ゲノム編集に関する倫理的議論のサーベイ

児玉聡
20150805

目的・方法

- ゲノム編集に関して、英米圏でどのような倫理的議論や規制に関わる議論がなされているか(また、なされていないか)、概観する
- RSS feedを用いて、主に2015年3月以降の英米圏のオンラインニュース記事をチェックし、そこに引かれている論文も含めて倫理的議論・規制に関わる議論を調べた(必ずしも網羅的ではない)

The researchers behind 'the biggest biotech discovery of the century' found it by accident KEVIN LORIA JUL 8 2015, Business Insider Aust.

Breakthrough Prize life science laureates Emmanuelle Charpentier and Jennifer A. Doudna arrive at the 2nd Annual Breakthrough Prize Award Ceremony at the NASA Ames Research Center on Sunday, November 9, 2014 in Mountain View, California.

The researchers behind 'the biggest biotech discovery of the century' found it by accident KEVIN LORIA JUL 8 2015, Business Insider Aust.

- They noticed that the system bacteria use to shut down viruses had an uncanny way of targeting specific sections of virus DNA — and that, with the correct programming, this system could seek out any section of DNA and slice it up. Not only that, if accompanied by other coding material, this process could also replace one section of DNA with a new section of DNA.
- They realised they'd found an incredibly precise tool.
- 外科手術用のメス：We've had gene-editing technology for decades, but now "we're basically able to have a molecular scalpel for genomes," says Doudna, a biologist at the University of California at Berkeley. "All the technologies in the past were sort of like sledgehammers."

The researchers behind 'the biggest biotech discovery of the century' found it by accident
KEVIN LORIA JUL 8 2015, Business Insider Aust.

- 基礎研究重要：The two scientists realised the potential applications for the system they were studying and then conducted experiments to show how it worked, which required both flashes of insight and a great deal of expertise. Yet still, “it’s serendipitous work — there’s an element of luck involved,” says Doudna.
- For that reason, she says this discovery highlights the importance of funding basic research, as that is the sort of work that can advance knowledge that then — unexpectedly — can lead to a transformative practical discovery.
- Funding for this type of work has fallen significantly over the past 50 years, according to a recent report out of MIT. Here’s a chart showing the drop in US funding for basic research from 1968 to 2015:
- “[Supporting basic research] is something that the US has done in the past,” says Doudna. “I think we’re in danger of losing that right now.”

By Shouguang Jin, Professor of molecular genetics and microbiology at University of Florida

Explainer: CRISPR technology brings precise genetic editing – and raises ethical questions
March 26, 2015 The Conversation

- Crispr: the equivalent of a surgical laser knife
- 倫理：ヒトを含む生物の生殖細胞や受精卵を操作可能
- 嚢胞繊維症、血友病、鎌形赤血球貧血症、ダウン症などの遺伝的欠陥(genetic defects)を治療できる可能性。
- これまでの遺伝子治療は正常な遺伝子を導入するだけのtemporary fix
- 理論的にはエンハンスメント(知性、見た目、寿命の向上)も可能
- まだ副作用がわかっていない。明確な規制もない
- そこで科学者グループ(NAPA meetingの人々)がヒト生殖細胞へのゲノム編集技術の臨床応用にモラトリアムを提案


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PERSPECTIVE
BIOTECHNOLOGY
A prudent path forward for genomic engineering and germline gene modification
David Baltimore[1], Paul Berg[2], Michael Botchan[3,4], Dana Carroll[5], R. Alta Charo[6], George Church[7], Jacob E. Corn[4], George Q. Daley[8,9], Jennifer A. Doudna[4,10,*], Marsha Fenner[4], Henry T. Greely[11], Martin Jinek[12], G. Steven Martin[13], Edward Penhoet[14], Jennifer Puck[15], Samuel H. Sternberg[16], Jonathan S. Weissman[4,17], Keith R. Yamamoto[4,18]
Author Affiliations
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アシロマ会議(1975、140名)にも参加した人が共著
NAPA meetings in Jan 2015

Napa Meeting Jan 2015

- ヒト生殖系列細胞への介入を議論。ミトコンドリア移植は論じず This group, all from the United States, and which included some of the leaders in the original 1970s discussions about recombinant DNA research at Asilomar and elsewhere, focused on the issue of human germline engineering, as the methods have already been demonstrated in mice (6) and monkeys (7). The Napa discussion did not address mitochondrial transfer (8, 9), a technique that does not use CRISPR-Cas9. Although characterized by some as another form of “germline” engineering, mitochondrial transfer raises different issues and has already been approved by the Human Fertilisation and Embryology Authority and by Parliament in the United Kingdom (10) and is being considered by the Institute of Medicine and the Food and Drug Administration in the United States (11). At the Napa meeting, “genome modification” and “germline engineering” referred to changes in the DNA of the nucleus of a germ cell.

Napa Recommendations

- 1) 当面、ヒト生殖系列ゲノム改変の臨床応用はすべきでない Strongly discourage, even in those countries with lax jurisdictions where it might be permitted, any attempts at germline genome modification for clinical application in humans, while societal, environmental, and ethical implications of such activity are discussed among scientific and governmental organizations. (In countries with a highly developed bioscience capacity, germline genome modification in humans is currently illegal or tightly regulated.) This will enable pathways to responsible uses of this technology, if any, to be identified.
- 2) ゲノム改変のELSIを論じるためのフォーラムを作るべし Create forums in which experts from the scientific and bioethics communities can provide information and education about this new era of human biology, the issues [redacted] the risks and rewards of using such powerful technology for a wide variety of applications including the potential to treat or cure human genetic disease, and the attendant ethical, social, and legal implications of genome modification.

Napa Recommendations

- 3) Crisprを用いた生殖系列遺伝子治療への臨床応用を視野にいれたヒト・非ヒトの基礎研究を支援すべし Encourage and support transparent research to evaluate the efficacy and specificity of CRISPR-Cas9 genome engineering technology in human and nonhuman model systems relevant to its potential applications for germline gene therapy. Such research is essential to inform deliberations about what clinical applications, if any, might in the future be deemed permissible.
- 4) 学際的な国際会議を開いて指針を作るべし Convene a globally representative group of developers and users of genome engineering technology and experts in genetics, law, and bioethics, as well as members of the scientific community, the public, and relevant government agencies and interest groups, to further consider these important issues, and where appropriate, recommend policies.

Anthony Wrigley, Senior Lecturer in Ethics at Keele University;
Ainsley Newson Senior Lecturer in Bioethics at University of Sydney

Genome editing poses ethical problems that we cannot ignore

March 31, 2015 The Conversation

- (ナフィールドのバックグラウンドペーパーの概要になっている。ナフィールドのペーパーは別の報告参照)
- これまでの遺伝子改変との連続性／非連続性
- 使用法：デュシェンヌ型筋ジスの遺伝子治療(動物モデル)、農薬・殺虫剤抵抗性のある穀物
- ガタカ、素晴らしき新世界の世界?：遺伝性疾患の根絶、病気への抵抗性向上、エンハンスメント(目・肌・髪の色、身長)

Anthony Wrigley, Senior Lecturer in Ethics at Keele University;
Ainsley Newson Senior Lecturer in Bioethics at University of Sydney

Genome editing poses ethical problems that we cannot ignore

March 31, 2015 The Conversation

- 生殖系列への介入は不可逆的編集(permanent edits)、次世代のすべての細胞に誤りが複製される可能性
- 次世代に影響しない遺伝子治療は現在はOK。ただし現時点で治っているのはsevere combined immunodeficiencyのみ
- 規制が後手に回るとデファクトの技術になりうる；その場合この技術にアクセスできない人は不利益を被る(正義の問題)

NATURE MEDICINE | EDITORIAL
Germline editing: time for discussion
Nature Medicine 21, 295 (2015) 07 April 2015

- (日本語要約入手可能)
- 3月5日のMIT Technology Review: 中国でCrisprを使ってヒトの体外受精胚をいじっているというううわさを書く
- 現時点ではまだヒト生殖細胞や受精卵には使用されていない
- TALENやZFNはオフターゲットの問題やタンパク質作製の困難さがあるがCrisprはそれらの困難の多くを克服
- ヒト生殖系列へのゲノム編集のモラトリアム提案(Lanphier et al. Sangamo BioSciences)—エンハンスメント目的での使用の可能性、規制のバックラッシュで体細胞へのゲノム編集ができなくなるかも

MIT Technology Review

FEATURED STORY

Engineering the Perfect Baby

Scientists are developing ways to edit the DNA of tomorrow's children. Should they stop before it's too late?

By Antonio Regalado on March 5, 2015

NATURE | COMMENT

Don't edit the human germ line

Edward Lanphier, Fyodor Urnov, Sarah Ehlen Haecker, Michael Werner & Joanna Smolenski

12 March 2015

Heritable human genetic modifications pose serious risks, and the therapeutic benefits are tenuous, warn Edward Lanphier, Fyodor Urnov and colleagues.

NATURE MEDICINE | EDITORIAL
Germline editing: time for discussion
Nature Medicine 21, 295 (2015) 07 April 2015

- ヒト生殖系列への介入については科学者でも議論が分かれている(Ethics of embryo editing divides scientists)。
- ゲノム編集を用いたエンハンスメントはもってのほかだが、鎌形赤血球貧血症など生殖細胞へのゲノム編集以外では治療ができない可能性があるものもある
- 安全性の問題も克服されるかもしれない
- 議論すべきこと：エンハンスメント使用の規制、遺伝子改変チャイルドの追跡調査の問題、アクセスの公平性
- 最近、ミトコンドリア置換術とヒト体細胞クローニングが成功。これらも生殖系列の変化を伴うので一緒に議論するのが有用
- The ISSCR has now weighed in on germline editing, as has a group of scientists, lawyers and ethicists in a Perspective in Science, both calling for a halt on the clinical application of germline nuclear genome editing and recommending that in vitro genome editing research be allowed to proceed.

Ethics of embryo editing divides scientists
David Cyranoski 18 March 2015,
Nature | News

- George Church, a geneticist at Harvard Medical School in Boston, Massachusetts, agrees that there should be a moratorium on embryo editing, but only “until safety issues are cleared up and there is general consensus that it is OK”. …
- 安全性をクリアすればOK：Church sees no fundamental problem with editing the germ line — he notes that even the somatic-cell therapies are still a form of artificial modification. He compares gene editing in embryos to in vitro fertilization, which people objected to until it was shown to be safe.

2015 – ISSCR Press Releases and Statements

The ISSCR Statement on Human Germline Genome Modification

19 March, 2015
View the PDF version of the statement

The International Society for Stem Cell Research calls for a moratorium on attempts at clinical application of nuclear genome editing of the human germ line to enable more extensive scientific analysis of the potential risks of genome editing and broader public discussion of the societal and ethical implications.

At this time, the ISSCR supports in vitro laboratory research, performed under proper ethical oversight, to enhance basic knowledge and to better understand the safety issues associated with human genome editing technologies, including their potential for application in somatic tissues. The ISSCR also calls for broad public and international dialogue on the capabilities and limitations of these technologies and on the implications of their application to the human germ line. The ISSCR is committed to playing a role in catalyzing both the scientific and broader ethical deliberations about germline genome editing.

Science | Thu Apr 23, 2015 3:22pm EDT
First experiment 'editing' human embryos ignites ethical furor REUTERS

- 先週末に中国人研究者たちがProtein & Cellというジャーナルにヒト胚のゲノム編集に関する投稿(3月30日に論文受領、4月1日にアクセプト)
- 筆頭執筆者のJunjiu Huang of Sun Yat-sen University in Guangzhouによれば、NatureとScienceは倫理面から落とした
- CRISPR/Cas9, and represents a biological version of a word-processing program's "find and replace" function. Scientists introduce enzymes that first bind to a mutated gene, such as one associated with disease, and then replace or repair it.

Science | Thu Apr 23, 2015 3:22pm EDT
First experiment 'editing' human embryos ignites ethical furor REUTERS

- 中国の研究 Huang's experiments provide evidence of what can go wrong with CRISPR. His team experimented on 86 one-cell human embryos, they reported, all from fertility clinics and, because of chromosomal defects, unable to develop into a baby. Their target was a gene called HBB, which can cause the blood disease beta-thalassemia.
- About a dozen embryos did not even survive the genome-editing, the scientists reported.
- Of the surviving embryos, many showed "off-target" effects, they reported, meaning genes other than HBB were altered. Other embryos suffered "untoward mutations." Only a handful of embryos contained the healthy DNA meant to repair the defective HBB genes.

The moral imperative to research editing embryos: The need to modify Nature and Science

Published April 23, 2015 | By Chris Gyngell

Chris Gyngell and Julian Savulescu

- NatureとScienceが中国の論文を落としたのは正しくなかった
- すでに霊長類を含む他の種でも胚へのゲノム編集介入は行われていた。ヒト体細胞でも行われていた
- CRISPRは細胞自身のDNA修復システムを使うので、胚でやってみるどうなるかは研究として重要
- ゲノム編集はテイサックス、ハンチントン、嚢胞性繊維腫を根絶する可能性

The moral imperative to research editing embryos: The need to modify Nature and Science

Published April 23, 2015 | By Chris Gyngell

Chris Gyngell and Julian Savulescu

- リスク：オフターゲットな改変は全身に拡がる可能性、リスクが大きすぎて現時点では生殖自体は試みるべきではない
- しかしHuangらは染色体が余分にあるnon-viableな胚に対してやった。普通なら流産する胚であり、IVFの余剰胚。誰にも危害を与えていない。リスクを理解するための研究であった。この研究は重要だった。
- しかしNatureもScienceも「倫理的理由」から落とした。両者に載ったコメンタリー(BaltimoreやLanphier)の議論はエンハンスメントへのSlippery Slopeだというものや、将来世代に対する予想のつかない影響を挙げていたが、これらはvague, emotive, and devoid of any real rational force。

The moral imperative to research editing embryos: The need to modify Nature and Science

Published April 23, 2015 | By Chris Gyngell

Chris Gyngell and Julian Savulescu

- 多くの技術は予測のつかない影響をもつし、エンハンスメントにも使われうる。これらは人命を救いうる研究を検閲するよい理由ではない
- 検閲が正当化される場合：H5N1トリインフルエンザの改変に関する二つの論文(致死率60%、インフルエンザと同じぐらいの感染率になる)；しかしこれをNatureとScienceは2012年に一本ずつ掲載した→一貫していないので基準を示すべき
- 英国だけでも毎年10万件の中絶。なぜこの研究が非難されるのか
- 結論：Huangらの方がNatureとScienceよりも倫理的

Protein & Cell July 2015, Volume 6, Issue 7, pp 476-479, Date: 26 Jun 2015
The moral imperative to continue gene editing research on human embryos

The moral imperative to research editing embryos: The need to modify Nature and Science

Published April 23, 2015 | By Chris Gyngell

Chris Gyngell and Julian Savulescu

Protein & Cell誌に改めて掲載
Julian Savulescu, Jonathan Pugh, Thomas Douglas, Christopher Gyngell,
The moral imperative to continue gene editing research on human embryos
Protein & Cell July 2015, Volume 6, Issue 7, pp 476-479, Date: 26 Jun 2015

China ignites debate over genetic engineering

by Michael Cook | 25 Apr 2015 | BioEdge

- イギリスでは批判が少ない In Britain, it was hard to find scientists who were opposed, let alone alarmed, by the news. "It's no worse than what happens in IVF all the time, which is that non-viable embryos are discarded," says John Harris, a utilitarian bioethicist at the University of Manchester, UK. "I don't see any justification for a moratorium on research."
- One of the UK's leading stem cell researchers, Robin Lovell-Badge, was almost enthusiastic. "I disagree with a moratorium, which is in any case unlikely to work well," he said. "Indeed I am fully supportive of research being carried out on early human embryos in vitro [in culture/in the lab], especially on embryos that are not required for reproduction and would otherwise be discarded."
- ミトコンドリア置換ですでにやっている：And Dr Anna Smajdor, a bioethicist at the University of East Anglia, said: "There is a whiff of hypocrisy about the moral outrage over reports that Chinese scientists have been modifying the DNA of embryos. Here in the UK we have given the go ahead to modifying the DNA of babies who will transmit these changes indefinitely to their offspring. The Chinese have tweaked DNA in embryos never destined to be born."

NATURE | NEWS
Embryo editing sparks epic debate
David Cyranoski & Sara Reardon 29 April 2015

- Although researchers agree that a moratorium on clinical applications is needed while the ethical and safety concerns of human-embryo editing are worked out, many see no problem with the type of research that Huang's team did, in part because the embryos could not have led to a live birth. "It's no worse than what happens in IVF all the time, which is that non-viable embryos are discarded," says John Harris, a bioethicist at the University of Manchester, UK. "I don't see any justification for a moratorium on research," he adds. Church, meanwhile, notes that many of the earliest experiments with CRISPR/Cas9 were developed in human induced pluripotent stem cells, adult cells that have been reprogrammed to have the ability to turn into any cell type, including sperm and eggs. He questions whether Huang's experiments are any more intrinsically problematic. iPS細胞はどうなの

NATURE | NEWS
Embryo editing sparks epic debate
David Cyranoski & Sara Reardon 29 April 2015

- NIH、米国では黄教授の研究は実施が認められない：Modifying human embryos is legal in China and in many US states. Asked whether Huang's study would have been funded under its rules, the US National Institutes of Health says that it "would likely conclude it could not fund such research", and is watching the technology to see whether its rules need to be modified.
- Because the embryos Huang's team used were initially created for in vitro fertilization, not for research, the work would already have overcome many of the ethical hurdles it would face in other countries too, adds Tetsuya Ishii, who studies bioethics and policy at the University of Hokkaido in Sapporo, Japan.

NATURE | BREAKING NEWS
NIH reiterates ban on editing human embryo DNA
Sara Reardon 29 April 2015

- NIH director Francis Collins: 胚のgene editing禁止を確認
- 安全性、次世代への影響、遺伝子スクリーニングなど他の手段があるためやるべきでない
- NIHは以前から禁止(1996年のDickey-Wicker修正条項--研究目的でヒト胚を作ること、破壊することを含む研究には公的資金を投じることを禁じる。ただし私的資金を用いた研究は州ごとに規制が異なる) non-viableな胚にも法が適用されるとの解釈

Crispr: is it a good idea to 'upgrade' our DNA? Zoë Corbyn
Sunday 10 May 2015 The Guardian

- 生殖系列への介入はしないというコンセンサスがこれまであった。Germ-line genome editing is highly controversial, even for medical purposes. Since the development of genetic engineering in the 70s there has been a "fairly undisturbed" consensus that human germ-line genetic modification – with the worries it raises about "playing God" and "designer babies" – is off bounds, says Peter Mills, assistant director of the UK Nuffield Council on Bioethics and the council's lead on genome editing. According to Unesco's Universal Declaration on the Human Genome and Human Rights, germ-line interventions "could be contrary to human dignity".

ユネスコ：ヒトゲノムと人権に関する世界宣言

- C.ヒトゲノムに関する研究
- 第10条
- ヒトゲノムに関するいかなる研究又はその応用も、特に生物学、遺伝学及び医学の分野におけるものも、個人の又は該当する場合は集団の人権、基本的自由及び人間の尊厳に優越するものではない。
- 第11条
- ヒトのクローン個体作製のような人間の尊厳に反する行為は、許されてはならない。国及び権限ある国際機関は、そのような行為を特定すること、並びにこの宣言に述べられている諸原則の尊重を確保するために講ずべき適切な措置を国内的に又は国際的に決定することに協力するよう要請される。

ユネスコ：ヒトゲノムと人権に関する世界宣言

- G.宣言の実施 第24条
- ユネスコ国際生命倫理委員会(IBC)は、本宣言に述べられている諸原則の普及に 貢献すべきであり、さらに、それら諸原則の適用及び論議の対象となる技術の発展によ って提起される論点の検討にも貢献すべきである。同委員会は、弱者集団などの関係当 事者と適切な協議を実施すべきである。同委員会は、この宣言のフォローアップについ て、特に生殖細胞系列の操作のような人間の尊厳に反する可能性のある行為の特定につ いて、ユネスコの手続き規則に則って総会に勧告を行い、助言を与えるべきである。

Crispr: is it a good idea to ‘upgrade’ our DNA? Zoë Corbyn Sunday 10 May 2015 The Guardian

- 着床前スクリーニングにない利点がある：Unlike embryo screening, germ-line editing would not require multiple embryos, which some couples don’t have. It could deal easily with multiple genetic conditions where finding unaffected embryos is a challenge. And it wouldn’t involve discarding any embryos, which some people feel uncomfortable with. “There is an argument for genome engineering in embryos to repair genes that clearly predispose to disease,” says Perry [Tony Perry, a molecular embryologist at the University of Bath]

Crispr: is it a good idea to ‘upgrade’ our DNA? Zoë Corbyn Sunday 10 May 2015 The Guardian

- エンハンスメント：Some people may even think it important to use Crispr to make better humans, not just preemptively stamp out disease. There are gene variants which confer extra-strong bones, low Alzheimer’s risk or viral resistance such as to HIV. Beyond that, what about enhancements such as living longer, improved cognition, or altered physical attributes?

Crispr: is it a good idea to 'upgrade' our DNA? Zoë Corbyn
Sunday 10 May 2015 The Guardian

- 英国では生殖細胞の研究はHFEAの管理、治療は議会の承認必要：The UK has a cautiously progressive regulatory system that would apply to developments in human germ-line editing. Any research on germ cells needs to be licensed by the Human Fertilisation and Embryology Authority (HFEA). Parliamentary approval would be needed for therapeutic use. According to a list of research projects using human embryos currently being carried out in the UK provided by the HFEA, none appear to involve genome editing. But Lovell-Badge says he is aware of "several groups" in Britain interested in using it to "answer some basic research questions". (Meanwhile the main public funder of research in the US - the NIH - says it won't fund any use of gene-editing technologies in human embryos.)

Embryo engineering a moral duty, says top scientist
By James Gallagher
Health editor, BBC News website 13 May 2015

- Dr [Tony] Perry was part of the teams to clone the first mice and pigs and says the new technology should be embraced.
- [Is it acceptable to edit DNA to prevent disease?]
- He told the BBC: "My view is this is such a wonderful opportunity to remove horrible diseases that it would be unethical not to explore it.
- "I think it is a sin of omission, if you have a method where you can prevent someone suffering and you don't take that opportunity then it is wrong, it is unethical.
- "But that needs to be in context of a full debate."
- He called on government and research bodies to fund such research…
- He said it was possible for society to accept the technology for medical purposes, but draw the line at "a population of Lara Crofts and Jason Bournes".

National Academy of Sciences To Tackle Ethics Of CRISPR-Cas9, Gene-Editing Technology
May 18, 2015 02:15 PM By Reuters

- 先月の中国のゲノム編集の応答として国際会議開催：the National Academy of Sciences (NAS) and its Institute of Medicine will convene an international summit this fall where researchers and other experts will "explore the scientific, ethical, and policy issues associated with human gene-editing research," the academies said in a statement.
- 委員会も作る：In addition, NAS - an honorary body that was chartered by Congress in 1863 and performs studies for the federal government and others - will appoint a multidisciplinary, international committee to study the scientific basis and the ethical, legal, and social implications of human gene editing.

National Academy of Sciences To Tackle Ethics Of CRISPR-Cas9, Gene-Editing Technology
May 18, 2015 02:15 PM By Reuters

- 新アシロマ会議：It is a step reminiscent of one in 1975, when NAS convened the Asilomar Conference. That led to guidelines and federal regulations of recombinant DNA, the gene-splicing technology that underlay the founding of Genentech and other biotech companies and revolutionized the production of many pharmaceuticals.

White House backs review of gene-editing technology by Michael Cook | 30 May 2015 | BioEdge

- オバマ政権も倫理を考えることを支持：The Obama Administration has backed calls for an in-depth ethical review of gene-editing technology. This move came swiftly after Chinese scientists announced that they had altered the genome of non-viable human embryos earlier in May. “The Administration believes that altering the human germline for clinical purposes is a line that should not be crossed at this time,” said John P. Holdren, the white House science advisor.
- Holdren says that great circumspection is needed:
- “Research along these lines raises serious and urgent questions about the potential implications for clinical applications that could lead to genetically altered humans. The full implications of such a step could not be known until a number of generations had inherited the genetic changes made — and choices made in one country could affect all of us.”

White House backs review of gene-editing technology by Michael Cook | 30 May 2015 | BioEdge

- 優生学に反対 Columbia University biology professor Robert Pollack published a strong letter in Science which sums up the unease among some scientists:
- This opening to germline modification is, simply put, the opening of a return to the agenda of eugenics: the positive selection of “good” versions of the human genome and the weeding out of “bad” versions, not just for the health of an individual, but for the future of the species…
- Rational eugenics is still eugenics. The best in the world will not remove the pain from those born into a world of germ-line modification but who had not been given a costly investment in their gametes. They will emerge with the complexity of a genome different from what this technology will be able to define as “normal.” I do not think anything short of a complete and total ban on human germline modification will do, to prevent this powerful force for rational medicine—one patient at a time—from becoming the beginning of the end of the simplest notion of each of us being “endowed by our Creator with certain inalienable rights.”

ゲノム編集の課題調査へ 政府の生命倫理調査会 Sankei 2015.6.3 19:57

- 政府の総合科学技術・イノベーション会議の生命倫理専門調査会は３日、狙い通りに遺伝子を壊したり置き換えたりする「ゲノム編集技術」を人間の受精卵に利用することについて、倫理的な課題を調査すると決めた。
- ゲノム編集技術をめぐっては４月、中国の研究チームが人間の受精卵の遺伝子改変を試みたとの論文を発表し、世界中の専門家に衝撃を与えた。米政府は「将来世代への影響が不透明で、現時点では超えてはいけない一線だ」と反対する声明を５月に発表している。
- ３日の調査会では、出席委員から「日本としても何らかの見解を示すべきだ」「早急な議論が必要」などの意見が出た。今後有識者から意見を聴き、課題を把握した上で調査会として見解をまとめるかどうか決める。ウェブに資料あり

US Congress moves to block human-embryo editing Sara Reardon 25 June 2015 (Nature News)

- FDAでヒト胚のゲノム編集の臨床研究を評価しない方向の予算案：The US House of Representatives is wading into the debate over whether human embryos should be modified to introduce heritable changes. Its fiscal year 2016 spending bill for the US Food and Drug Administration (FDA) would prohibit the agency from spending money to evaluate research or clinical applications for such products…
- The House legislation comes during a time of intense debate on such matters, sparked by the announcement in April that researchers in China had edited the genomes of human embryos. The US National Institutes of Health (NIH) moved quickly to remind the public that a 1996 law prevents the federal government from funding work that destroys human embryos or creates them for research purposes.
- Privately funded research on editing the human germline remains legal in the United States. But the pending House bill seeks to make it harder to test embryo editing in clinical trials. A provision in the legislation would prevent the FDA from using federal funds to evaluate or permit research that involves either viable embryos with heritable genetic modifications, or sperm or eggs that could be used to create such an embryo.

CRISPR, the disruptor
Heidi Ledford
03 June 2015 Nature news

- 動植物：旧来の方法と違って自然に起きた変異かどうか見わけがつかない CRISPR's ability to precisely edit existing DNA sequences makes for more-accurate modifications, but it also makes it more difficult for regulators and farmers to identify a modified organism once it has been released. “With gene editing, there's no longer the ability to really track engineered products,” says Jennifer Kuzma, who studies science policy at North Carolina State University in Raleigh. “It will be hard to detect whether something has been mutated conventionally or genetically engineered.”
- 米国はまだ動物のゲノム編集について規制がない That rings alarm bells for opponents of genetically modified crops, and it poses difficult questions for countries trying to work out how to regulate gene-edited plants and animals. In the United States, the Food and Drug Administration has yet to approve any genetically modified animal for human consumption, and it has not yet announced how it will handle gene-edited animals.

CRISPR, the disruptor
Heidi Ledford
03 June 2015 Nature news

- 植物はすべては規制されない：Under existing rules, not all crops made by genome editing would require regulation by the US Department of Agriculture (see Nature **500**, 389–390; 2013). But in May, the agriculture department began to seek input on how it can improve regulation of genetically modified crops — a move that many have taken as a sign that the agency is re-evaluating its rules in light of technologies such as CRISPR.

US regulation misses some GM crops
Heidi Ledford
20 August 2013 Nature News

- 植物の遺伝子改変規制は古いルールを準用している：The regulation of GM crops in the United States is based on laws that were not tailor-made for the technology. The Animal and Plant Health Inspection Service (APHIS), the branch of the agriculture department responsible for overseeing GM crops, has so far stuck to a strict interpretation of a 1957 law designed to protect agriculture against plant pests that was co-opted in 1986 to regulate GM crops. At that time, GM crops were nearly always engineered using Agrobacterium tumefaciens, a bacterial pest that can insert DNA into plant genomes.
- In 2011, APHIS regulators announced that a herbicide-tolerant Kentucky bluegrass would not fall under their purview, because the lawn-and-garden company developing it did not use Agrobacterium or any other plant-pest DNA to engineer the grass. The company, Scotts Miracle-Gro of Marysville, Ohio, instead used a gene gun to fire DNA-coated gold particles into plant cells. Some of that DNA is then incorporated into the genome.

US regulation misses some GM crops
Heidi Ledford
20 August 2013 Nature News

- Helios Gene Gun は in vivo にてさまざまな標的に直接、迅速に幅広く遺伝子を導入できるハンドヘルドタイプの便利な装置です。 ユニットは調整可能な低圧のヘリウムパルスを使用して、DNA、RNA、または生体材料でコーティングされた金のマイクロキャリアを小さなプラスチック製のカートリッジの内壁から直接標的細胞に導入します。外来性の遺伝子もタンパク質も送達しません。http://www.bio-rad.com/ja-jp/product/helios-gene-gun-system

CRISPR, the disruptor
Heidi Ledford
03 June 2015 Nature news

- GENE DRIVE: Usually, a genetic change in one organism takes a long time to spread through a population. That is because a mutation carried on one of a pair of chromosomes is inherited by only half the offspring. But a gene drive allows a mutation made by CRISPR on one chromosome to copy itself to its partner in every generation, so that nearly all offspring will inherit the change. This means that it will speed through a population exponentially faster than normal (see 'Gene drive') — a mutation engineered into a mosquito could spread through a large population within a season. If that mutation reduced the number of offspring a mosquito produced, then the population could be wiped out, along with any malaria parasites it is carrying.

CRISPR, the disruptor
Heidi Ledford
03 June 2015 Nature news

- GENE DRIVE: But many researchers are deeply worried that altering an entire population, or eliminating it altogether, could have drastic and unknown consequences for an ecosystem: it might mean that other pests emerge, for example, or it could affect predators higher up the food chain. And researchers are also mindful that a guide RNA could mutate over time such that it targets a different part of the genome. This mutation could then race through the population, with unpredictable effects.
- “It has to have a fairly high pay-off, because it has a risk of irreversibility — and unintended or hard-to-calculate consequences for other species,” says George Church, a bioengineer at Harvard Medical School in Boston. In April 2014, Church and a team of scientists and policy experts wrote a commentary in Science6 warning researchers about the risks and proposing ways to guard against accidental release of experimental gene drives.

CRISPR, the disruptor
Heidi Ledford
03 June 2015 Nature news

- At the time, gene drives seemed a distant prospect. But less than a year later, developmental biologist Ethan Bier of the University of California, San Diego, and his student Valentino Gantz reported that they had designed just such a system in fruit flies7. Bier and Gantz had used three layers of boxes to contain their flies and adopted lab safety measures usually used for malaria-carrying mosquitoes. But they did not follow all the guidelines urged by the authors of the commentary, such as devising a method to reverse the engineered change. Bier says that they were conducting their first proof-of-principle experiments, and wanted to know whether the system worked at all before they made it more complex.
- GENE DRIVEも規制を検討：For Church and others, this was a clear warning that the democratization of genome editing through CRISPR could have unexpected and undesirable outcomes. “It is essential that national regulatory authorities and international organizations get on top of this — really get on top of it,” says Kenneth Oye, a political scientist at the Massachusetts Institute of Technology and lead author of the Science commentary. “We need more action.” The US National Research Council has formed a panel to discuss gene drives, and other high-level discussions are starting to take place. But Oye is concerned that the science is moving at lightning speed, and that regulatory changes may happen only after a high-profile gene-drive release.

Easy DNA Editing Will Remake the World. Buckle Up. Amy Maxmen WIRED 20150723

- At the end of the [1975 Asilomar] meeting, [David] Baltimore and four other molecular biologists stayed up all night writing a consensus statement. They laid out ways to isolate potentially dangerous experiments and determined that cloning or otherwise messing with dangerous pathogens should be off-limits. A few attendees fretted about the idea of modifications of the human “germ line”—changes that would be passed on from one generation to the next—but most thought that was so far off as to be unrealistic. Engineering microbes was hard enough. The rules the Asilomar scientists hoped biology would follow didn't look much further ahead than ideas and proposals already on their desks.

Easy DNA Editing Will Remake the World. Buckle Up. Amy Maxmen WIRED 20150723

- 自主規制か外的管理か That's why she [Doudna] convened the meeting in Napa [Jan 24th, 2015]. All the same problems of recombinant DNA that the Asilomar attendees tried to grapple with are still there—more pressing now than ever. And if the scientists don't figure out how to handle them, some other regulatory body might. Few researchers, Baltimore included, want to see Congress making laws about science. "Legislation is unforgiving," he says. "Once you pass it, it is very hard to undo."
- In other words, if biologists don't start thinking about ethics, the taxpayers who fund their research might do the thinking for them.

Easy DNA Editing Will Remake the World. Buckle Up. Amy Maxmen WIRED 20150723

- ヒト胚への介入の倫理と法理：But straight-out editing of a human embryo sets off all sorts of alarms, both in terms of ethics and legality. It contravenes the policies of the US National Institutes of Health, and in spirit at least runs counter to the United Nations' Universal Declaration on the Human Genome and Human Rights. (Of course, when the US government said it wouldn't fund research on human embryonic stem cells, private entities raised millions of dollars to do it themselves.) Engineered humans are a ways off—but nobody thinks they're science fiction anymore.

Easy DNA Editing Will Remake the World. Buckle Up. Amy Maxmen WIRED 20150723

- 科学者の方が倫理的 In an odd reversal, it's the scientists who are showing more fear than the civilians. When I ask [Harvard geneticist George] Church for his most nightmarish Crispr scenario, he mutters something about weapons and then stops short. He says he hopes to take the specifics of the idea, whatever it is, to his grave. But thousands of other scientists are working on Crispr. Not all of them will be as cautious. "You can't stop science from progressing," Jinek says. "Science is what it is." He's right. Science gives people power. And power is unpredictable.

ゲノム編集で受精卵操作「禁止すべきだ」　日米学会声明
合田禄
2015年8月1日00時35分 朝日デジタル

- 狙った通りに遺伝子を改変できる「ゲノム編集」という技術でヒトの受精卵を操作することについて、日本遺伝子治療学会と米国遺伝子細胞治療学会は３１日、「倫理的な問題などについて社会的な合意が得られ、解決するまで厳しく禁止すべきだ」とする共同声明を発表した。
- ゲノム編集は、従来の遺伝子組み換えよりも簡単に遺伝子を操作でき、研究現場で急速に普及している。中国の研究チームが今年４月、この技術でヒト受精卵の遺伝子を操作したとする論文を発表し、議論を呼んでいた。親が望む特徴をもつ「デザイナーベビー」につながりかねない技術として、世界中の研究者で議論が起きていた。
- 共同声明では、ゲノム編集で受精卵を操作すると、その受精卵だけでなく世代をまたいで影響し、何世代も先にならないとその影響が分からないことなど、倫理的問題があると指摘。「まずヒト以外の動物で研究するべきだ」とした。一方、受精卵ではない普通の細胞をゲノム編集することについては、「問題ない」との見方を示した。（合田禄）

まとめ

- ヒト体細胞のゲノム編集研究はOK、臨床研究も数年後か
- ヒト生殖細胞の研究もin vitroは倫理的にOK。ただし米国では法規制で公的資金を用いてはできない。英国ではHFEAの管掌
- 臨床応用は安全性、必然性、将来世代に引き継がれる、エンハンスメントなどの理由からダメ。ただし批判あり。ヒトゲノム宣言に反するという意見
- 中国のヒト受精卵研究は生殖系列に手を付けたので批判が多いが、non-viableなので問題ないとする意見もある。Nature, Scienceの対応に批判あり(出版倫理)
- 動植物は基本的にOK。米国では規制が不明確。カルタヘナの話はなし。Gene driveは要検討
- 「切るだけ」と「挿れる」の区別を論じているものは見当たらない

ゲノム編集で考えるべき分類(案)

	ヒト体細胞	ヒト生殖細胞	動物体細胞	動物生殖細胞	植物
基礎研究					
臨床応用(治療)					
エンハンスメント					
実用化・商業化	N/A	N/A			

実用化・商業化とは、食べてよいか、自然に戻してよいかなど

まとめ：ゲノム編集で考えるべき分類(案)
(○×等は倫理的許容可能性の例)

	ヒト体細胞	ヒト生殖細胞	動物体細胞	動物生殖細胞	植物
基礎研究	○	?	○	○	○
臨床応用(治療)	○	×	○	○	(不明)
エンハンスメント	×	×	(不明)	○	○
実用化・商業化	N/A	N/A	(不明)	?	?

実用化・商業化とは、食べてよいか、自然に戻してよいかなど