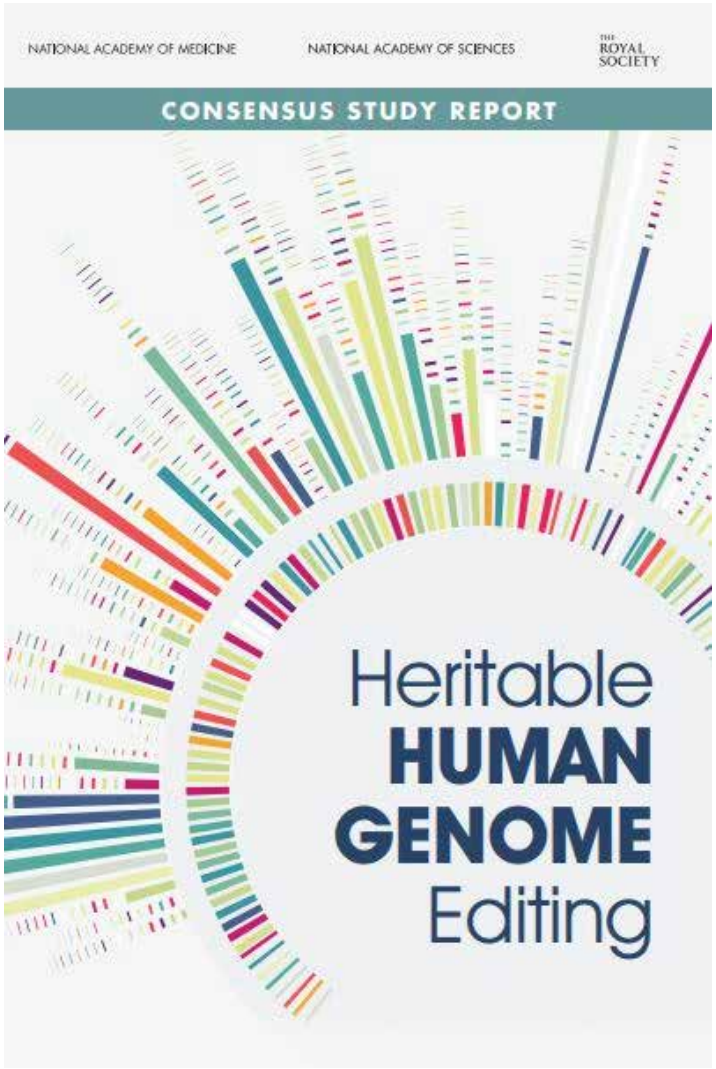
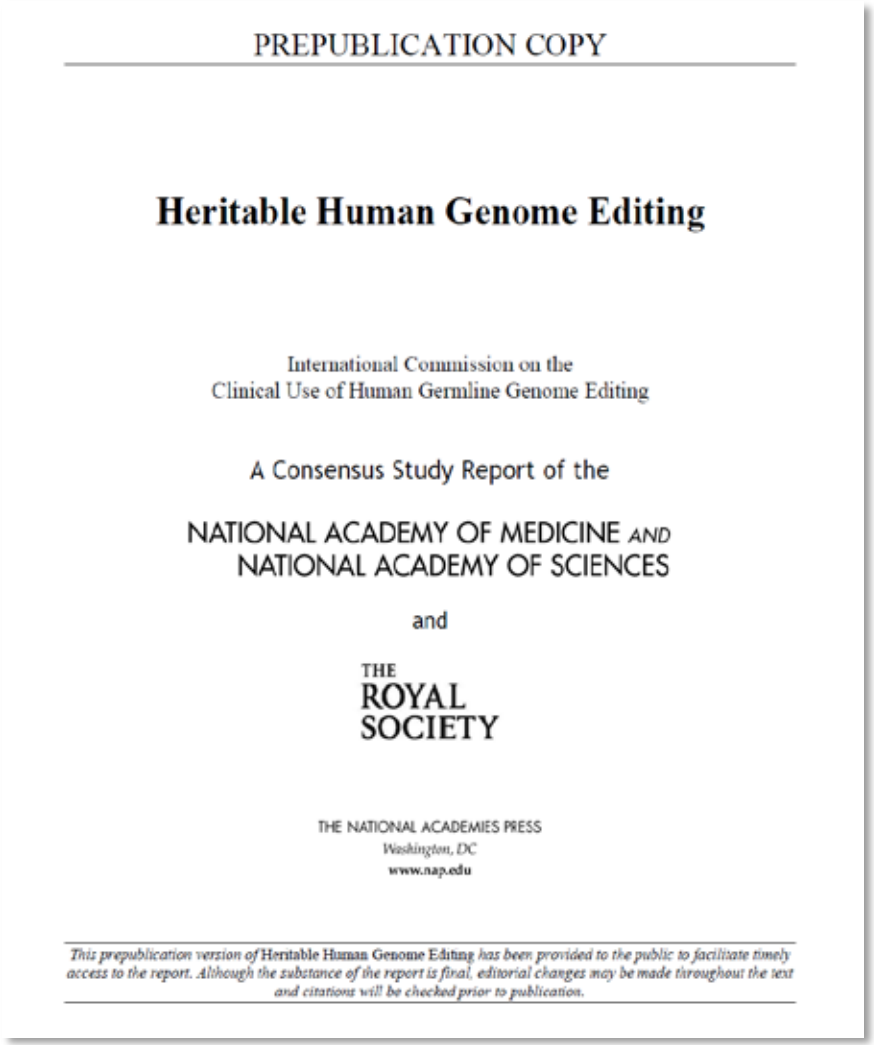
ヒト胚へのゲノム編集に関する国際委員会の報告について

資料２－１

Heritable Human Genome Editing（HHGE）(2020) 報告書

第124回生命倫理専門調査会
2020年10月29日
国立成育医療研究センター　阿久津英憲

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Heritable Human Genome Editing

International Commission on the
Clinical Use of Human Germline Genome Editing

A Consensus Study Report of the

NATIONAL ACADEMY OF MEDICINE *AND*
NATIONAL ACADEMY OF SCIENCES

and

THE
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Heritable Human Genome Editing（HHGE）(2020) 報告書について

Heritable human genome editing （HHGE）について

- 基礎的な実験研究は、例えば、ゲノム編集技術を開発したり、病気のメカニズムを理解したり、初期の発生を理解したりするのに利用できる。ゲノム編集は、多くの種類の細胞、動物モデル、または研究に用いられる初期ヒト胚で行うことができる。しかし、この研究は実験室でしか行われておらず、人での妊娠は決して起こりません。

- 研究目的で行われる生殖細胞系ゲノムの編集と臨床目的で行われる編集を区別するために、報告書は以下の用語を使用する:
  a) “genome editing in human embryos”という語句、またはそのような編集が基礎および、前臨床検査研究（preclinical laboratory research）の一部として行われる場合の同等の記述。
  b) “HHGE”とは、結果として得られた胚を、挙児の目的に、子宮へ移植することを意味する。臨床的意義で、”any editing in germline cells”を意味する。

International Commission on the Clinical Use of Human Germline Genome Editing

委員会の構成と体制

“**International Commission on the Clinical Use of Human Germline Genome Editing**”（以下、「委員会」とす）は、米国科学アカデミー（NAS）/医学アカデミー（NAM）と英国王立協会（The Royal Society）により招集され、10カ国-計18名の専門家により構成されている。

さらに、International Oversight Board of leaders from national academies of sciences and international institutionsが14名の著名な専門家から構成され、委員会の運営、報告書の査読など監視委員会として組織されている。

背景と目的

ゲノム編集技術の急速な進歩の中、2018年に受精卵ゲノム編集による“デザイナーベビー”が中国で生まれた。この技術に関連する科学的、社会的、倫理、法令、ガバナンス等の問題を早急に検討するよう世界的な要請として再燃してきた。委員会は、ゲノム編集技術や生殖補助医療などに関連する最新の医学･科学的情報を幅広く収集し、科学的、医学的、規制上の要件だけでなく、これらの要件に密接に関連する社会的、倫理的な問題などから受精卵ゲノム編集の臨床利用の可能性を審議し現段階の理解および今後、グルーバルな枠組みで必要とする働きなど具体的に報告書としてまとめ社会へ提示する。

活動

2019年6月に全体での活動を開始した。一般にも開放したPublic meetingを2シリーズ（2019年8月ワシントンDC；2019年11月ロンドン）開催し、2020年1月に委員会のみの会議をワシントンDCで行った。他に、2019年10月には、各分野の専門家によるWebinarが実施された。世界各地から各分野の有識者、計44名を本委員会で招請した。

パブリックコメントも収集した。Public meetingはHP上で動画視聴可能であり、そこでも広くコメントを収集し、報告書作成へ活用した。

International Oversight Board

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- **Victor Dzau**, U.S. National Academy of Medicine
- **John Skehel**, The Royal Society of the U.K.

Members

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- **K. Vijay Raghavan**, Government of India
- **Janet Rossant**, The Gairdner Foundation and University of Toronto
- **Rajiv Shah**, The Rockefeller Foundation

Sponsors

Department of Health and Human Services	National Academy of Medicine Initiatives Fund	National Academy of Sciences Cicerone Endowment Fund
Rockefeller Foundation	The Royal Society (UK)	Wellcome Trust

3つの重要なポイント

1. No clinical use of HHGE should be considered until it has been clearly established that it is possible to efficiently and reliably make precise genomic changes without undesired changes in human embryos. Further research is necessary

HHGEの臨床利用は認められない

2. Before any country decides to approve the use of HHGE, there should be national and international mechanisms to ensure that the preclinical requirements have been met for initial responsible use

HHGEの使用を適切に検証、評価する自国内および国際的なしくみが必要

3. Any clinical use of HHGE should proceed cautiously, with initial uses restricted to a limited set of circumstances as per the criteria set out in the report

臨床利用となるHHGEは、非常に限られた状況に限定されるべき

Evaluating initial applications for HHGE

遺伝病の理解とともに、HHGEの臨床利用に関して安全性と有効性について

- **Criteria for safe and effective HHGE have not yet been met.** Neither the editing technologies nor the technologies for sequencing embryonic DNA to check on-target and off-target effects are reliable enough for clinical use.

HHGEの安全性と有効性を担保する厳格な基準

- **stringent standards for preclinical evidence** to ensure that **precise genomic changes** can be made in human embryos **without undesired changes and without altering normal embryo development**.
- Standards for any initial human uses of HHGE need to be set high, because there are uncertainties associated with a new technology and some aspects of safety and efficacy.
- Decisions to permit any clinical use of HHGE rest with individual countries and should be made on a case-by-case basis, informed by international discussions.
- International cooperation on HHGE to provide for 3 functions is also critical:
    1. An International Scientific Advisory Panel to conduct regular technical assessments of progress in areas of genome editing and assisted reproductive technologies;
    2. An international body to recommend whether it could be appropriate to cross HHGE thresholds, which will include assessing not only scientific progress but also what ethical and societal concerns are raised by new classes of uses;
    3. A mechanism for raising concerns about research or conduct of HHGE.

Translational pathway for initial use

HHGEの安全性と有効性を担保する厳格な基準

プレクリニカルリサーチで検証

- Preclinical research in cell and animal models to develop and validate the editing methodology
- Sufficient preclinical evidence from human embryos to demonstrate
  - Reliably accurate on-target changes
  - No off-target changes introduced by the editing reagents
  - No mosaicism caused by the editing reagents

受精胚細胞生検での検証：**1細胞レベルでの確実性**

- Clinical evaluation of an embryo to be used in a pregnancy to verify
  - Intended edit and no unintended changes in one or a few biopsied cells
  - Comparable developmental milestones as an unedited embryo

IC、長期フォローアップの仕組み

- Protocols for seeking informed consent and conducting long-term follow-up

Categorising applications for HHGE

HHGEの適用可能性を分類
ーゲノム編集の効果
ー遺伝子型と表現型の因果関係
ー遺伝病を遺伝するリスクがある見込みのある親が、その疾患のない遺伝的に関連した子供をもつために利用できる既存の選択肢

The Commission categorized possible applications of HHGE based on:

- Phenotype that editing is intended to influence
- Causal relationship between genotype and phenotype
- Existing options available to prospective parents at risk of passing on a genetic disease to have a genetically related child without that disease

Six categories of possible applications

- Category A – serious monogenic (single gene) diseases in which all children would inherit the disease
- Category B – serious monogenic diseases in which some children would inherit the disease
- Category C – monogenic conditions with less serious impacts
- Category D – polygenic diseases
- Category E – applications not related to heritable disease
- Category F – monogenic conditions that cause infertility

Recommendation for any initial use

HHGEの適応対象は非常に限られる

Analysis of the potential harms, benefits and uncertainties in the science, led to recommendation that any initial use of HHGE be restricted to circumstances that meet four criteria:

- Serious monogenic disease
- Common variant known not to cause disease
- No unaffected embryos subject to editing and transfer
- No or very poor options for having a genetically–related child without the disease

Governance arrangements for HHGE (national)

”HHGEの科学的研究に加えて、技術の使用を承認する前に実施すべきガバナンス機能についても調査した。委員会は、HHGEを承認するかどうかの意思決定において国家主権を認めるが、そのような決定が特定の目的のためにHHGEを使用することが適切であるかどうかについて国際的な議論によって知らされることを望む。”

- Decisions about whether or not to approve HHGE will ultimately be made by countries
- Any country considering HHGE should have mechanisms and competent regulatory bodies to ensure that a number of conditions are met. If a country is not able to meet all of these conditions, no clinical use of HHGE should occur in that country. Conditions include:

  - Decision-making informed by findings from independent international assessments of the progress in scientific research and on the safety and efficacy of HHGE
  - Case by case evaluation
  - Transparency

Governance arrangements for HHGE (international)

”国内及び国際的な議論は、技術の安全性及び有効性の継続的な評価によって情報提供されるべきである。この評価を実施するために、委員会は国際科学諮問委員会International Scientific Advisory Panel （ISAP）を設立することを勧告する。”

Three functions for international oversight of HHGE:

1. **Ongoing evaluation of the science and technology on which HHGE** would depend
   - International Scientific Advisory Panel (ISAP) to assess progress & research developments required to reach technical or translational milestones
   - Assess whether preclinical requirements have been met for any circumstances of clinical use
   - Advise on scientific and clinical risks and potential benefits
2. Debate whether it could be appropriate to cross HHGE thresholds to new class of uses, including ethical and societal concerns raised
   - International body to convene debates about crossing any HHGE thresholds. Diverse membership, beyond scientific and clinical expertise
   - Role in defining each proposed new class of use and its limitations
   - Recommend whether it could be appropriate to cross the threshold of permitting a new class of use
3. A mechanism for raising concerns about research or conduct of HHGE.
   - We reiterate need for this function but don’t specify mechanism

Taking the Commission's work forward

- Public briefings at conferences and Academy events
- Report being considered by World Health Organisation's Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing
- Revisiting the conclusions and recommendations at the Third International Summit on Human Genome Editing

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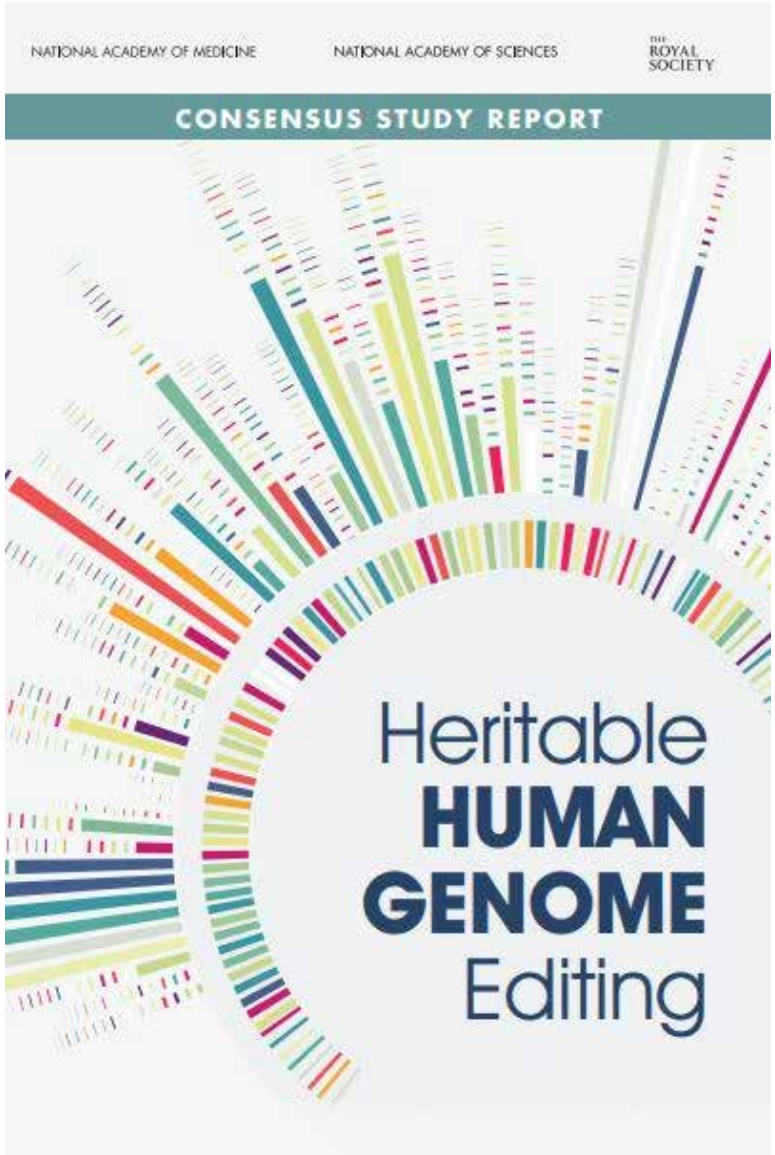

Report Release Webinar

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