

ISSCRガイドラインと当面のヒト生殖細胞作製の課題

ISSCR Guidelines for Stem Cell Research and Clinical Translation: The 2021 update

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Box 2. Categories of research

A brief summary of the categories of research from the 2021 ISSCR Guidelines for Stem Cell Research and Clinical Translation. For more detailed guidance, please see <https://www.isscr.org/guidelines>.

Category 1A—Exempt from review by a specialized oversight process

- Most *in vitro* pluripotent stem cell research
- Most *in vitro* organoid research
- Transfer of human stem cells into postnatal animal hosts

Category 1B—Reportable but not typically reviewed by a specialized oversight process

- Non-integrated stem cell-based embryo models
- *In vitro* culture of chimeric embryos (human cells into non-human embryos)
- *In vitro* gametogenesis without fertilization or generation of embryos

Category 2—Reviewed by a specialized oversight process

- Procurement of embryos, or gametes for the creation of embryos, for *in vitro* research
- Derivation of cell lines from human embryos
- Genetic alteration of embryos or gametes
- *In vitro* culture of human embryos for research until the formation of the primitive streak or 14 days from fertilization, whichever comes first
- Human cells transplanted into nonhuman embryos that are gestated in a non-human uterus
- Integrated stem cell-based embryo models
- Transferring human embryos following MRTs into a human uterus

Category 3A—Not allowed: Currently unsafe

- Heritable genome editing for reproductive purposes
- Transferring mtDNA-modified (not including MRTs) embryos into a uterus
- Using gametes differentiated from human stem cells for reproduction

Category 3B—Not allowed: Lacks compelling scientific rationale and/or is ethically concerning

- Gestating human stem cell-based embryo models
- Human reproductive cloning
- Breeding human-animal chimeras where there may be human germ cells.
- Transferring human-animal chimeric embryo(s) to a human or non-human primate uterus
- Transferring human embryo(s), irrespective of origins, to an animal uterus

In vitro-derived gametes

If, however, the research entails testing gametes derived after any period of *in vitro* culture by fertilization and/or the creation of embryos, this must be subject to review, approval, and ongoing monitoring, as appropriate, through a specialized oversight process capable of evaluating the unique aspects of the science and the associated ethical issues. This latter research is therefore firmly in Category 2.

- 生殖細胞の分化メカニズムの理解
→ *in vitro* gametogenesisは発生中のヒト生殖細胞を知る唯一の方法
→ ゲノム編集との組み合わせにより不妊の遺伝的要因が解明に期待
(今後)
→ 配偶子を作る分化培養系の開発が必要
→ 配偶子の機能評価には受精の可否が必要
- 体外培養による配偶子の供給源
→ 実験動物の結果からサルなどを用いた基礎研究が必要

結論

- 生殖細胞系列の発生過程は*in vitro* gametogenesisで再現できる: マウスではほぼすべての過程、ヒトでは始原生殖細胞、その他大動物は始原生殖細胞
- 始原生殖細胞の発生において、種特異的なメカニズムは存在する。
 - *in vitro* gametogenesisがそのメカニズムを探る唯一の方法
 - ゲノム編集技術と組み合わせることによりメカニズムの理解が加速
- *in vitro* gametogenesisで得られる配偶子には質的なばらつきがあり、生殖目的の利用には慎重な検討を要する。