DRAFT CIRM Guidance for Oversight of Integrated Human Embryo Models

Advances in stem cell science have resulted in the development of "integrated embryo models" for the study of human development and disease etiology. Embryo models are organized three-dimensional structures derived from pluripotent stem cells that mimic the developmental processes that occur in early human embryos.[1]

Because human pluripotent cells serve as the building blocks for these models, CIRM-funded protocols are governed by our Medical and Ethical Standards Regulations which require scientific and ethical oversight by Stem Cell Research Oversight (SCRO) Committees. CIRM's regulations require different levels of oversight depending on nature and purpose of the experiment. Generally, protocols involving the use of pluripotent stem cells require the "notification" of the SCRO committee. Protocols involving the use of human embryos required heightened oversight including SCRO review, approval, and annual renewal consistent with established research guidelines.[2]

SCRO committees have requested clarification of how protocols involving the development of embryo models should be overseen in the context of CIRM's regulations. CIRM considers these models to be in vitro research involving pluripotent stem cells requiring SCRO notification. However, the emergence of "integrated embryo models" has resulted in constructs that demonstrate advanced developmental potential.[3] Given this developmental potential, the International Society for Stem Cell Research and scholars have suggested a deliberative oversight framework consistent with SCRO review, approval and annual renewal of protocols involving integrated embryo models.[4,5] This framework includes the recommendation that there be a compelling scientific justification for the use of integrated embryo models that cannot be otherwise addressed by alternative approaches.

CIRM's existing Medical and Ethical Standards include a requirement to provide an "acceptable scientific rationale" as part of the review, approval and renewal of research protocols. Therefore, CIRM recommends that (1) protocols involving integrated embryo models be subject to full heightened SCRO review and oversight, and (2) the reason of the use of the integrated model shall be included in the scientific rationale.

In addition to these SCRO oversight requirements, specificized activities are not eligible for CIRM funding (e.g. prohibited activities). These activities include:

- The introduction of any stem cells, whether human or nonhuman, into human embryos.

---

[1] https://www.isscr.org/isscr-news/isscr-statement-on-new-research-with-embryo-models
[2] https://www.nationalacademies.org/our-work/guidelines-for-human-embryonic-stem-cell-research
[3] https://www.cell.com/cell/fulltext/S0092-8674(23)00807-3
[4] https://www.isscr.org/guidelines/blog-post-title-one-ed2td-6fcdk
[5] https://www.nature.com/articles/d41586-023-03062-x

- The transfer to a uterus of a genetically modified human embryo.

While CIRM does not consider integrated embryo models to be equivalent to human blastocysts or embryos resulting from the in-vitro fertilization of human gametes, the above restrictions should be applied to integrated embryo models.