



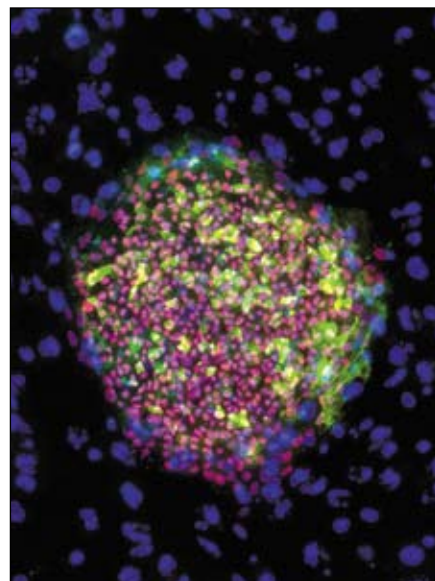
Bruce Conklin explaining the consent form to a potential donor.



Predicting the Future

Obtaining Consent
for Future Stem Cell Research

The discovery of iPS cells provides an unprecedented means to study and possibly cure diseases.



The discovery of human induced pluripotent stem (iPS) cells has radically changed stem cell biology. It opened a whole new and extremely effective strategy for studying stem cells. It made the technology of stem cells readily available to many new researchers. And it transformed the ethical debate about using embryonic stem cells. While many scientists believe that there are no ethical questions concerning iPS cells, other scientists are less certain.

As often happens in science, one advance reveals new challenges, and iPS cells are no exception. iPS cells and donor cells are genetically identical. iPS cells can be grown indefinitely, and they might be used for purposes that are as yet “predictions about the future.”

Gladstone senior investigator Bruce Conklin and two colleagues, Bernie Lo of UCSF and Katerina Aalto-Setälä of the Regene Institute for Regenerative Medicine in Finland, raised this issue in a recent paper in *PLoS Biology*.

“iPS cells are a fundamental breakthrough in the study of developmental biology and regenerative medicine,” said Dr. Conklin. “This extraordinary tool will take us places we cannot yet know. For that reason, we need to very carefully design an appropriate consent process for donating somatic cells for iPS cell derivation.”

The requirement for informed and voluntary consent is well established in international agreements—examples include the Helsinki Declaration and the Council for International Organizations of Medical Sciences “International Ethical Guidelines for Biomedical Research Involving Human Subjects”—and in U.S. law. The International Society for Stem

Cell Research, the National Academy of Sciences, and the California Institute for Regenerative Medicine have proposed guidelines for stem cell research.

One of the keys of the U.S. regulations is that donated material be “de-identified” to reduce any possible violation of patient confidentiality. Various surveys have shown that a majority of people are willing to donate tissue under these circumstances.

It’s tough to make predictions, especially about the future.

—Yogi Berra

“The traditional consent process has worked well for most situations in the past,” said Dr. Conklin. “However, informed consent for certain aspects of iPS cell research are more complicated.”

He notes several examples. Large-scale genome sequencing might increase the risk of discovery of donor identity. Future researchers might also know the donor’s susceptibility to genetic diseases. Some donors may have objections to mixing of human and animal species.

“Two areas of iPS cell research might be particularly troublesome—transplantation and reproductive research,” said Dr. Conklin. Donors may not have fully realized that their donated cells might be used for transplantation. Also since iPS cells might be around for years before transplantation, a recipient may have health concerns about transplanted cells. Were they from a person who has since developed cancer or another serious disease? Perhaps the most serious concern is reproductive biology. In the future, human

iPS cells might be differentiated into primordial germ cells and mature gametes that could be used in fertility treatments.

Dr. Conklin and his colleagues suggested some guidelines for obtaining informed consent. They recommend a tiered process. The first level would involve permission to obtain somatic cells for derivation and for a specified list of basic research procedures. The second level would be for transplantation studies. They further believe that consent for reproductive research should be obtained later—and only if it is really needed. Finally, they recommend that permission be obtained to contact donors in the future. This option would allow researchers to talk to donors about research that was unknown at the time of the original donation. However, it must be noted that de-identification is not appropriate as a means of avoiding prior consent.

“iPS cells have given us an unprecedented opportunity to understand development and to cure an array of serious diseases,” said Dr. Conklin. “And while they solve many ethical questions, they raise others. We hope the biomedical community will examine these new ethical considerations now to facilitate future research. Figuring out how to obtain informed consent is a prerequisite for that work.”

Aalto-Setälä K, Conklin BR, Lo B (2009) Obtaining consent for future research with induced pluripotent cells: Opportunities and challenges. *PLoS Biol.* 7:e42.