ヒト胎児を利用した研究報告

Lineage tracing of human development through somatic mutations

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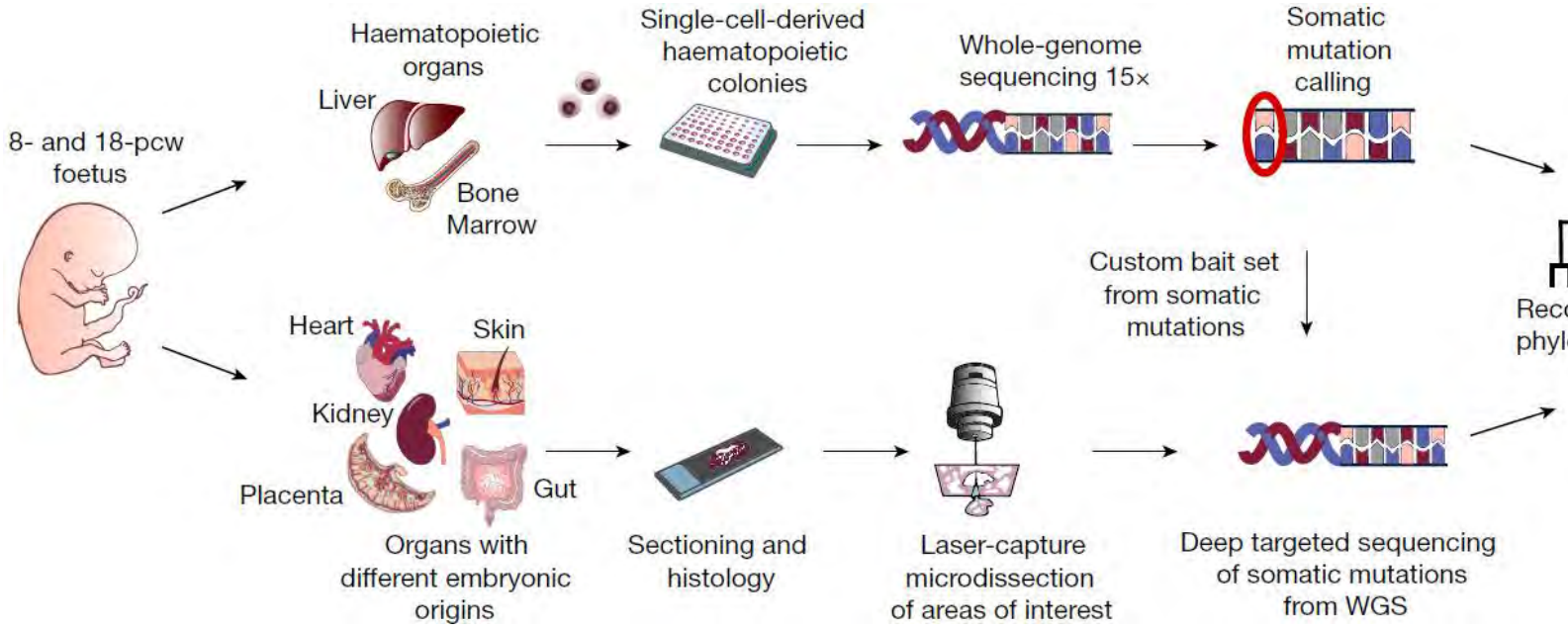
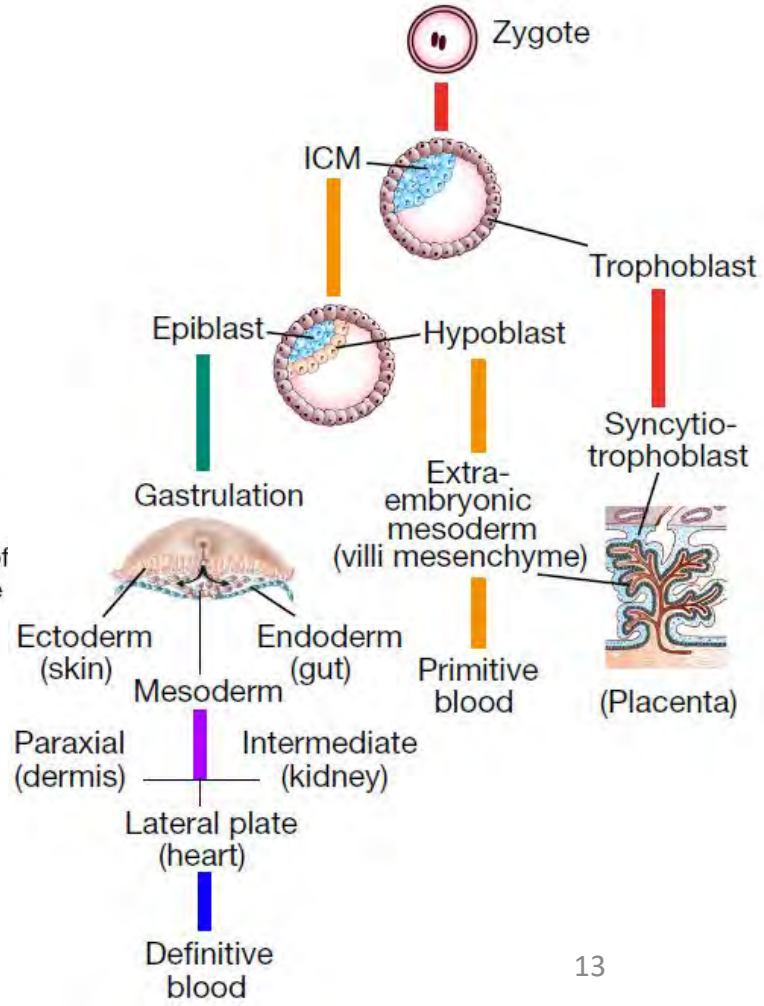
Michael Spencer Chapman[1,2,3,8], Anna Maria Ranzoni[1,4,5,8], Brynelle Myers[1,4,5], Nicholas Williams[1], Tim H. H. Coorens[1], Emily Mitchell[1,3,4], Timothy Butler[1], Kevin J. Dawson[1], Yvette Hooks[1], Luiza Moore[1,6], Jyoti Nangalia[1,4,5], Philip S. Robinson[1,7], Kenichi Yoshida[1], Elizabeth Hook[6], Peter J. Campbell[1,4,9]✉ & Ana Cvejic[1,4,5,9]✉





ヒト胎児を利用した研究報告

Single-cell transcriptomic characterization of a gastrulating human embryo

Richard C. V. Tyser[1,6], Elmir Mahammadov[2,3,4,6], Shota Nakanoh[5], Ludovic Vallier[5], Antonio Scialdone[2,3,4,7]✉ & Shankar Srinivas[1,7]✉

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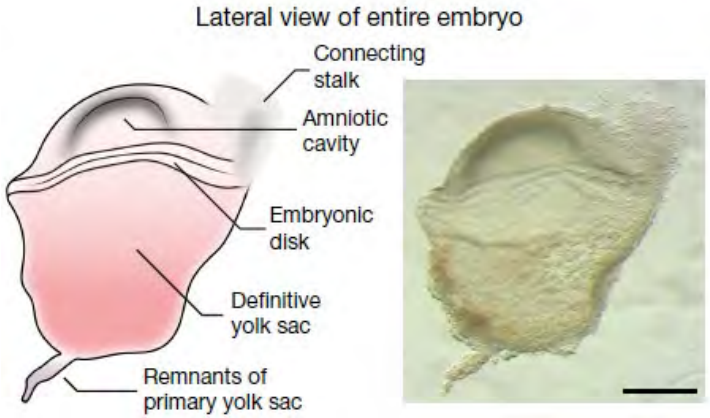
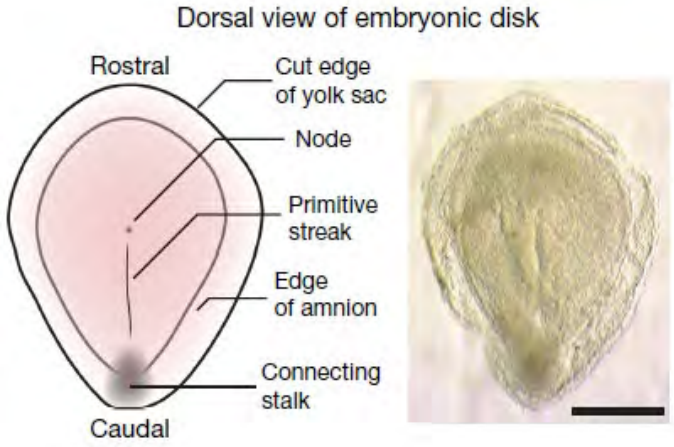
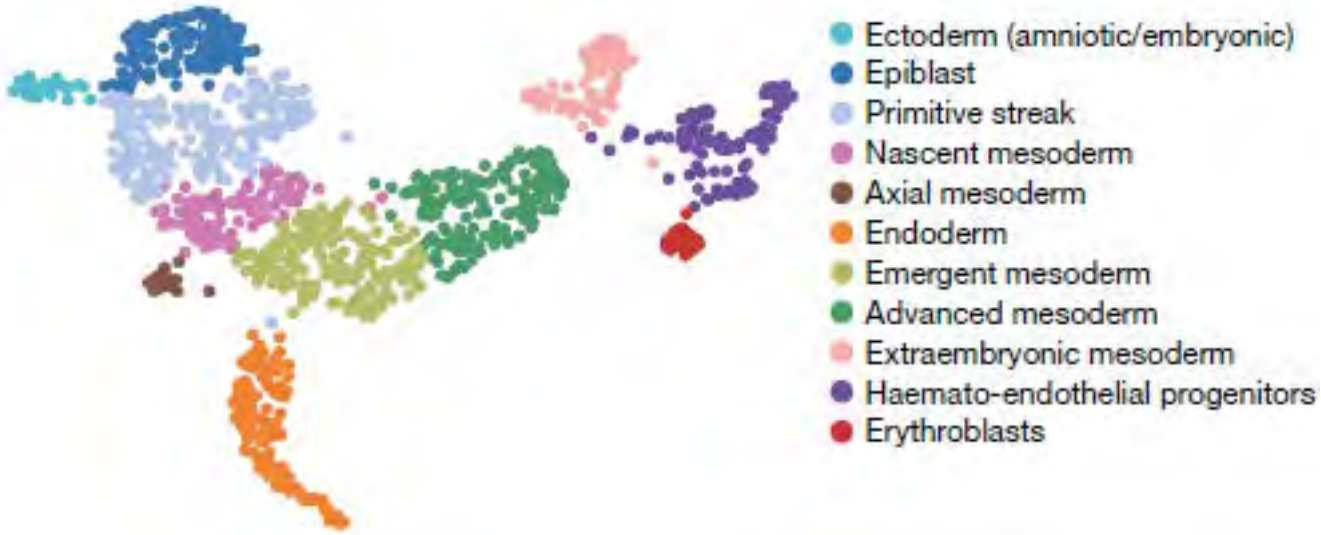




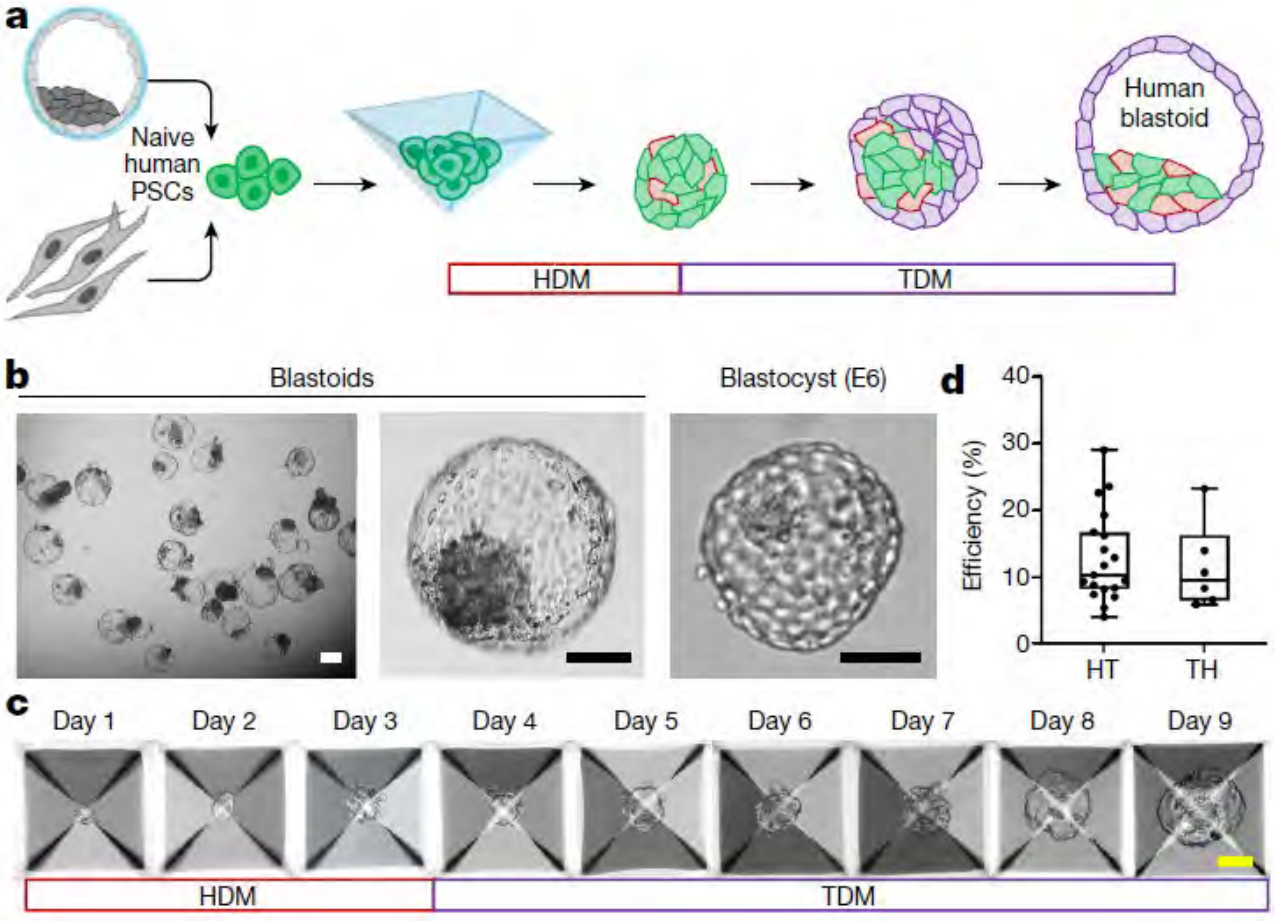


胎児を利用せずにヒト発生モデルを構築

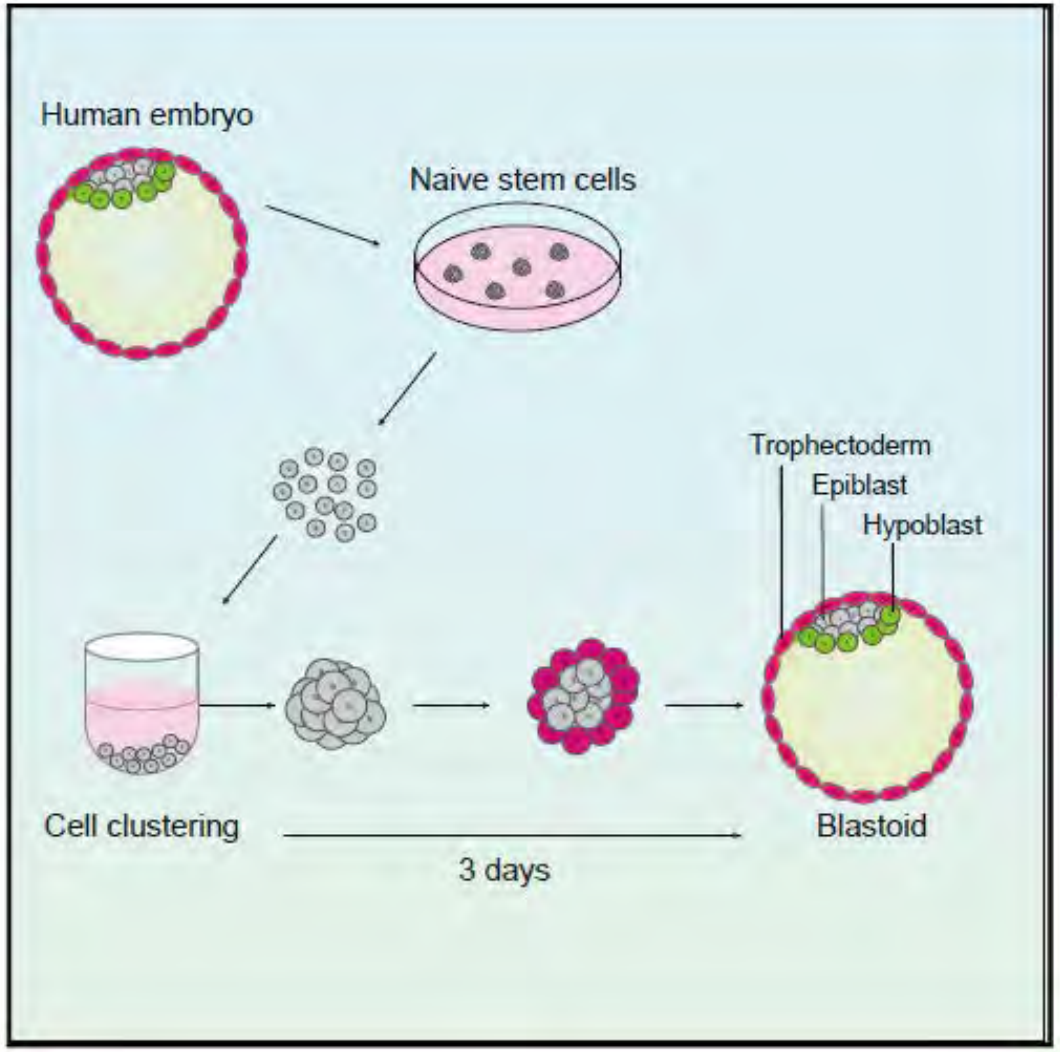
- 世界的な流れとして、ヒト検体（胎児）を使った研究は急増している
- 日本では、かなり困難な状況
- ヒト検体はコントロール・レファレンス
- 実際の研究としては倫理面・マテリアル量的にも困難

多能性幹細胞を利用できないか

幹細胞を利用した胚モデル:ヒトブラストイド



Yu et al., Nature, 2021



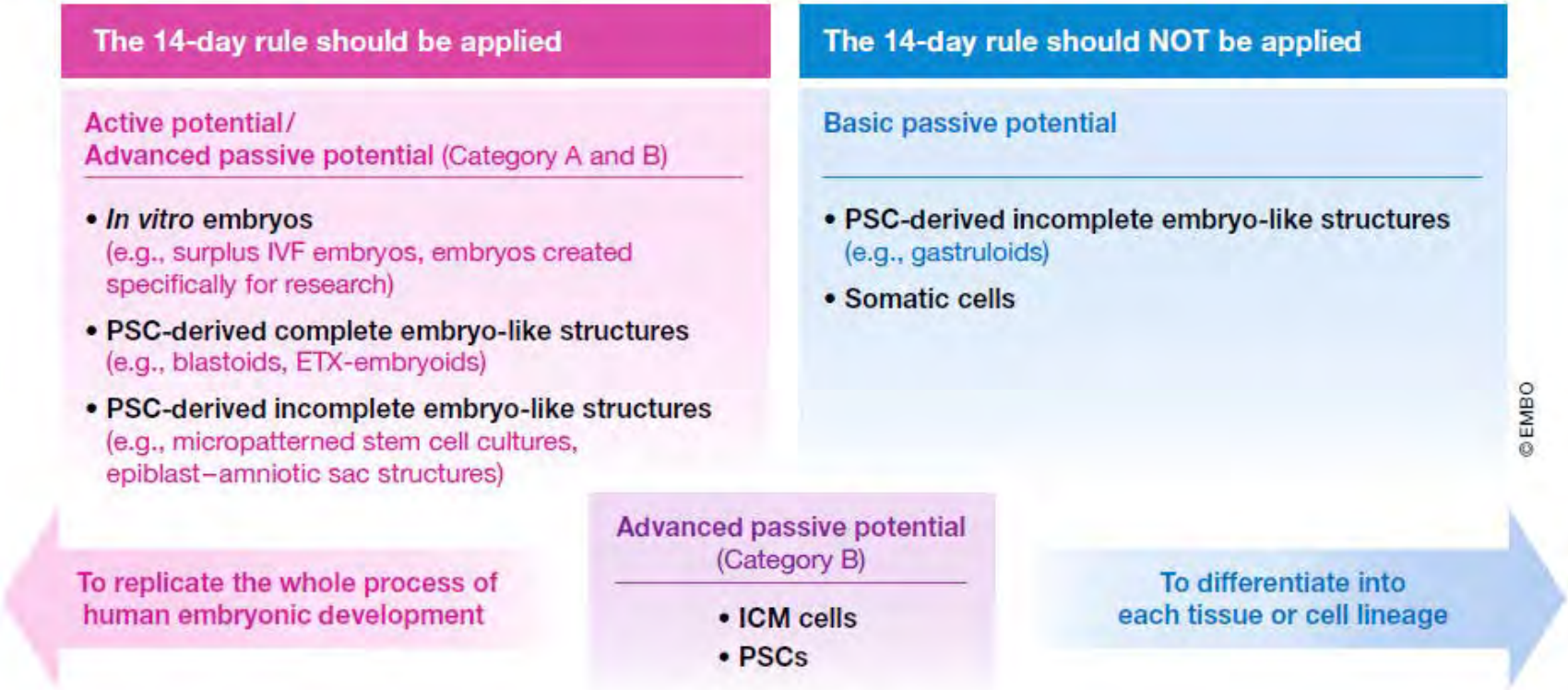
Yanagida et a., Cell Stem Cell 2021

幹細胞を利用した胚モデル:ヒト胚オルガノイド

The moral status of human embryo-like structures: potentiality matters?

The moral status of human synthetic embryos

Tsutomu Sawai[1,2,*], Tomohiro Minakawa[3], Jonathan Pugh[4], Kyoko Akatsuka[2], Jun K Yamashita[3] & Misao Fujita[1,2]



EMBO reports 2021

国際幹細胞学会の幹細胞を用いたガイドライン

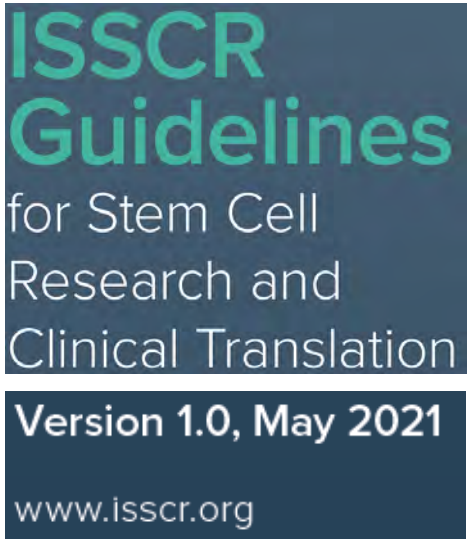
CATEGORY 1	CATEGORY 2	CATEGORY 3
1A **Exempt from review by a specialized oversight process** • Most *in vitro* pluripotent stem cell research • Most *in vitro* organoid research • Transfer of human stem cells into postnatal animal hosts	**2** **Reviewed by a specialized oversight process** • Procurement 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 occurs 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 MRT into a human uterus	**3A** **Not allowed; currently unsafe** • Heritable genome editing • Transferring mtDNA-modified (not including MRT) embryos into a uterus • Using gametes differentiated from human stem cells for reproduction
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		**3B** **Not allowed: lacks compelling scientific rationale 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 ape uterus • Transferring human embryo(s), irrespective of origins, to an animal uterus

カテゴリー1B
一般的な研究申請を要する

幹細胞を用いた不完全なヒト胚モデルを作製(ヒト胚を構成するすべての細胞を含まない)

カテゴリー2
専門的な倫理申請を要する

幹細胞を用いて完全なヒト胚モデルを作製する(ヒト胚を構成するすべての細胞を含む)



国際幹細胞学会の幹細胞を用いたガイドライン：14日ルール

CULTURE OF HUMAN EMBRYOS BEYOND FORMATION OF THE PRIMITIVE STREAK OR 14 DAYS

It is currently not technically feasible to culture human embryos beyond formation of a primitive streak or 14 days post-fertilization. However, culture systems are evolving, making this a possibility in the near future. Understanding the primitive streak, early germ layer development and primordial germ cell formation in humans is crucial to improve our understanding of and interventions for infertility, *in vitro* fertilization, pregnancy loss, and developmental disorders that occur or originate soon after implantation. Research using embryos is also crucial to validate integrated stem cell-based embryo models, which in the future may provide a more practical alternative to understanding some aspects of early human development.

Recommendation 2.2.2.1: Given advancements in human embryo culture, and the potential for such research to yield beneficial knowledge that promotes human health and well-being, the ISSCR calls for national academies of science, academic societies, funders, and regulators to lead public conversations touching on the scientific significance as well as the societal and ethical issues raised by allowing such research. Should broad public support be achieved within a jurisdiction, and if local policies and regulations permit, a specialized scientific and ethical oversight process could weigh whether the scientific objectives necessitate and justify the time in culture beyond 14 days, ensuring that only a minimal number of embryos are used to achieve the research objectives.

幹細胞を利用した胚オルガノイド研究の今後：私見

- 新たな生命倫理問題が出現した
  - ヒト胚オルガノイドはヒト個体を細胞から作り出すリスク
    - 実際には、現時点ではかなり遠い

- 胚オルガノイド研究を日本において推進する必要があるか？
  - 胚オルガノイド研究のヒト健康に対するメリットがあるのか？→イエス
    - ✓ ヒト胚オルガノイドは最も生理的な分化誘導方法
    - ✓ ヒト胚を使用する必要がなくなる

- 胚オルガノイド研究の今後と考えるべき問題点
  - メリットから「世界」では研究が一気に進むだろう
    - ✓ 日本においても社会に説明し、対話する必要がある
    - ✓ ヒト胚・胎児利用に比べ日本社会では許容できるのでは（iPS細胞研究に対する理解）
  - 個体として成し得ない限りは、許容されるのではないか