with the next Ethics Committee meeting on November 12, 2010.

Federal Stem Cell Policy Developments

Dr. Daines turned the floor over to Ms. Roxland to discuss recent developments in federal stem cell policy.

Ms. Roxland began with a short history of the *Sherley v. Sebelius* case. The original complaint, filed in August 2009, included a number of named plaintiffs, including Nightlight Christian Adoptions, Embryos, and Adult Stem Cell Researchers.

The complaint, filed in the Federal District Court of the District of Columbia, challenged the new National Institutes of Health (NIH) guidelines for stem cell research on two grounds. The plaintiffs alleged that the guidelines: (1) violated the Dickey-Wicker Amendment, which prohibits federal funding of research involving the creation or destruction of an embryo or fetus; and (2) were issued in violation of the Administrative Procedures Act because they did not incorporate public comment, particularly negative comment.

Initially, the District Court dismissed the case, finding that the plaintiffs lacked standing to sue. On appeal, the Court of Appeals for the District of Columbia reversed the ruling as to the adult stem cell researchers only, allowing their case to proceed. The court based its ruling on the plaintiffs' claim that the new guidelines subjected them to increased competition for funding. The case went back to the District Court, and on August 23, 2010, it issued a preliminary injunction suspending NIH funding of stem cell research.

Because the court's reasoning could be construed to apply to all research involving human embryonic stem cells, including research involving the Bush Administration lines, the NIH issued a directive to halt all such research to its funded researchers. Thereafter, on September 9, 2010, the Court of Appeals granted an administrative stay of the injunction pending its review of the motion for an emergency stay. Meanwhile, the merits of the case remained before the District Court.

Discussion and Possible Action on Request for Applications for Journalism Programs

Dr. Daines turned the floor over to Dr. Sturman to discuss the draft RFA for Journalism Program awards. Dr. Sturman reminded members that in September of 2009, the Ethics Committee had prioritized its targeted audiences for education initiatives, and that journalists had placed second. He stated the RFA had been developed for journalism schools with both

undergraduate and graduate programs and allowed them to propose ideas that would offer both educational and professional opportunities.

Dr. Sturman noted that the journalism schools had taken different approaches. For example, some were interested in creating a documentary or book, while others were interested in programs for journalism undergraduates or reporters. He recommended offering up to four awards, over a five year period, which would total a million dollars, or \$200,000 a year for each awards. Dr. Sturman stated that only one application would be allowed per institution and opened up the floor for discussion.

Several members expressed support of the RFA and acknowledged a tremendous need for a primer on stem cells containing basic information for journalists. Dr. Hohn stated that national newspapers, such as the Washington Post and the New York Times, have science writers whose scientific understanding was quite good; but that the smaller, regional newspapers often did not and could benefit from the projects.

Dr. Sturman commented that television reporters also need sources of information that they could turn to quickly and noted a recent article, “Knowledge Based Journalism is not an Oxymoron,” describing a program funded by the Carnegie-Knight Initiative on the Future of Journalism Education. The program participates with New York schools, and has created a resource that provides journalists, journalism students and teachers with access to authoritative materials on a wide range of policy subjects.

Ms. Wils suggested that NYSTEM offer a primer course at the annual meeting to attract journalists to begin the educational process or to show them where they can find resources. Dr. Spiegel stated that an alternative approach for the annual meeting could be a press session devoted to particularly high impact papers. Dr. Hohn inquired whether the program had funds available to send journalists or journalism students to a national stem cell meeting, with a press event following the meeting. Dr. Fischbach suggested seeking journalists with a science background.

Dr. Sturman responded by stating that he had learned from past experiences that few journalists could be expected to attend the meeting unless their registration fee was waived and that few would devote a full day. He stated that staff had proposed a variety of possible projects and that the RFA was not restricted to any one concept except that schools were required to interact with other parts of the university, in particular the science faculty.

Dr. Fischbach then moved to authorize NYSTEM staff to issue the RFA for Journalism Programs as proposed. Ms. Wils seconded the motion. The motion passed.

Presentation: Differences in Trans-differentiation Research

Dr. Daines reminded members that they had requested periodic updates on stem cell research and turned the floor over to Dr. David Anders to present information regarding recent developments in “trans-differentiation” research.

Dr. Anders advised members that trans-differentiation is an offshoot of the reprogramming field. He noted that cellular reprogramming may be defined as the resetting of a

cell's gene expression program. Dr. Anders stated that the challenge to remaking differentiated adult cells is that they are in an inherently stable state. He noted it was recognized many years ago that nonetheless, under special circumstances, terminally differentiated cells can be reprogrammed, for example through fusion with a pluripotent cell, or by nuclear transfer. The seminal contribution of Dr. Yamanaka in 2006 was to demonstrate that this process can be mimicked by expressing a small set of regulatory factors that push a terminally differentiated cell back to a pluripotent state, like that of embryonic stem cells, which can then be re-differentiated to desired cell types. These "master regulators" induce a self-reinforcing pluripotency program, and ultimately a stable, pluripotent phenotype.

Dr. Anders stated that Dr. Yamanaka's research suggested a new approach to produce individualized and disease-specific pluripotent cells that has since been verified by many laboratories, and applied in diverse ways to studies of numerous diseases (with several prominent examples by NYSTEM-funded scientists) in hopes of developing new therapies. He also noted that Dr. Yamanaka's findings suggested a further possibility, that of applying a similar approach to directly reprogram one differentiated cell type into another differentiated cell type. An example would be converting a skin cell into a heart cell (trans-differentiation). He noted this type of direct conversion has been referred to as "lineage reprogramming." Dr. Anders advised members that during development, a regulated cascade of events takes place in response to developmental cues that progressively restrict developmental potential and determine cell fate.

Dr. Anders advised members that the first example of applying the Yamanaka combinatorial approach for lineage reprogramming came from the laboratory of Dr. Doug Melton, whose group showed that co-expressing three genes, using virus vectors to infect the pancreas of immune compromised mice, was sufficient to convert fully differentiated adult mouse exocrine cells in the pancreas into beta cells which secreted insulin. Dr. Anders noted that the study didn't show islet formation, but that the efficiency of the process was sufficient to lower the fasting glucose level in mice that had been rendered diabetic.

Dr. Anders then discussed Dr. Marius Wernig's success in trans-differentiation of fibroblasts into neurons, identifying three necessary and sufficient factors from a large starting collection of candidates. He noted that the Dr. Wernig and his colleagues showed that these neurons were functional by standard criteria, able to synapse and transmit signals. Dr. Anders noted that this work was the first demonstration of direct conversion of cells from one primary germ layer into differentiated cells normally derived from another germ layer—a mesoderm to ectoderm conversion – and that this supported the potential generality of the approach.

Dr. Anders stated that the most recent published example was from the laboratory of Deepak Srivastava in California, who showed that fibroblasts can be reprogrammed directly into cardiomyocytes (heart muscle cells) using three factors. He summarized how the researchers looked in more detail than in previous lineage reprogramming studies at the epigenetic changes, and showed that those epigenetic changes were consistent with what would be expected in conversion of fibroblasts to a myoblast, which were functional in vitro. Dr. Anders stated that another significant finding was that these cells could be reprogrammed in vivo, in the context of the model animal heart.

Lastly, Dr. Anders summarized the different requirements for reprogramming to pluripotency, as initially described by Yamanaka and colleagues, and the examples of lineage reprogramming that each require a unique set of conditions. He stated that recent findings suggest lineage

programming may become a widely useful tool, and that it is an exciting development, but it remains to be determined whether these are limited cases.

Dr. Anders advised members that all the work so far described in the literature has been with animal models. As is the case with reprogramming to pluripotency, a great deal of work remains to be done to understand the molecular basis of lineage reprogramming, to improve efficiency, to ensure that the fidelity of reprogramming is adequate, and to address unresolved safety questions. He concluded by stating that this is an exciting area, which extends the range of tools that researchers are using to search for new therapies.

Adjourn

Dr. Daines then asked for a motion to adjourn the Funding Committee meeting. Dr. Hohn so moved. Dr. Spiegel seconded the motion. The motion passed and the meeting was adjourned.

*s/ Janet Cohn
Executive Secretary to the
Empire State Stem Cell Board
Approved: May 23, 2011*