

APPROVED MEETING MINUTES

**California Department of Public Health Human Stem Cell Research Advisory Committee
July 28, 2008 Teleconference, 3:00pm-4:00pm PST**

**California Department of Public Health (CDPH) Human Stem Cell Research (HSCR) Advisory
Committee Members**

David Magnus, PhD
Henry Greely, JD
Bernard Lo, MD
Bertram Lubin, MD
Samuel Cheshier, MD, PhD
Margaret McLean, PhD
Fred Gage, PhD
Elliot Dorff, PhD
Radhika Rao, JD

CDPH

Shabbir Ahmad, Manager, Human Stem Cell Research Program, CDPH
Amber Christiansen, Human Stem Cell Research Program, CDPH
Heidi Mergenthaler, Human Stem Cell Research Program, CDPH
Patricia Rodriguez, CDPH Legal Counsel

Members of the Public

Lindsey Parhan, UC San Francisco
Marcy Darnovsky, Center for Genetics and Society
Laura Cavanaugh, UC San Francisco
Geoff Lomax, California Institute for Regenerative Medicine (CIRM)
Susan Stayn, Stanford University

Agenda Item 1: Opening Remarks and Introductions

Agenda Item 2: Approval of Minutes

The minutes from the December 5, 2007 meeting were approved without objection.

Dr. Ahmad of CDPH provided an update on the activities of the CDPH Human Stem Cell Research (HSCR) Program. The HSCR Program released reporting forms (HSCR1260-1 and HSCR1260-2) for research involving human embryonic stem cells/lines and assisted oocyte production. The forms are based on the mandates from Senate Bill 1260 (Ortiz, 2006) and are due to the HSCR Program August 1. Thus far the HSCR Program has received reporting forms from five SCRO Committees.

Dr. Ahmad also mentioned that CIRM had invited the Program to provide an update on the reporting forms at CIRM's Standards Working Group meeting on July 25th, 2008. The Program gave a brief presentation about the reporting forms. During the meeting, two issues arose with regard to whether projects partially funded by CIRM needed to report to CDPH and concern was expressed with regard to the potential re-identification of oocyte donors through the various demographic variables collected in form HSCR1260-2. Dr. Ahmad indicated that CDPH's internal legal counsel would review these issues.

Dr. Ahmad also noted that the next meeting of the HSCR Advisory Committee is scheduled for October 1, 2008.

Agenda Item 3: Should CDPH revise guidelines regarding informed consent requirements for induced pluripotent stem cell research?

Professor Greely opened the discussion about whether the Committee should recommend revising the CDPH Guidelines with regard to informed consent requirements for induced pluripotent stem cells (iPSC). This is an issue raised by the ability to make iPSCs, by taking somatic cells and reprogramming them to become pluripotent, in ways that seem to closely mimic human embryonic stem cells (hESC). The issue here is whether the somatic cells that are used to generate those iPSCs and similar cell lines need to have been donated with the same kind of special hESC specific consent that the National Academy of Sciences (NAS) standards, the CIRM regulations and the CDPH Guidelines require for donation of embryos, oocytes, and sperm. At the time the NAS standards were developed, it was likely that the only perceived use of somatic cells in this context was for somatic cell nuclear transfer (SCNT), which is an ethically sensitive type of research.

Professor Greely further explained that iPSCs are used to create pluripotent stem cell lines with the ultimate goal of using these lines to study specific diseases and develop treatments that minimize a negative immune response. For the Committee's purposes, of import is that this technique does not involve embryos or SCNT.

Professor Greely noted that CIRM's changes to its regulations that address the issue of informed consent for iPSCs, California Code of Regulations Sections 100080, 100090, and 100100, were adopted on June 29th, 2008; therefore, the CDPH Guidelines and CIRM regulations are currently inconsistent with each other.

The most relevant CIRM changes are in sections 100080 and 100090. Section 100080(a)(3) allows for the use of a stem cell line derived from non-identifiable human somatic cells if the derivation did not result from SCNT or the creation/use of a human embryo and the somatic cells are not able to be re-identified through an associated code or link. Section 100090(a), now says that the requirements of 100080(a)(2) must have been met and that the requirements for anything subsequent of Section 100100(b) for informed consent must be met.

Section 100100(b) is the detailed stem cell specific consent requirements of the regulations stemming from the NAS guidelines and paralleled by the CDPH Guidelines. This includes, for example, the informed consent requirements that inform donors that their cells may be used to create cell lines that are used indefinitely, that their cells may be genetically modified, or that their cells may be put into non-human animals.

Under the amendments to sections 100080 and 100090, this type of specific informed consent is not required when deriving pluripotent cell lines from somatic cells provided the somatic cells are unidentifiable and did not result from an embryo or SCNT. CDPH's Guidelines still require that if researchers want to reprogram a somatic cell into an iPSC line, then that somatic cell would have had to have been taken from the donor with the informed consent process detailed in Section 100100. Researchers are particularly interested in using iPSC lines that are well-established and well-characterized; however, under the current CDPH Guidelines, most of these older iPSC lines do not meet the requirements for informed consent.

After providing this background, Professor Greely asked for comments about whether the Committee should recommend to the Department that it change its guidelines to parallel the CIRM regulations with respect to somatic cells that have previously been acquired, as well as with respect to somatic cells that may be acquired in the future and used for this purpose. Professor Greely noted that in the past the Committee has tried to remain as consistent as possible with the CIRM regulations.

Professor Greely's main argument for exempting somatic cells from the more extensive informed consent requirements is that research involving iPSCs does not raise the same kinds of ethical concerns for donors that research involving embryos and oocytes does. Dr. Dorff agreed that the ethical concerns are different and he recommended changing the CDPH Guidelines to be consistent with CIRM. Dr. Lubin agreed with revising the CDPH Guidelines.

Professor Greely interjected that he thought researchers in California were already performing research involving iPSCs and had concerns that this was in violation of the Guidelines.

Dr. Lo continued, indicating he agreed with the others that the Guidelines should be changed not only for consistency purposes with CIRM, but also to maintain consistency with the common rule as interpreted by federal agencies. The California researchers using iPSCs are following the federal regulations with respect to human subjects and the use of existing de-identified biological materials. Dr. Lo also pointed out that the exclusion from the detailed informed consent requirements does not apply if a researcher plans to use iPSCs to create an embryo or for use in SCNT; therefore, the extensive informed consent requirements still apply for the more ethically sensitive types of research.

Dr. Gage agreed that the CDPH Guidelines should be consistent with CIRM's changes. He felt this new science was very important and would help facilitate and support California's stem cell research goals. Dr. Magnus also agreed with changing the CDPH Guidelines and noted that, in practice, it would be difficult to enforce detailed informed consent requirements because it is so common for graduate students/researchers to use different cell lines to try to induce pluripotency.

Professor Rao agreed with changing the CDPH Guidelines. She also asked for clarification on the informed consent requirements if a researcher is collecting somatic cells with the intent of using them to develop iPSCs, as opposed to using previously donated somatic cells. Professor Greely asked Dr. Lomax to explain the distinction CIRM uses for existing versus newly collected somatic cells.

Dr. Lomax explained that if CIRM-funded research involved collecting somatic cells with the intent of deriving a covered stem cell line, then the detailed consent provisions of section 100100(b) would apply. Dr. Lomax explained that CIRM was having its grantees use the more detailed consent requirements but that it could not dictate how somatic cells are collected by other researchers that may eventually be used by CIRM grantees.

For clarification, Professor Greely gave the example of a researcher interested in studying Huntington's disease and collecting somatic cells from someone with Huntington's in order to develop iPSCs. In this case, the researcher would have to use the consent requirements in section 100100(b). But if the researcher obtained already-collected somatic cells from a Huntington's patient, then the research does not fall under section 100100(b). Dr. Gage had concerns that if you had a population of patients whose disease was well-characterized but no cell lines already existed from these patients, then the detailed consent process needed to

collect somatic cells from these patients would be much more difficult than if cell lines had by chance been previously created. Dr. Lomax explained that presumably the researcher would know the patients from whom somatic cells were needed and, therefore, it would be easy to obtain detailed consent. Professor Greely noted that consent under the common rule would be required anyway in this scenario. Dr. Gage inquired as to the need for requiring a more detailed consent form. Dr. Lomax responded that the CIRM Standards Working Group determined it was reasonable to require a certain level of consent and was trying to establish the most effective consent possible from the point of procurement. Professor Greely added that one could also argue that even though this research does not involve embryos or SCNT, iPSC lines are being created with a donor's DNA and genome, which could have unexpected long-term consequences.

Dr. Gage wondered if there was a loophole in this process such that a researcher could apply for IRB approval to biopsy patients and create cell lines from the biopsied cells. Once the cell lines were developed, the researcher could apply for a separate IRB approval to use the cell lines for a different purpose, which would not require the same level of consent since the cell lines were already established. Dr. Magnus and Dr. Lubin thought that obtaining comprehensive consent from the beginning would be the most efficient approach.

Professor Rao raised the issue again with regard to whether the consent requirements should be different for derivation involving existing somatic cells versus newly created cells. Professor Greely reiterated that CIRM's regulations require detailed consent if, at the time of procurement, the researcher plans to use the somatic cells to derive a new iPSC line. Dr. Lomax emphasized that CIRM views the consent requirements in the context of a CIRM grant proposal; therefore, CIRM's approach is to require comprehensive consent at the time of collection for CIRM funded research. Dr. Magnus agreed that requiring thorough consent from the beginning was a good approach but thought that requiring the same level of consent for existing cells was too much. Dr. Cheshier also thought that cells that had already been derived should be allowed for use. He added that it would not be logistically difficult to include more language to consent forms in order to satisfy new consent requirements. Dr. McLean agreed that the requirements should be less rigorous for existing cells versus newly collected cells when deriving new cell lines.

Professor Greely did not think it would be appropriate to attempt to draft language during a conference call. He proposed the Committee vote on whether to recommend to the Department that it amend its Guidelines to be consistent with the CIRM regulatory changes such that existing cell lines do not need the same detailed informed consent as research involving newly collected cells. The Committee agreed to this recommendation. Professor Greely said he or others would work on the draft language.

Professor Greely introduced a topic for the Committee's upcoming October 1 meeting. He mentioned that Rob Streiffer from the University of Wisconsin published an article in Science about the consent forms used for the NIH approved hESC lines. The article indicates the BresaGen consent form did not include research and the Cellartis consent form only included language about studying how long cells could be kept alive in culture before being discarded. There is concern with both of these in that they never obtained consent for making embryonic stem cell lines. Professor Greely mentioned the Committee would likely see this issue come up even before the October 1 meeting.

Meeting adjourned.