

**ESSCB Statement Regarding
the Conduct of hESC Research Involving Chimeras**

Approved November 14, 2011

Introduction

After extensive deliberation, the Empire State Stem Cell Board voted to require that NYSTEM grantees adhere to the guidelines of the National Academy of Sciences (NAS) or the International Society for Stem Cell Research (ISSCR) when conducting chimera research involving human embryonic stem (hES) cells.¹ The statement below memorializes the Board's discussions and identifies key ethical issues related to the conduct of this research.²

Background

Inter-species chimeras ("chimeras") are created by transplanting cells or tissues from an organism of one species (the "donor") into an organism of another species (the "host"). The resulting chimeric animal is mosaic, with some cells or tissues containing DNA only from the host and others containing DNA only from the donor, but no cells or tissues with combined DNA from both the host and the donor.³

Creation of chimeras has become commonplace in medicine, such as when a surgeon transplants a heart valve from a pig into a human patient to replace a faulty valve. Use of chimeras has also been recognized as an important tool in medical research for understanding cellular, tissue, and organ function, and often is considered essential in the pre-clinical stage of research for therapeutic assessment. For instance, scientists for the last few decades have created tumors in immune-deficient mice in order to study the disease progression of cancer and to discover possible therapies.

Experiments involving chimeras are employed in the field of stem cell research, notably when hES cells are transplanted into non-human animals. This type of experiment can raise significant ethical concerns, particularly if hES cells are inserted into animal species that have a high degree of genetic similarity to humans. Although it is not practicable at this time to predict with certainty the extent of the contribution of hES cells to such chimeras, the possibility that these

¹ Empire State Stem Cell Board, *Appendix A-2, Contract Policy Statements and Conditions*, § E.2 (Mar. 2010), available at http://stemcell.ny.gov/docs/NYSTEM_Appendix_A-2_03-10.pdf. On September 27, 2010, the Ethics Committee voted 7-1, with Father Thomas Berg abstaining from the vote, to approve the chimera research standards.

² On September 13, 2011, the Ethics Committee voted 7-1, with Jann Armantrout opposing, to approve this statement regarding chimera research. On November 14, 2011, the Funding Committee voted 9-1 to approve this statement, with Dr. Mario Loomis abstaining.

³ Chimeras are distinct from "hybrids" and "cybrids," neither of which this statement is intended to address. Hybrid animals are formed by interbreeding species or fusing genetic material of two distinct species. Every cell in a hybrid animal contains recombined genetic material. By comparison, cybrids – or cytoplasmic hybrids – generally are created by removing the nuclear material from the host egg from one species of animal (leaving only the cytoplasm of the host egg) and inserting a nucleus from a donor egg. The cells of the resulting cybrid are comprised overwhelmingly the DNA of the donor, with a minute portion of host's mitochondrial DNA.

animals may develop human characteristics or experience changes in sentience and cognition give rise to ethical issues. In addition, chimera research raises concerns that focus on animal welfare, including that animals used in experiments are treated as humanely as possible.

Recognizing the scientific importance and genuine ethical concerns surrounding chimera research involving hES cells, the Ethics Committee spent more than a year examining and discussing the appropriate standards for guiding scientists conducting such research with NYSTEM funds. The Ethics Committee began by reviewing ethical and scientific literature on chimeras, studying how various institutional bodies oversee chimera research, and hearing scientific presentations by experts.

The Ethics Committee also identified a number of elements of chimera research involving hES cells that give rise to ethical concerns. These elements include:

- The developmental stage of the host animal – hES cells that are introduced in an early stage of animal development may have greater potential to fully integrate into the host animal as it grows;
- The type of tissue that may be affected by the hES cells – Experiments that generate chimerism of the brain are of greater concern than protocols affecting other cells because of possible effects on the host animal’s cognitive abilities;
- The species of the host animal – Species that are more genetically similar to humans are more likely to be able to integrate and utilize human cells; and
- Ability of the chimeric animal to breed – Breeding of animals with chimerism of the germ line increases the possibility that human traits will be passed to offspring in potentially undesired or ethically-concerning ways.

ESSCB Recommendations

A system of rigorous oversight combined with guidelines to aid in the review of chimera protocols, was reasonable and necessary. In addition to currently-mandated oversight mechanisms, including Institutional Animal Care and Use Committees (IACUC)⁴ and Institutional Review Boards (IRB),⁵ Embryonic Stem Cell Research Oversight (ESCRO) committees should also oversee the ethical aspects of chimera protocols involving hES cells to ensure compliance with ethical principles.

The level and rigor of the ESCRO review should correspond to the sensitivity of the experiment in question. Depending on the scientific and ethical aspects of the research, the protocol may warrant additional scrutiny and evaluation by the ESCRO committee and require a greater level of scientific justification to persuade the committee that the goals of the experiment cannot be

⁴ 9 C.F.R. 2.31. IACUCs require, amongst other things, that a protocol proposing research involving animals has substantial scientific merit, uses the fewest number of animals possible, and contains procedures to avoid undue pain. *See also* N.Y. Pub. Health Law Art. 5, § 504.

⁵ 45 C.F.R. 46. *See also* N.Y. Pub. Health Law Art. 24-A.

accomplished using alternative methods. Such a vigilant and in-depth evaluation demands the full attention and participation of the scientist and the ESCRO during the review process and ensures that only hES cell and chimera research that is ethically and scientifically sound would be approved.

In a small but important number of situations, chimeric research should be prohibited at this time because of the broad consensus that such research is unethical. For example, research involving implantation of a hES cell - non-human animal chimera into a human uterus for gestation, or inter-breeding of two animals with chimerism of the germ line, should not be permitted to proceed.

Rather than setting new and unique standards, NYSTEM grantees should follow the chimera standards provided in either the NAS or ISSCR Guidelines. Both sets of guidelines are commonly utilized by researchers conducting hES cell and chimera research, and have established high standards for review and evaluation of protocols. The guidelines also significantly overlap in the types of experiments explicitly prohibited as well as the oversight mechanisms.

In anticipation of future advances in science and technology, the Board intends to periodically revisit the standards and guidelines governing chimera research to account for new developments.