# Forschung mit Embryonen

2015: 97796 IVF – 57998 Transfers

Was könnte, möchte und darf man mit überschüssigen Embryonen machen?

# Gesetzliche Regelungen

1. **Embryonenschutzgesetz**
2. **Stammzellgesetz**
3. **Samenspendenregistergesetz seit 1. Juli 2018**

1. **IVF und ICSI  nur mit dem Ziel einer Schwangerschaft (Instrumentalisierungsverbot**)
2. **Leben beginnt ab Zygote**
3. **Verbot die Keimbahn zu verändern**

1. **Keine Geschlechterauswahl**
2. **PID nur nach medizinischer Indikation**
3. **IVF und ICSI nur mit Einwilligung beider Spender** (Ehe!)
4. Keine Befruchtung nach dem Tod des Mannes
5. Keine Veränderung der Keimbahn
6. *Keine Gentherapie?*
7. Klonen verboten
8. **Chimären oder Hybridbildung** verboten
9. Import Stammzellen nur wenn vor 2007 und aus überschüssigen Embryonen

- Forschung dann nur wenn wissenschaftlich begründet

# Religiöse Einflüsse und Betrachtungen

1. Religionen: Unterschiedliche Sichtweise, wann menschliches Leben beginnt
2. Bewertung Ehe/Partnerschaft durch Religion
3. Christentum: Unterschiedliche Bewertung der Sakramente
4. Akzeptanz gleichgeschlechtlicher Partnerschaften und allein erziehende Eltern
5. Geschichte der Eugenik

Siehe **Dignitas Personae (Kongregation für die Glaubenslehre)**:

1. Bildung der menschlichen Existenz mit Bildung der Zygote und Achtung als Person
2. Recht auf Unversehrtheit von Empfängnis bis Tod
3. Einheit der Ehe
4. Geschlechtlichkeit bedingt Akt der Zeugung

## Begründungen der Kirche zur Ablehnung von IVF und PID :

- Für das Leben weniger wird das Töten vieler in Kauf genommen.
- Kindeswunsch rechtfertigt nicht Produktion.
- Leben und Identität darf nicht in Hände Dritter gelegt werden

Einfrieren von Embryonen ist Abtreibung (da viele nicht überleben)
Überschüssige Embryonen dürfen nicht zu Forschungsmaterial degradiert werden
**Kryokonservierung von Eizellen ist moralisch unannehmbar**
Embryonenreduktion ist Abtreibung
**PID ist Eugenik und damit höchst verwerflich**.
Der Wert eines menschlichen Wesens darf nicht nach Maßstäben der
Normalität und des physischen Wohlbefindens beurteilt werden.
**PID unterstützt Kindstötung und Euthanasie. Es darf keine Diskriminierung ausgeübt werden**.
Interzeptive (Spirale, Pesar, Pille danach) und kontragestive (RU486)
sind als Abtreibung zu werten.

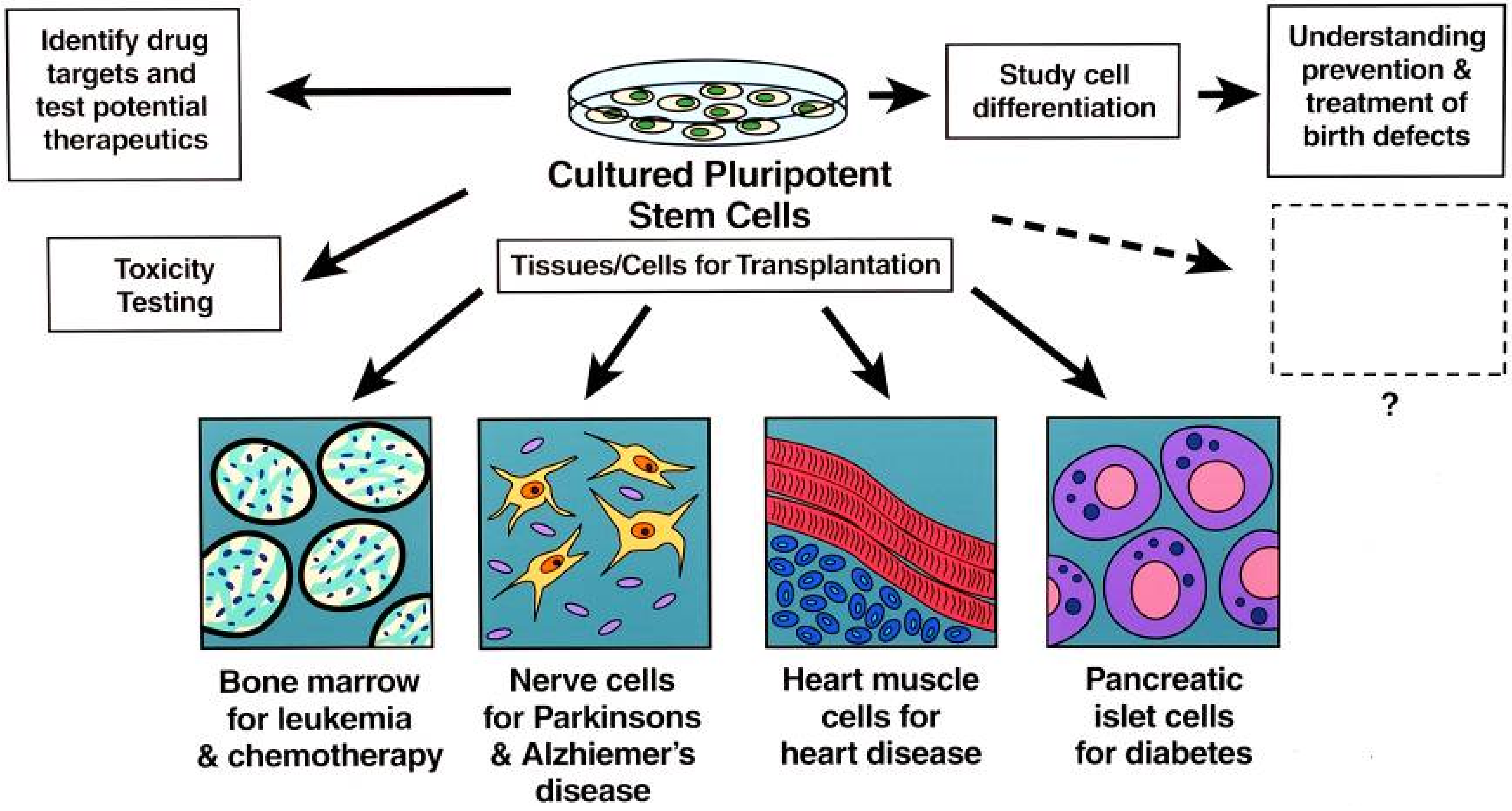
# Eugenik als Gefahr?

1. PID seit 2013 erlaubt
2. Embryonenscreening (2012 erstes Kind mit bekanntem Genom)
3. Kinder bekommen unabhängig vom Alter
4. Spermienselektion (Geschlechterselektion)
5. Oozytenselektion nach Einfrieren

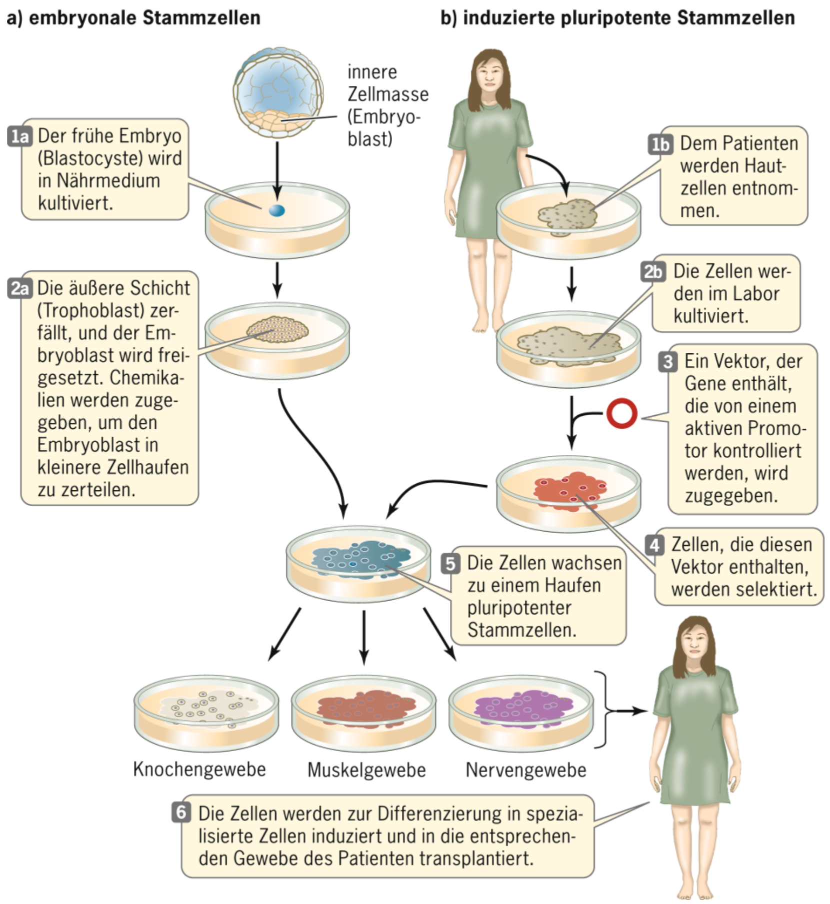
# Wo auf der Welt geht was?

| | KB | IVF | ICSI | Kryo Embryo | Eizell-Embryo-spende | Leih-mutter | IVF/ICSI Lesben/Single | repr. Klonen | ESC/ Forsch | PID |
|---|---|---|---|---|---|---|---|---|---|---|
| **Deutschland** | ✓ Ehe | ✓ Ehe | ✓ Ehe | –/✓ | –/✓ | – | – | – th Kl iPS ? | – import ✓ | –/✓ |
| **Dänemark** | ✓ | ✓ | ✓ | ✓ 2 Jahre | –/✓ | – | ✓ | – th Kl ✓ | –/✓ | –/✓ |
| **Österreich** | ✓ | ✓ | ✓ | ✓ 10 Jahre | – | – | ✓ | – | – | – |
| **Britannien** | ✓ † | ✓ † | ✓ † | ✓ 10 Jahre | ✓ | –/✓ | ✓ | – th Kl ✓ | ✓ | ✓ 14. Tag |
| **USA** (unterschied öffentlich/privat) | ✓ † | ✓ † | ✓ † | –/✓ | –/✓ | ✓ | ✓ | – / – th Kl ✓ | –/✓ | –/✓ |
| **Israel** (Japan) | ✓ (Ehe) | ✓ (Ehe) | ✓ (Ehe) | ✓ | ✓ | ✓ | ✓ | ✓ (kein Transfer) | ✓ | ✓ |
| **China** | ✓ | ✓ | ✓ | ✓ | ✓ | – | ? ! | – th Kl ✓ | ✓ | ✓ ! |
| **Indien** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ ! | – th Kl ✓ | ✓ 14. Tag | ✓ ! |
| **Belgien** (Spanien, Russland) | ✓ | ✓ | ✓ | ✓ | ✓ | nicht verboten | ✓ | – th Kl ✓ | –/✓ 14. Tag | –/✓ |

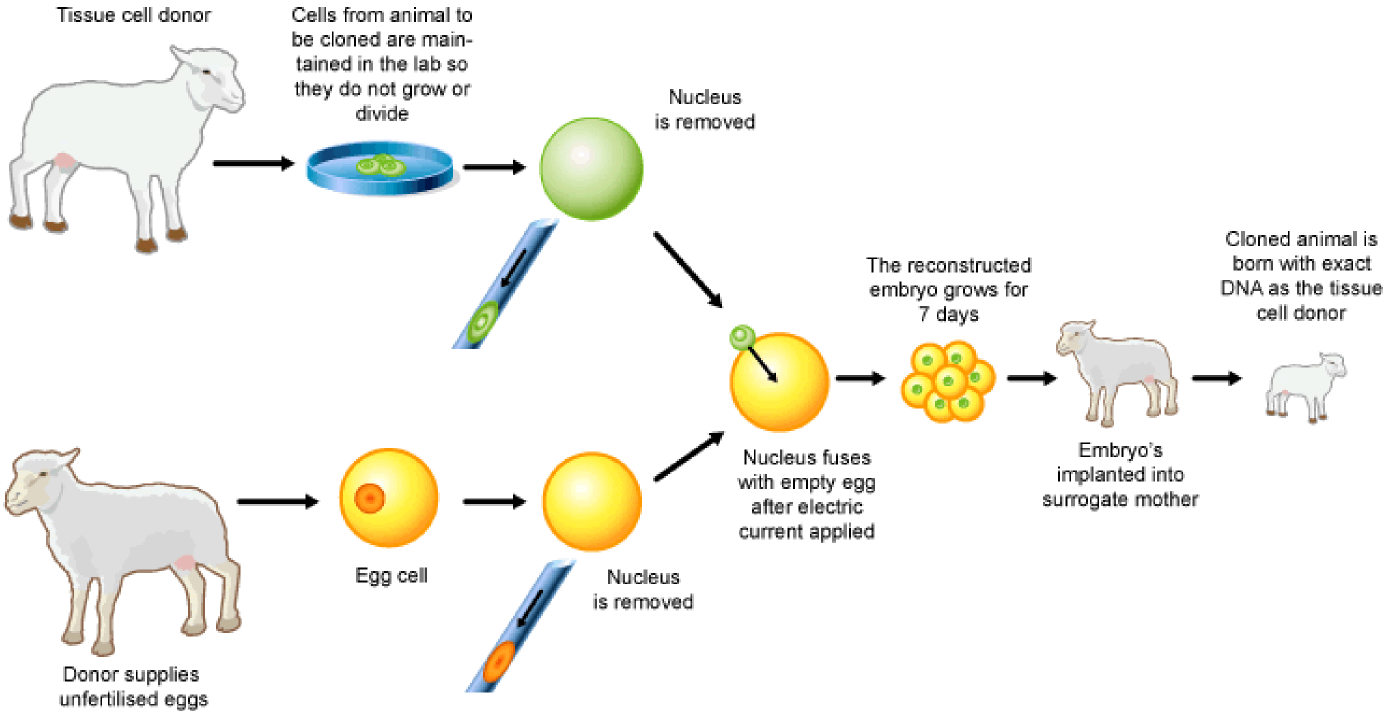
# Anwendung von hES Zellen in der Biomedizin



# Therapeutisches Klonen



# Klonen



Tissue cell donor
Cells from animal to be cloned are maintained in the lab so they do not grow or divide
Nucleus is removed
The reconstructed embryo grows for 7 days
Cloned animal is born with exact DNA as the tissue cell donor
Nucleus fuses with empty egg after electric current applied
Embryo's implanted into surrogate mother
Egg cell
Nucleus is removed
Donor supplies unfertilised eggs

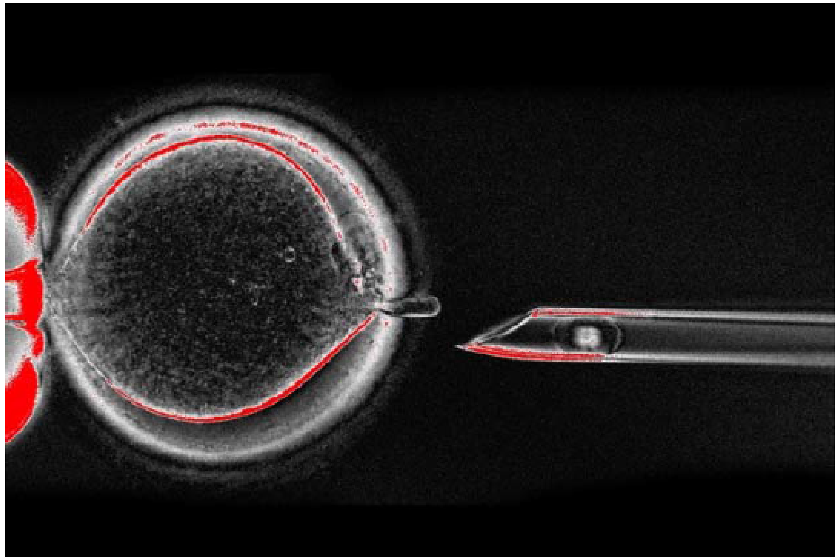
*NATURE* | NEWS

# UK moves closer to allowing ‘three-parent’ babies

**Scientists say mitochondrial-replacement therapy is ready for tests in the clinic.**

**Ewen Callaway**

30 November 2016



*Center for Embryonic Cell and Gene Therapy of Oregon Health & Science Univ.*

A pipette pulls out the nuclear genetic material from an unfertilized egg — a step in mitochondrial-

# Bekämpfung von Krankheiten

Anmelden

GESUNDHEIT

Schlagzeilen | Wetter | DAX 11.565,87 | TV-Programm | Abo

Nachrichten > Gesundheit > Schwangerschaft & Kind > Künstliche Befruchtung > Ukraine: Baby mit drei Eltern geboren

Ukraine

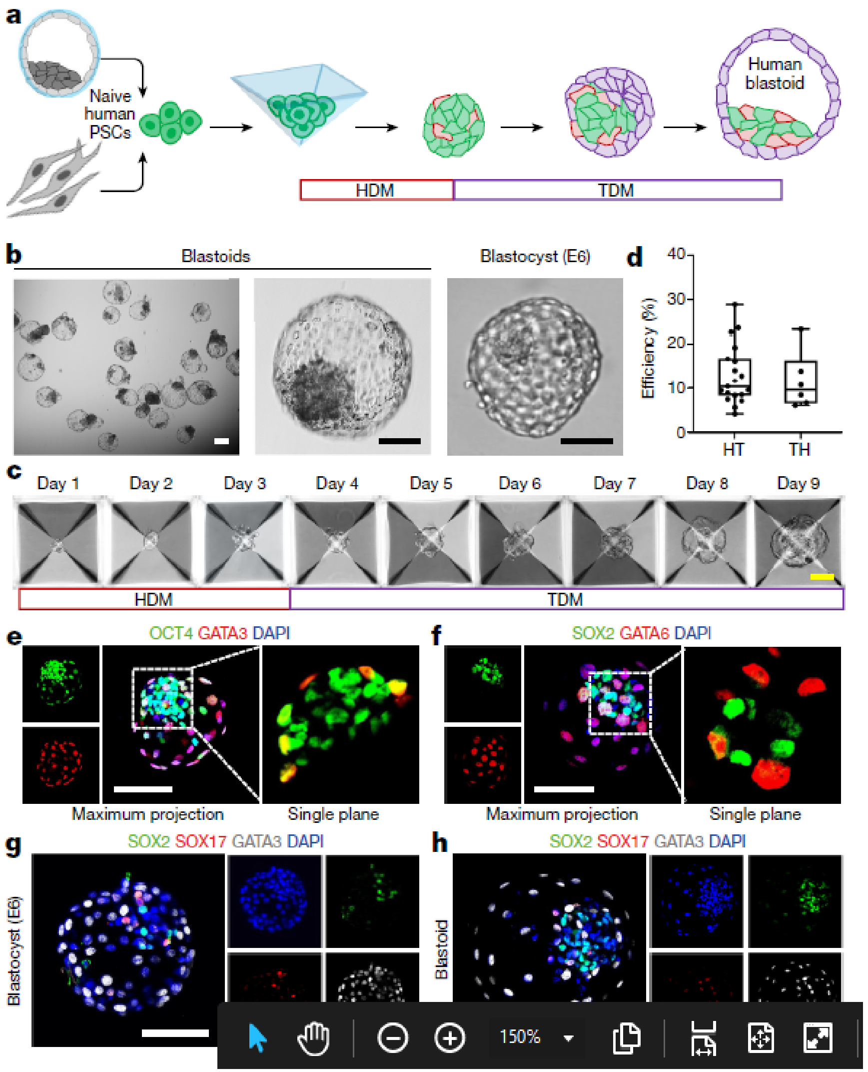
## Baby mit drei Eltern geboren

**In der Ukraine ist ein Baby mit zwei Müttern und einem Vater geboren worden. Alle drei Elternteile sind mit dem Kind genetisch verwandt. Kritiker sind entsetzt.**

imago

Künstliche Befruchtung: Mit einer Pipette wird ein Spermium in eine Eizelle injiziert

# Blastozystenähnliche Strukturen aus menschlichen pluripotenten Stammzellen




Aus Yu et al. Nature, 2021

# Porcine germline genome engineering

Luhan Yang[a,1], George Church[b,1], Hong-Ye Zhao[c], Lusheng Huang[d], Yangbin Gao[a], Hong-Jiang Wei[c], and Geoffrey Yang[e]

[a]Department of Research and Development, Qihan Bio Inc., Hangzhou, Zhejiang 311200, China; [b]Department of Genetics, Harvard Medical School, Boston, MA 02115; [c]Key Laboratory of Animal Gene Editing and Animal Cloning in Yunnan Province, Yunnan Agricultural University, Kunming 650201, China; [d]State Key Laboratory of Pig Genetic Improvement and Production Technology, Jiangxi Agricultural University, Nanchang, Jiangxi 330045, China; and [e]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115

Edited by Dana Carroll, University of Utah, Salt Lake City, UT, and approved September 29, 2020 (received for review March 26, 2020)

Crispr/Cas

An early human embryo, the focus of controversy.

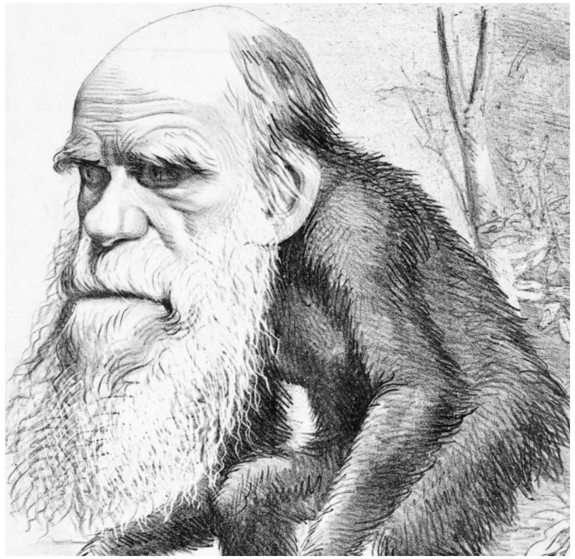
BIOETHICS

# Embryo engineering alarm

Researchers call for restraint in genome editing

# Chimären: Zusammengesetzte Lebewesen





# Chimären in der Kunst

ANNUAL REVIEWS

*Annual Review of Cell and Developmental Biology*

# Lessons from Interspecies Mammalian Chimeras

Fabian Suchy[1] and Hiromitsu Nakauchi[1,2]

[1]Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine, Stanford, California 94305; email: nakauchi@stanford.edu

[2]Division of Stem Cell Therapy, Institute of Medical Science, University of Tokyo, Tokyo 108-0071, Japan

2016

Bourret *et al. Stem Cell Research & Therapy* (2016) 7:87
DOI 10.1186/s13287-016-0345-9

Stem Cell Research & Therapy

REVIEW Open Access

CrossMark

# Human–animal chimeras: ethical issues about farming chimeric animals bearing human organs

Rodolphe Bourret[1], Eric Martinez[1], François Vialla[2], Chloé Giquel[1], Aurélie Thonnat-Marin[1] and John De Vos[3,4,5*]

nature › news › article

NEWS · 26 JULY 2019

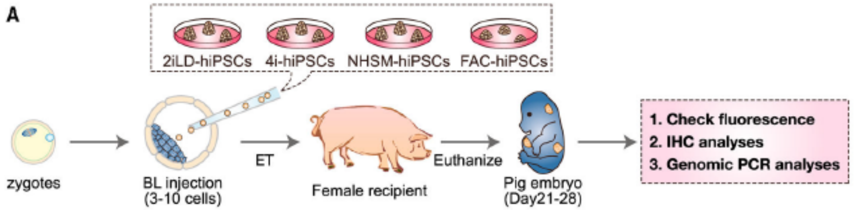
# Japan approves first human-animal embryo experiments

The research could eventually lead to new sources of organs for transplant, but ethical and technical hurdles need to be overcome.

David Cyranoski

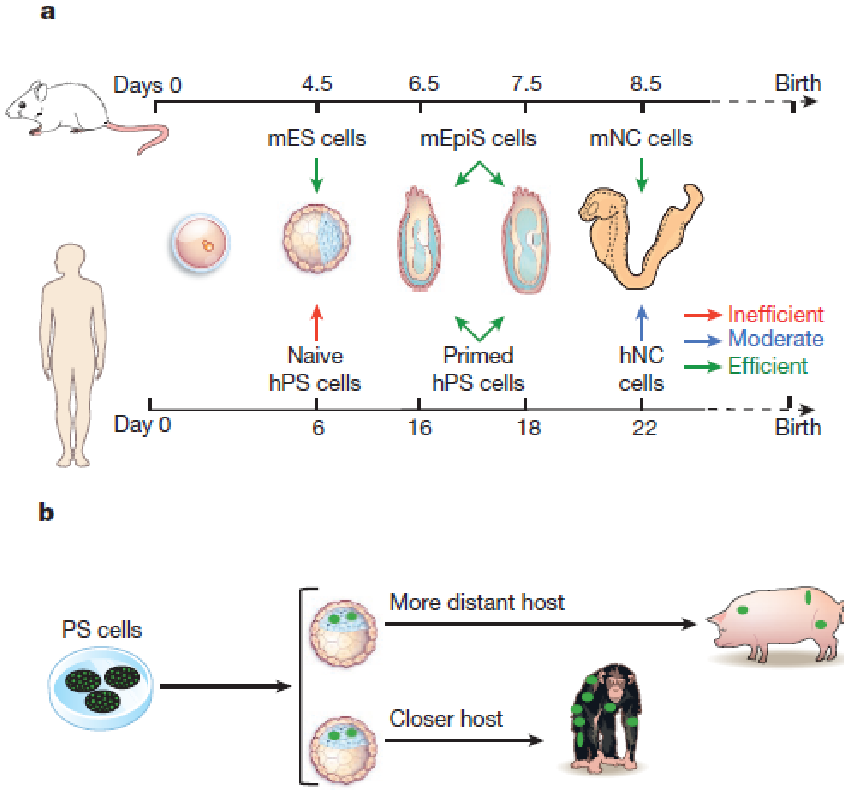
2019

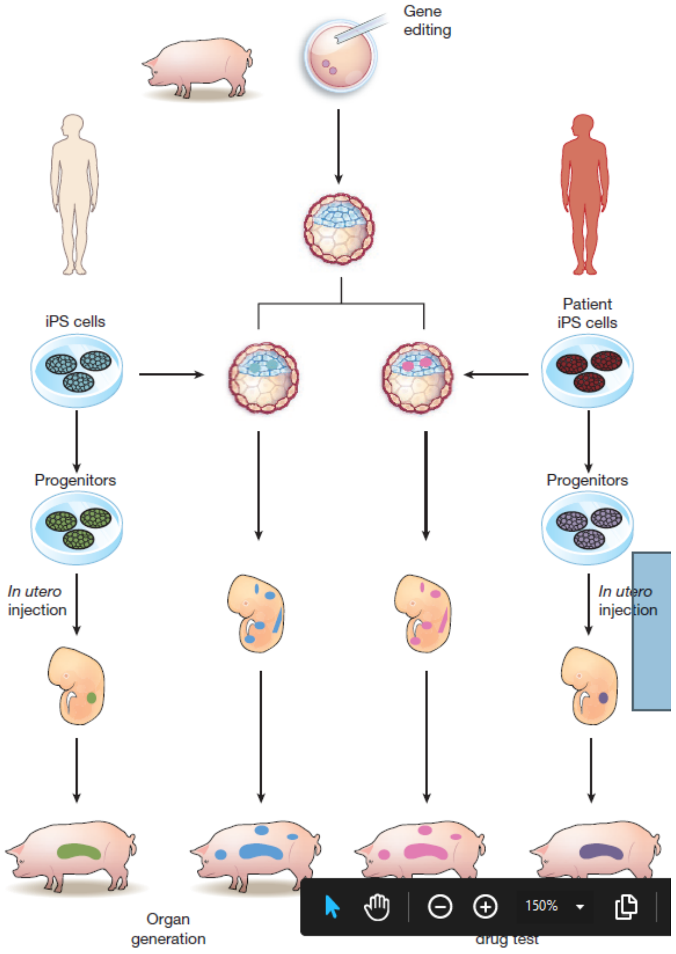
# Strategien um die Entwicklung von Mensch/Tier Chimären zu verbessern




B

| Cell line | Blastocyst origin | Total Normal size |
|---|---|---|
| 2iLD | Morula/EB | 6 |
| | 2C | 5 |
| | ZG | 2 |
| | subtotal | 13 |
| FAC | BI | 20 |
| | 2C | 9 |
| | 2C | 7 |
| | 2C | 7 |
| | ZG | 0 |
| | ZG | 2 |
| | PT | 2 |
| | subtotal | 47 |
| 4i | ZG | 6 |
| | ZG | 6 |
| | ZG | 2 |
| | subtotal | 14 |
| NHSM | ZG | 1 |
| | 2C | 4 |
| | 2C | 10 |
| | 2C | 8 |
| | PT | 2 |
| | subtotal | 25 |
| Total | | 99 |
| Non-injected | | 17 |


## Porcine germline genome engineering

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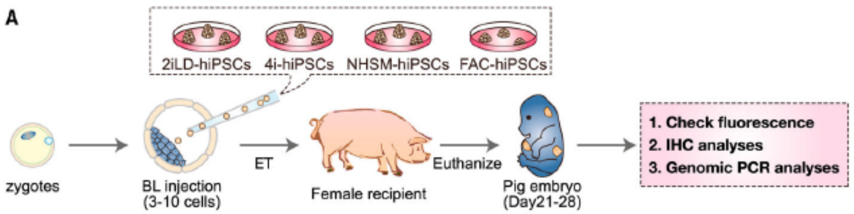
aus Wu et al., Nature, 2016

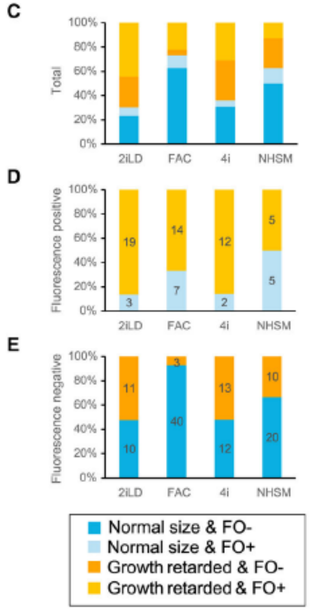
# Manipulation des Schweinegenoms

A




B

| Cell line | Blastocyst origin | Total: Normal size | Total: Growth retarded | Fluorescence positive (FO+): Normal size | Fluorescence positive (FO+): Growth retarded |
|---|---|---|---|---|---|
| 2iLD | Morula/EB | 6 | 13 | 1 | 8 |
| | 2C | 5 | 0 | 2 | 0 |
| | ZG | 2 | 17 | 0 | 11 |
| | subtotal | 13 | 30 | 3 | 19 |
| FAC | Bl | 20 | 6 | 3 | 5 |
| | 2C | 9 | 4 | 3 | 4 |
| | 2C | 7 | 2 | 0 | 2 |
| | 2C | 7 | 1 | 0 | 1 |
| | ZG | 0 | 1 | 0 | 0 |
| | ZG | 2 | 0 | 0 | 0 |
| | PT | 2 | 3 | 1 | 2 |
| | subtotal | 47 | 17 | 7 | 14 |
| 4i | ZG | 6 | 6 | 0 | 1 |
| | ZG | 6 | 13 | 1 | 5 |
| | ZG | 2 | 6 | 1 | 6 |
| | subtotal | 14 | 25 | 2 | 12 |
| NHSM | ZG | 1 | 6 | 0 | 4 |
| | 2C | 4 | 2 | 1 | 0 |
| | 2C | 10 | 3 | 2 | 0 |
| | 2C | 8 | 3 | 1 | 1 |
| | PT | 2 | 1 | 1 | 0 |
| | subtotal | 25 | 15 | 5 | 5 |
| Total | | **99** | **87** | **17** | **50** |
| Non-injected | | 17 | 0 | 0 | 0 |

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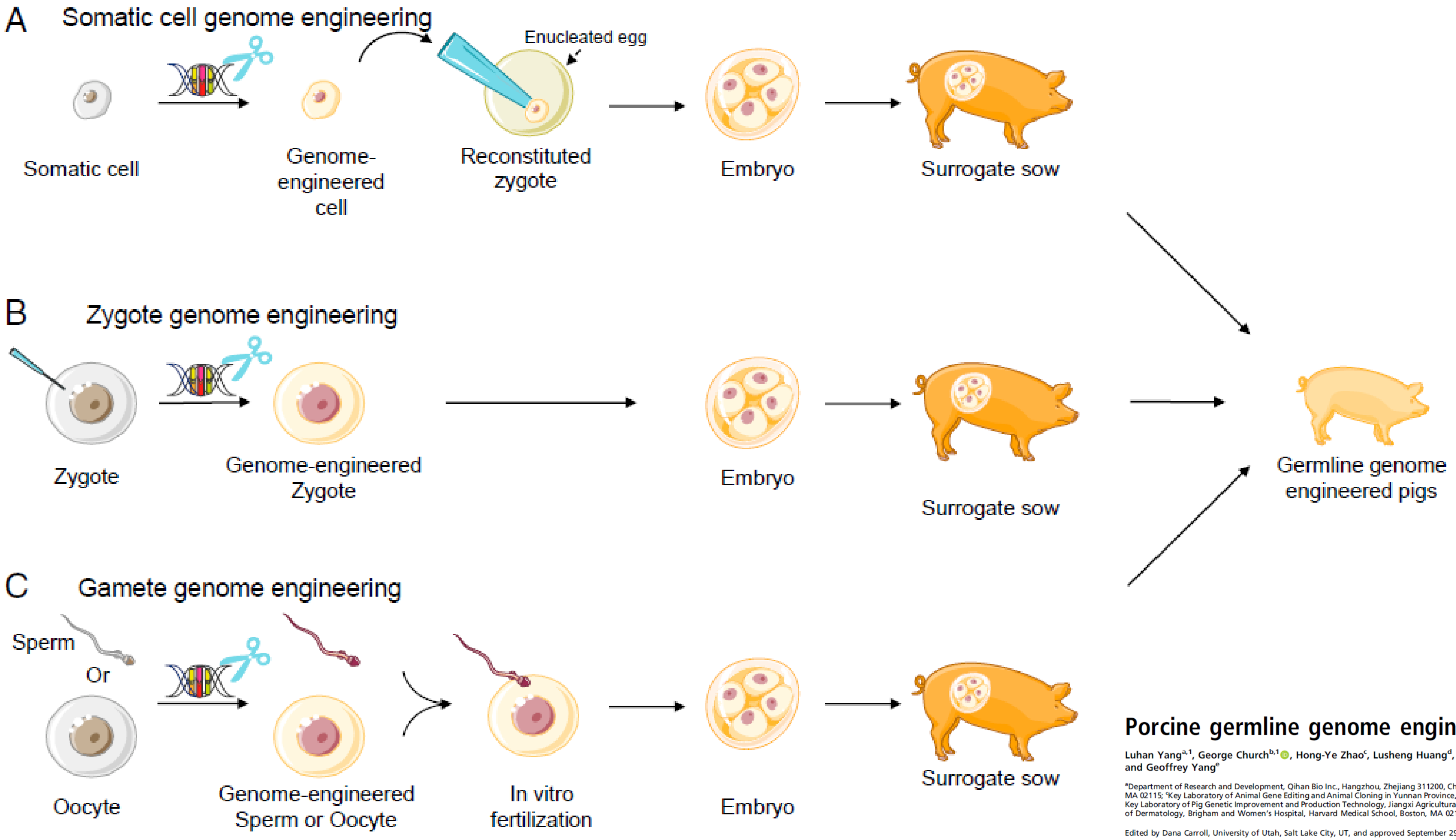
2020

# Genmanipulierte Schweine für die Xenotransplantation




**Porcine germline genome engineering**

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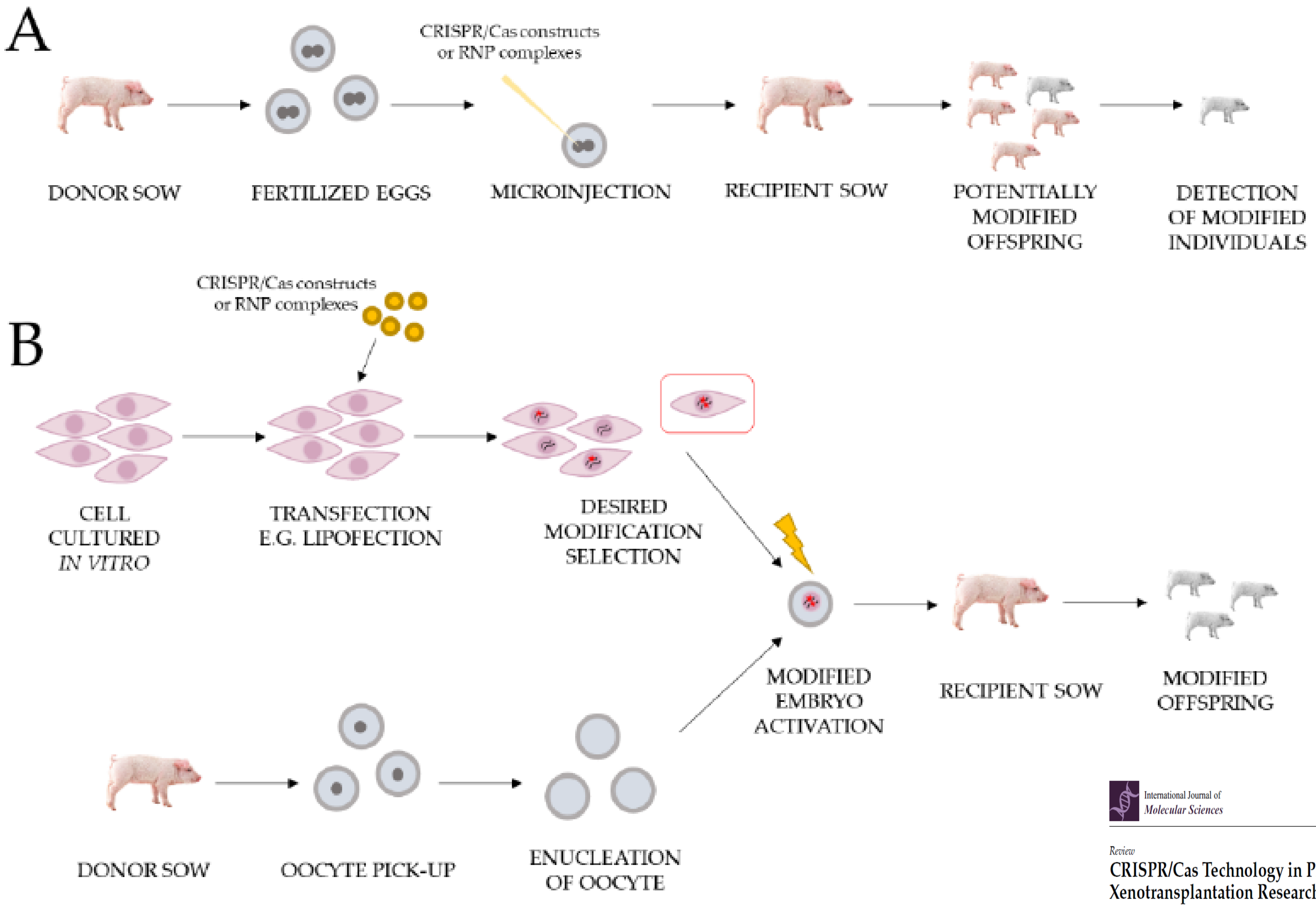



International Journal of Molecular Sciences
MDPI
Review
CRISPR/Cas Technology in Pig-to-Human Xenotransplantation Research
Natalia Ryczek [1,*], Magdalena Hryhorowicz [2], Joanna Zeyland [2], Daniel Lipiński [2] and Ryszard Słomski [3]

2021

# Affen/Mensch Chimären

2018

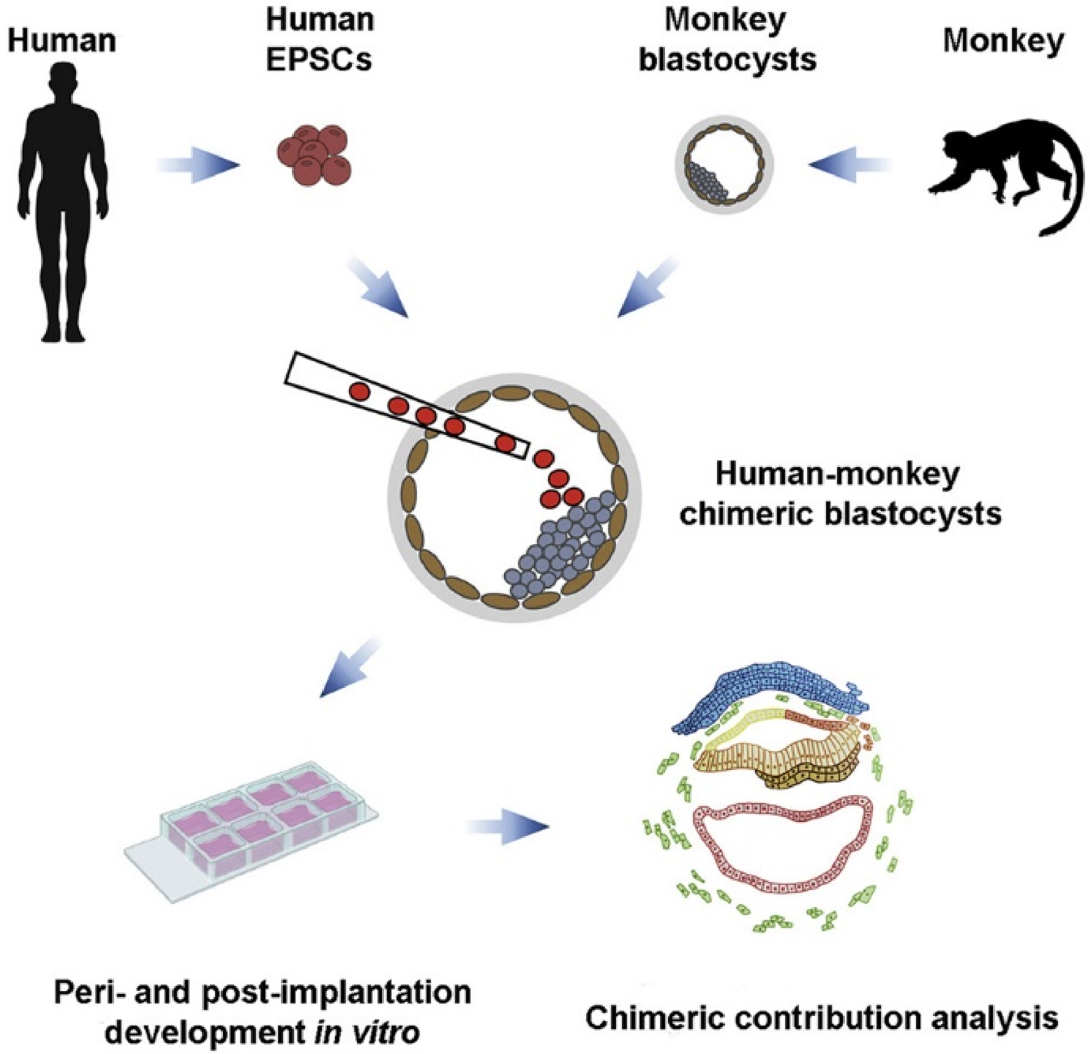
STEM CELLS AND DEVELOPMENT
Volume 27, Number 23, 2018

DOI: 10.1089/scd.2018.0162

CONCISE REVIEW

Human–Monkey Chimeras for Modeling Human Disease: Opportunities and Challenges

Alejandro De Los Angeles,[1] Insoo Hyun,[2] Stephen R. Latham,[3]
John D. Elsworth,[1] and D. Eugene Redmond, Jr.[4]



# FIRST MONKEY–HUMAN EMBRYOS SPARK DEBATE OVER HYBRID ANIMALS

The chimaeras lived up to 19 days – but some scientists question the need for such research.

By Nidhi Subbaraman

Scientists have successfully grown monkey embryos containing human cells for the first time – the latest milestone in a rapidly advancing field that has drawn ethical questions.

In the work, published on 15 April in *Cell*[1], the team injected monkey embryos with human stem cells and watched them develop. They observed human and monkey cells divide and grow together in a dish, with at least 3 embryos surviving to 19 days after fertilization. "The overall message is that every embryo contained human cells that proliferate and differentiate to a different extent," says Juan Carlos Izpisua Belmonte, a developmental biologist at the Salk Institute for Biological Studies in La Jolla, California, and a leader of the work.

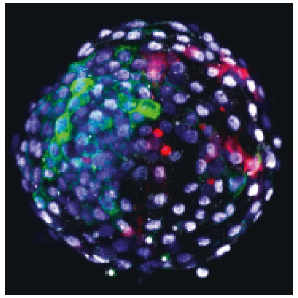
Researchers hope that some human–animal hybrids – known as chimaeras – could provide better models in which to test drugs, and be used to grow human organs for transplants. Members of this research team were the first to show, in 2019, that they could grow monkey embryos in a dish for up to 20 days after fertilization[2]. In 2017, they reported a series of other hybrids: pig embryos grown with human cells, cow embryos grown with human cells, and rat embryos grown with mouse cells[3].

## Touchy subject

The latest work has divided developmental biologists. Some question the need for such experiments using closely related primates – these animals are not likely to be used as model animals in the way that mice and rodents are. Non-human primates are protected by stricter research-ethics rules than are rodents, and biologists worry such work is likely to stoke public opposition.

"There are much more sensible experiments in this area of chimaeras as a source of organs and tissues," says Alfonso Martinez Arias, a developmental biologist at Pompeu Fabra University in Barcelona, Spain. Experiments with livestock animals, such as pigs and cows, are "more promising and do not risk challenging ethical boundaries", he says. "There is a whole field of organoids, which can hopefully do away with animal research."

Izpisua Belmonte says that the team does not intend to implant any hybrid embryos



WEIZHI JI, KUNMING UNIV. SCIENCE AND TECHNOLOGY

The monkey–human blastocyst.

into monkeys. Rather, the goal is to better understand how cells of different species communicate with each other during the embryo's early growth phase.

Attempts at growing human–mouse hybrids are still preliminary, and chimaeras need to be more effective and healthier before they can be useful. Scientists suspect that such hybrids might have trouble thriving because the two species are evolutionarily distant, so the cells

> "Some people may see that you're creating morally ambiguous entities."

communicate through different means. But observing cellular cross-talk in monkey–human embryo chimaeras – which involve two more closely related species – could suggest ways to improve the viability of future human–mouse models, Izpisua Belmonte says.

In the study, researchers fertilized eggs extracted from cynomolgus monkeys (*Macaca fascicularis*) and grew them in culture. Six days after fertilization, the team injected 132 embryos with human extended pluripotent stem cells, which can grow into a range of cell types inside and outside an embryo. The embryos each developed unique combinations of human and monkey cells and deteriorated at varying rates: 11 days after fertilization, 91 were alive; this dropped to 12 embryos at day 17 and 3 embryos at day 19.

"This paper is a dramatic demonstration of the ability of human pluripotent stem cells to be incorporated into the embryos of cynomolgus monkeys when introduced into the monkey blastocysts," says Magdalena Zernicka-Goetz, a developmental biologist at the California Institute of Technology in Pasadena. She noted that this team, like others in the past, was not able to control which cells developed into which tissues – a key step to master before such models can be used.

Martinez Arias was not convinced by the results. "I expect better evidence", especially of the later stages of development, he says. That embryo numbers rapidly plummeted as day 15 of development approached suggests to him "that the things are very sick".

Combining human cells with closely related primate embryos prompts questions about the status and identity of the resulting hybrids. "Some people may see that you're creating morally ambiguous entities there," says Insoo Hyun, a bioethicist at Case Western Reserve University in Cleveland, Ohio. He says this team was thorough in following existing guidelines. "I think they did quite a bit of due care to be mindful of regulations and ethical issues."

## Research restrictions

Meanwhile, international guidelines are catching up to the field's advances – next month, the International Society for Stem Cell Research (ISSCR) is expected to publish revised guidelines for stem-cell research. These will address non-human-primate and human chimaeras, says Hyun, who is leading an ISSCR committee discussing chimaeras. That group's guidelines currently prohibit researchers from letting human–animal chimaeras mate. Also, the group recommends extra oversight when human cells could integrate with an animal host's developing central nervous system.

Many countries – including the United States, the United Kingdom and Japan – have at points limited research on chimaeras involving human cells. Japan lifted its ban on experiments with animal embryos containing human cells in 2019.

In 2015, the US National Institutes of Health (NIH) announced a moratorium on federal funding for studies in which human cells would be injected into animal embryos. In 2016, the funding agency proposed lifting the ban but restricting research to hybrids created after gastrulation, when the early nervous system begins to form. More than four years later, the funding ban is still in place. An NIH spokesperson says the agency is awaiting the May ISSCR update "to ensure our position reflects the input from the community", but did not provide a timeline for release of the agency's rules.

1. Tan, T. et al. Cell **184**, 2020–2032 (2021).
2. Niu, Y. et al. Science **366**, eaaw5754 (2019).
3. Wu, J. et al. Cell **168**, 473–486 (2017).





2021

**Quellen**


Max Planck Institut für ausländisches und internationaler Strafrecht

Dignitas personae

BMBF (biotechnologie.de)

Pro Familia Reproduktives Reisen (BMBF)

Embryonenschutzgesetz (D)

Stammzellengesetz (D)

Human Fertilisation and Embryology Regulations (USA)

Pierre Jouannet Juli 2014; Wie pflanzen wir uns
In Zukunft fort? Mensch 2.0 (Spektrum Spezial);

Jahrbuch 2021, Deutsches IVF Register

Nature, Science und angegebene Publikationen

www.statista.com