



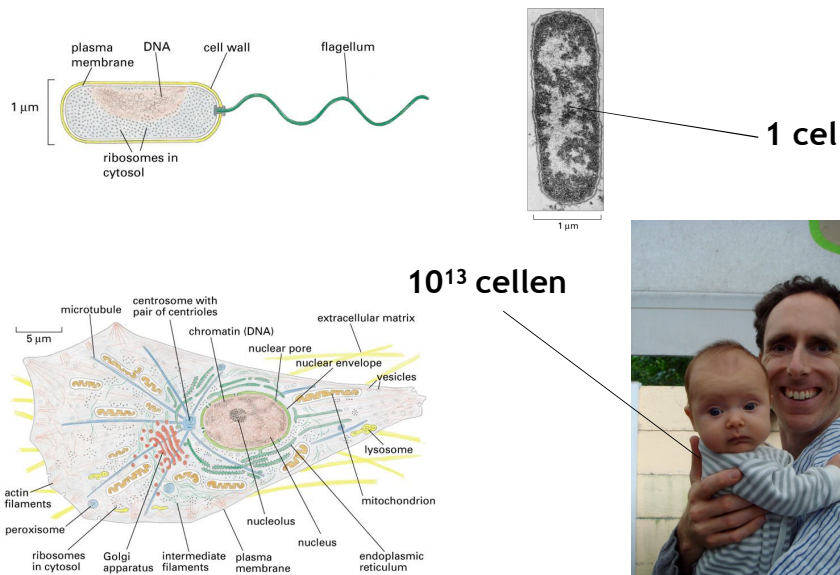
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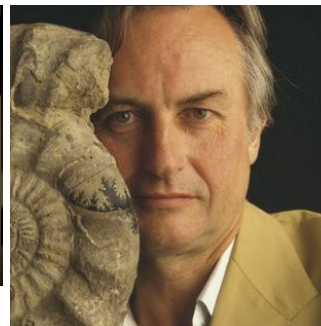
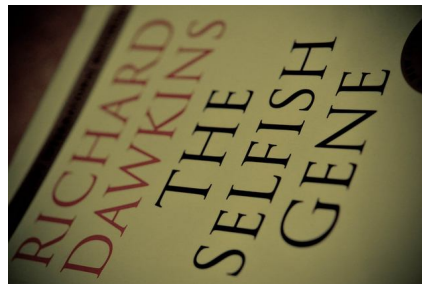
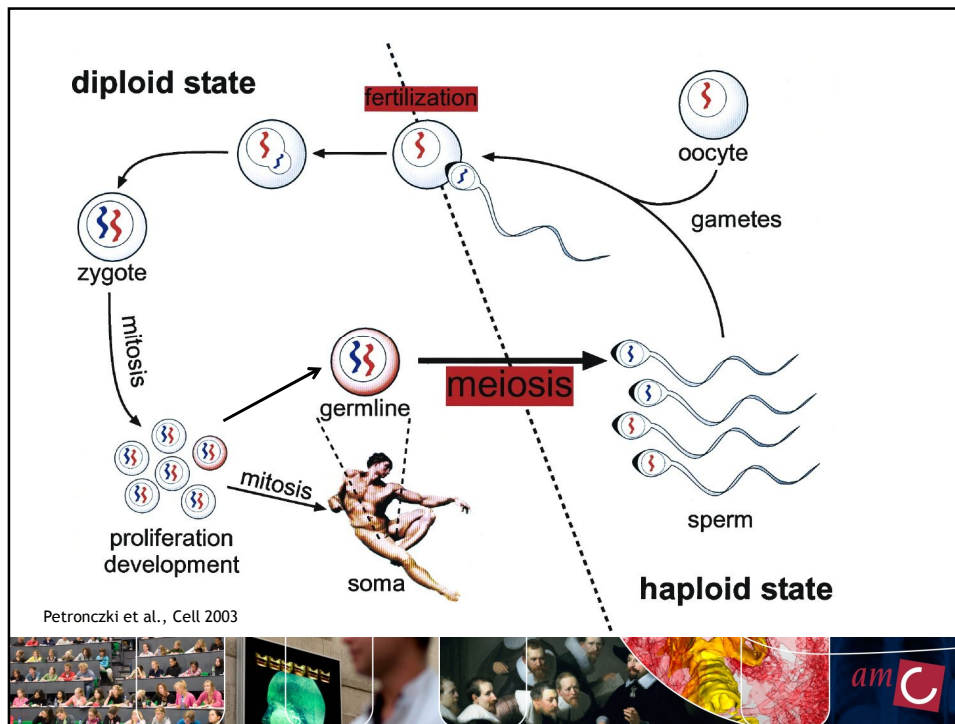
am  *center for reproductive medicine*

Genetic modification of gametes and embryos

Geert Hamer, PhD

Reproductive Biology Laboratory
Center for Reproductive Medicine
Research Theme Reproduction and Development
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Richard Dawkins, *The selfish gene* 1976.

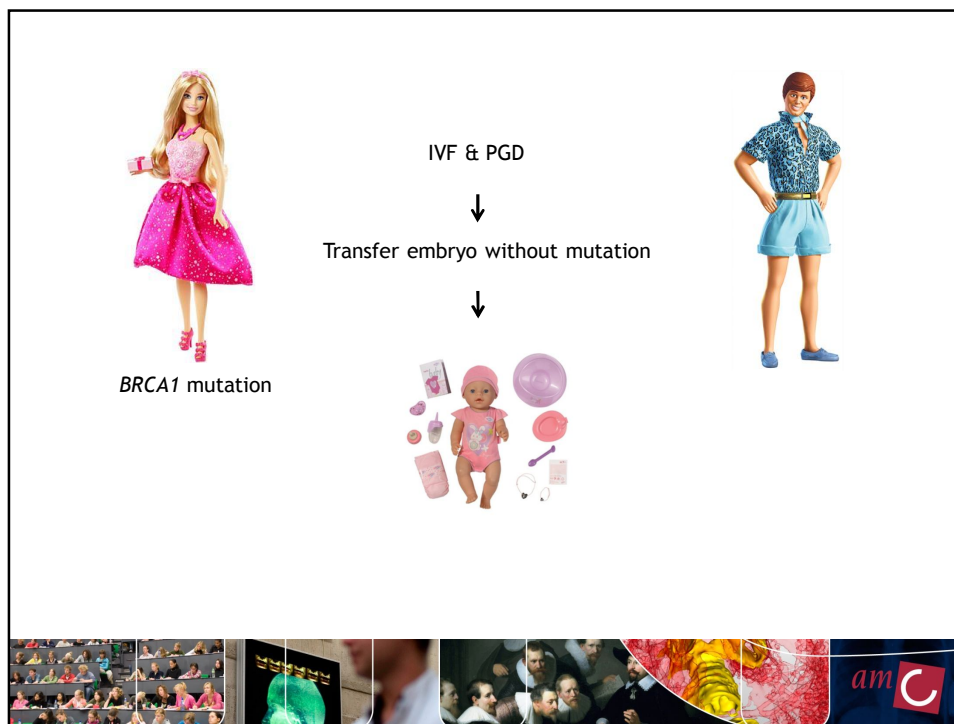
Thomas Kirkwood, *Disposable soma theory*, 1977.

They are the only cells that biology really cares about,
Ralph Brinster about germ cells, 2012



Honey, I have a genetic disease ...





Protein Cell 2015, 6(5):363–372
DOI 10.1007/s13238-015-0153-5

 CrossMark **Protein & Cell**

RESEARCH ARTICLE

CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes

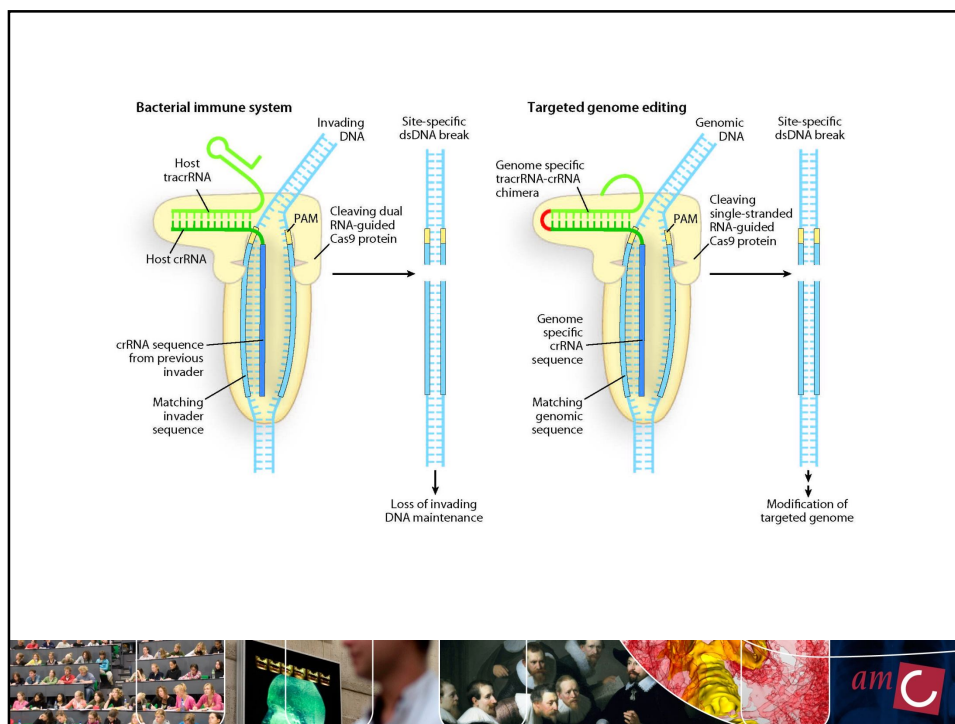
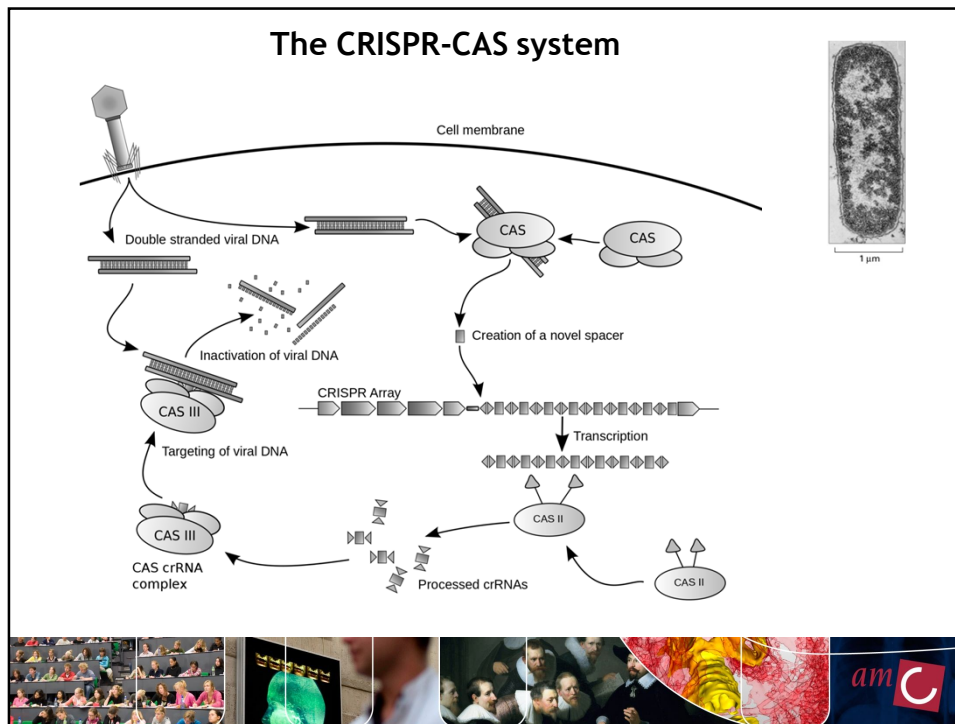
Puping Liang, Yanwen Xu, Xiya Zhang, Chenhui Ding, Rui Huang, Zhen Zhang, Jie Lv, Xiaowei Xie, Yuxi Chen, Yujing Li, Ying Sun, Yaofu Bai, Zhou Songyang, Wenbin Ma, Canquan Zhou[✉], Junjiu Huang[✉]

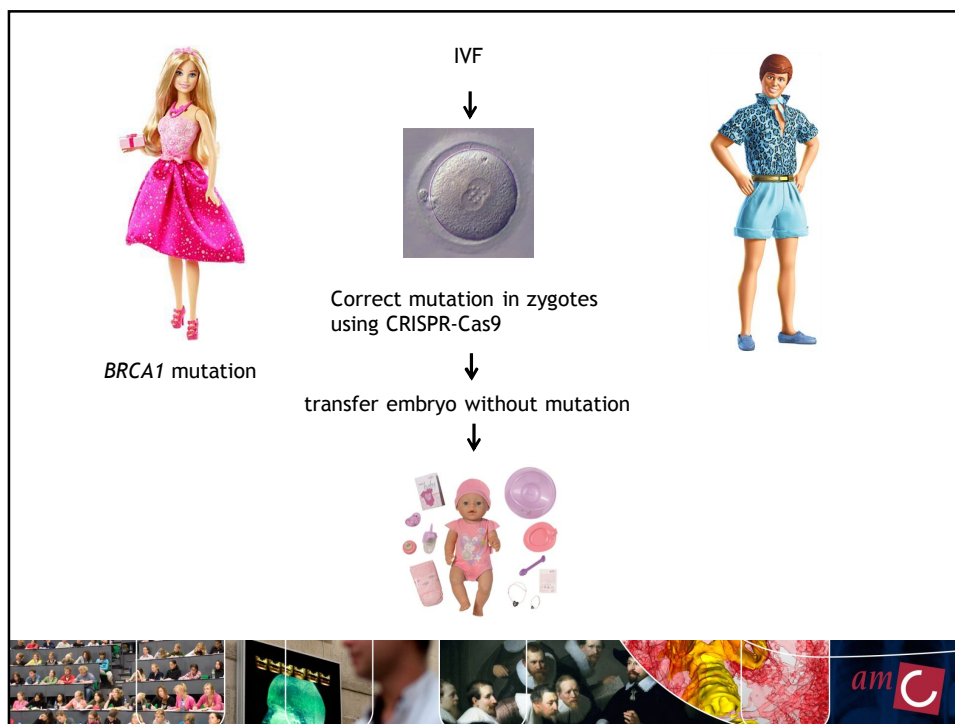
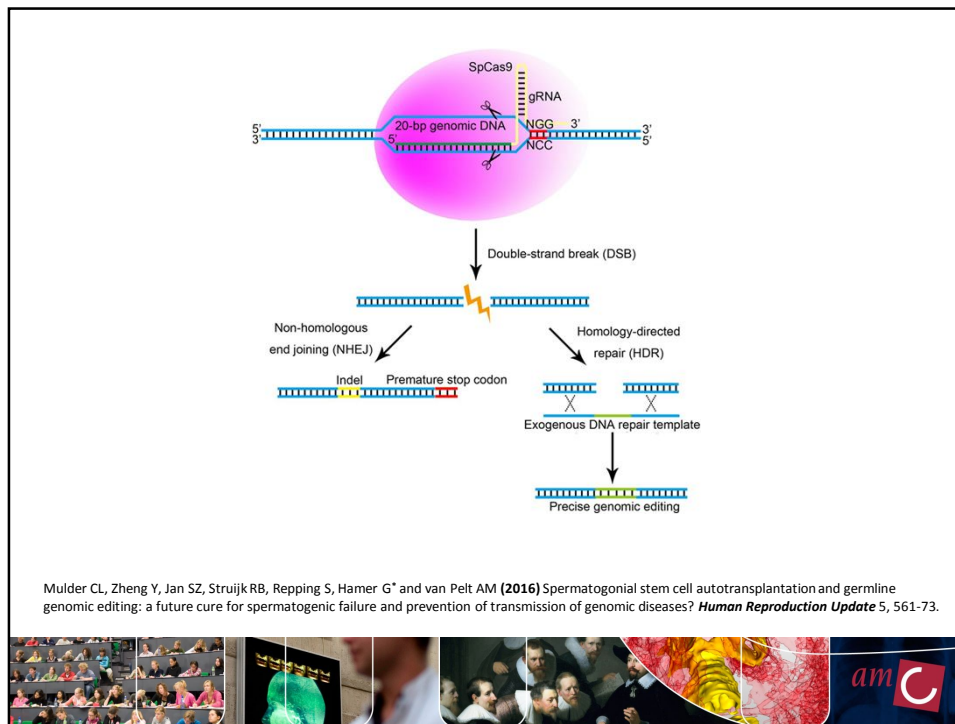
Guangdong Province Key Laboratory of Reproductive Medicine, the First Affiliated Hospital, and Key Laboratory of Gene Engineering of the Ministry of Education, School of Life Sciences, Sun Yat-sen University, Guangzhou 510275, China

✉ Correspondence: hjunjiu@mail.sysu.edu.cn (J. Huang), zhoucanquan@hotmail.com (C. Zhou)

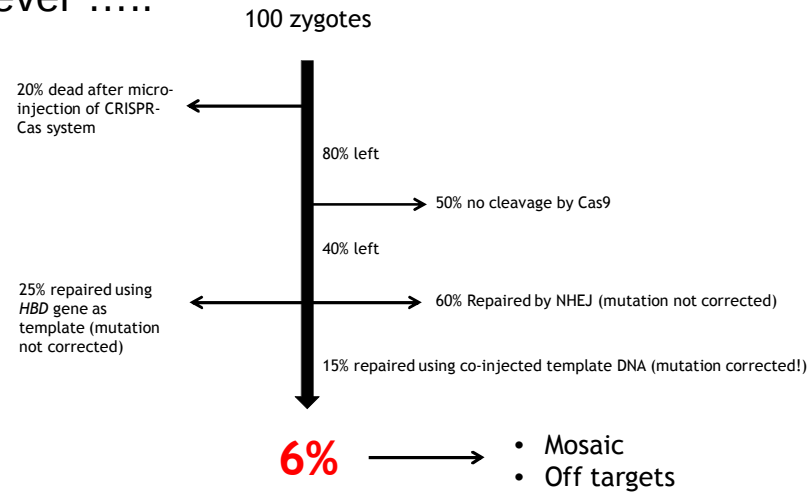
Received March 30, 2015 Accepted April 1, 2015







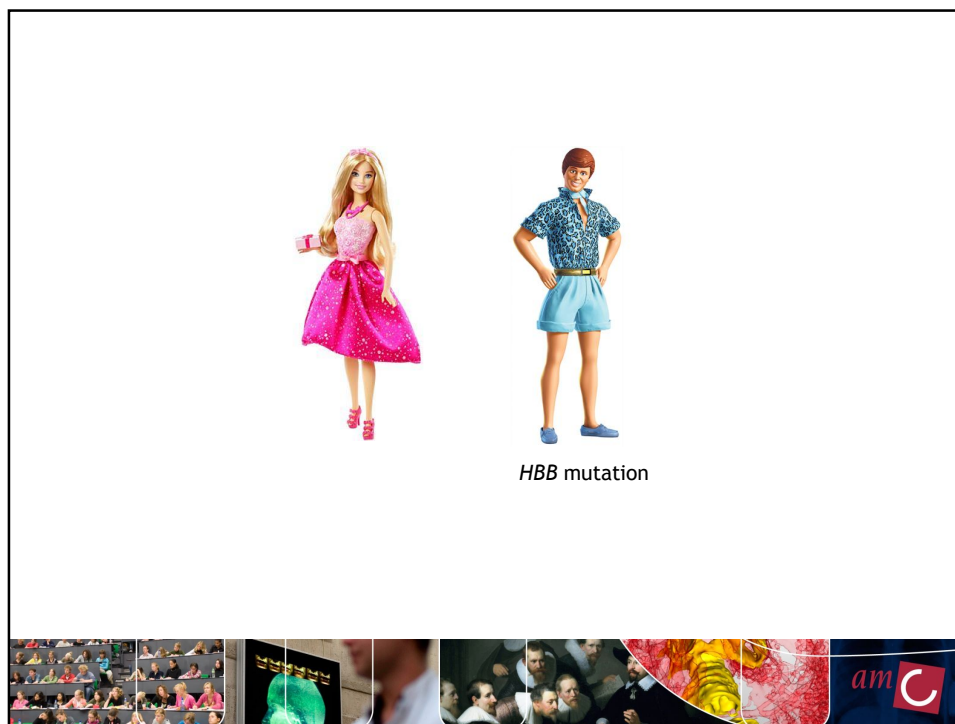
However



Moreover

PGD will be needed to identify and characterize the corrected embryos!!!





Targeted Germline Modifications in Rats Using CRISPR/Cas9 and Spermatogonial Stem Cells

Karen M. Chapman,¹ Gerardo A. Medrano,¹ Priscilla Jaichander,¹ Jaideep Chaudhary,¹ Alexandra E. Waits,¹

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<http://dx.doi.org/10.1016/j.celrep.2015.02.040>

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ORIGINAL ARTICLE

Cell Research (2015) 25:67-79.

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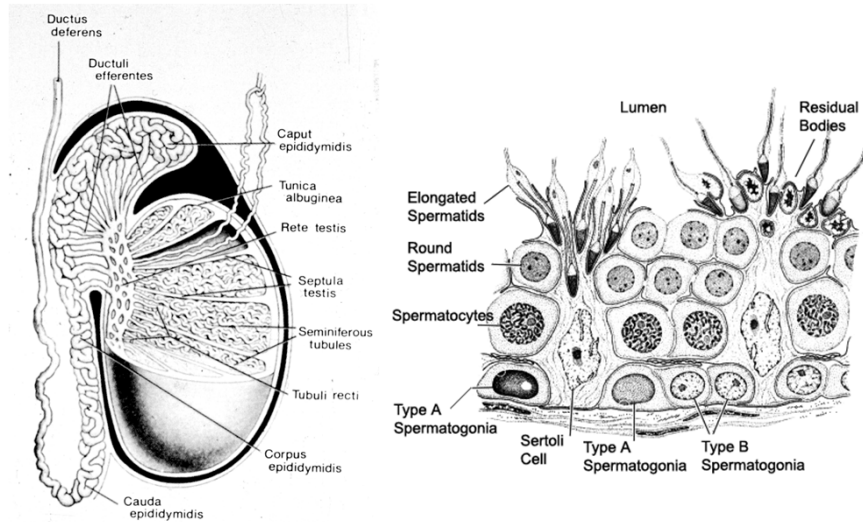


Correction of a genetic disease by CRISPR-Cas9-mediated gene editing in mouse spermatogonial stem cells

Yuxuan Wu^{1,2,*}, Hai Zhou^{1,2,3,*}, Xiaoying Fan^{4,*}, Ying Zhang^{2,5,*}, Man Zhang^{1,2,*}, Yinghua Wang^{1,2}, Zhenfei Xie^{1,2},
Meizhu Bai^{1,2,6}, Qi Yin^{1,2}, Dan Liang^{1,2}, Wei Tang¹, Jiaoyang Liao^{1,2}, Chikai Zhou^{1,2}, Wujuan Liu^{1,2}, Ping Zhu¹,
Hongshan Guo¹, Hong Pan^{1,2}, Chunlian Wu¹, Huijuan Shi¹, Ligang Wu^{2,5}, Fuchou Tang¹, Jinsong Li^{1,2,6}



Spermatogenesis



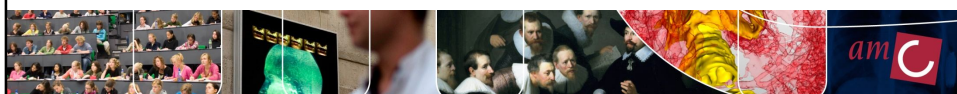
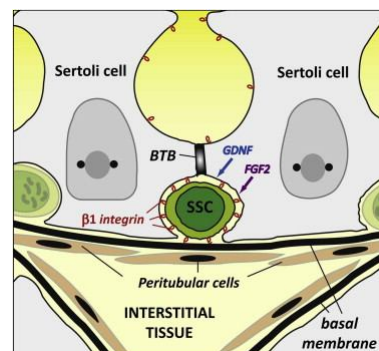
Spermatogonial stem cells

Daily Sperm Production
 $\pm 50-100 \times 10^6 = 1000/\text{sec}$

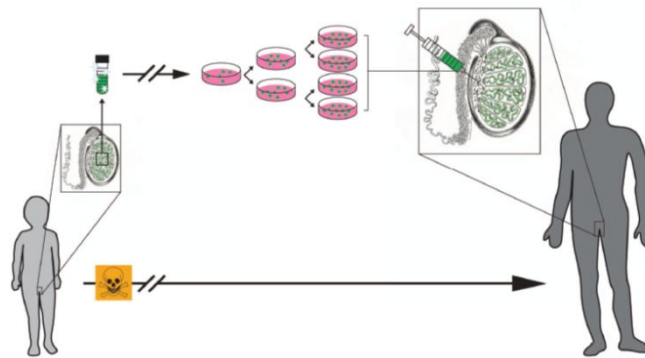
0.03 % of all germ cells

Spermatogonial stem cells form a basis for life long spermatogenesis

Balance between self-renewal and differentiation

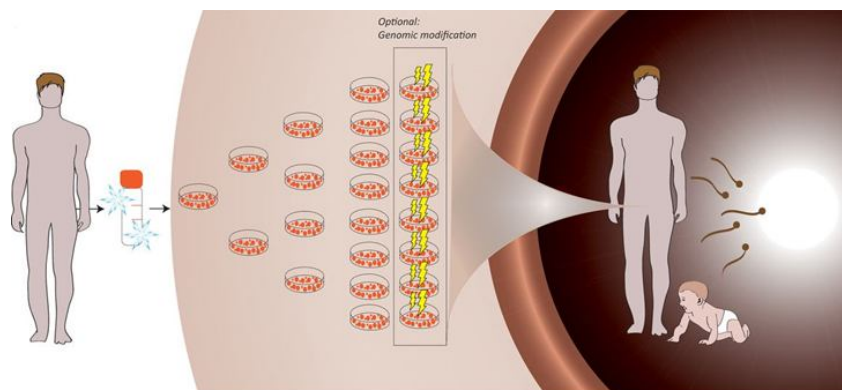


Fertility preservation for boys undergoing gonadotoxic cancer treatment

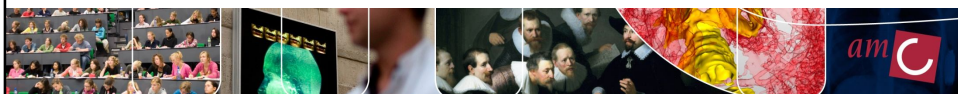


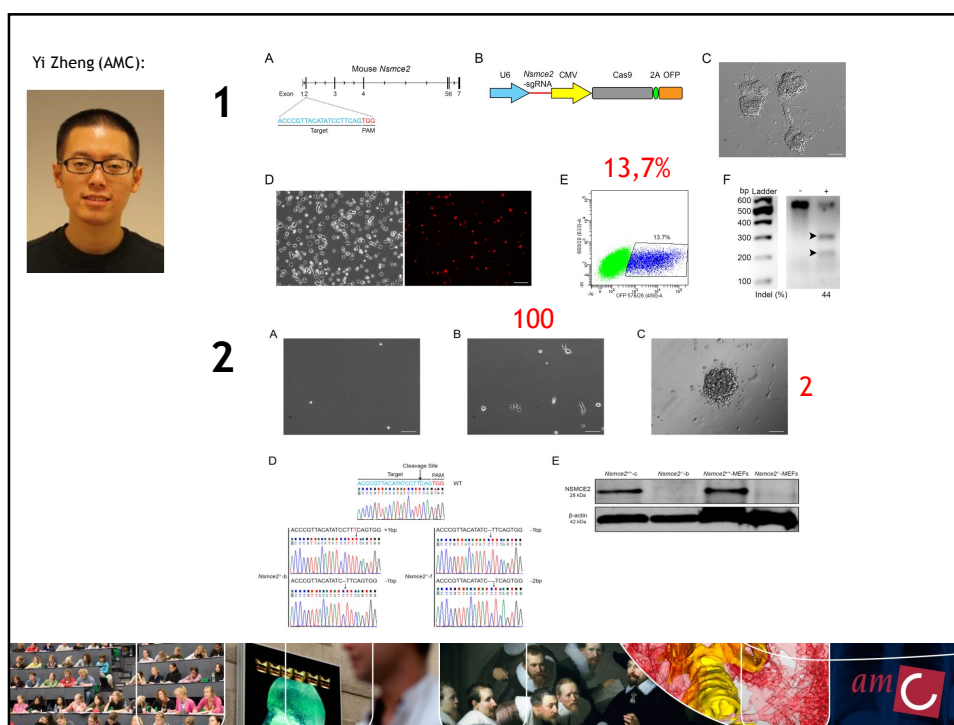
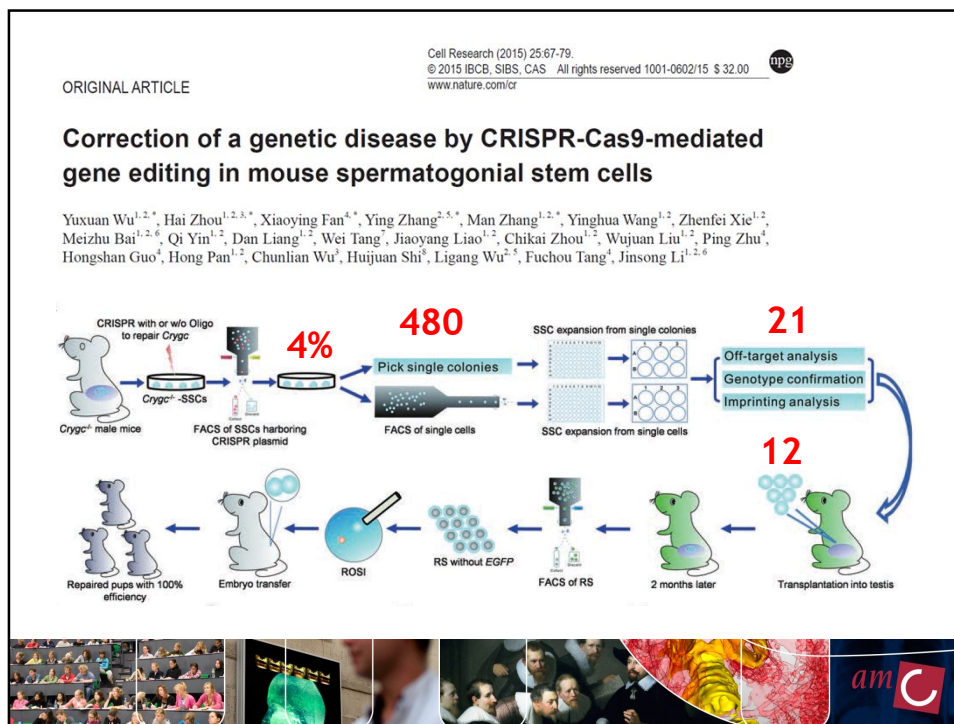
Sadri-Ardekani et al., JAMA 302, 2127, 2009

Sadri-Ardekani et al., JAMA 305, 2416, 2011



Mulder CL, Zheng Y, Jan SZ, Struijk RB, Repping S, Hamer G* and van Pelt AM (2016) Spermatogonial stem cell autotransplantation and germline genomic editing: a future cure for spermatogenic failure and prevention of transmission of genomic diseases? *Human Reproduction Update* 5, 561-73.








HBB mutation



- Culture spermatogonia from testis biopsy
- Correct mutation, screen colonies
- Autotransplantation
- Fertilize Barbie

















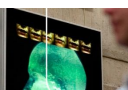




HBB mutation



- Culture spermatogonia from testis biopsy
- Correct mutation, screen colonies
- **Remove Ken's remaining germ cells !!!**
- Autotransplantation
- Fertilize Barbie **(or ICSI)**




















Targeted Germline Modifications in Rats Using CRISPR/Cas9 and Spermatogonial Stem Cells

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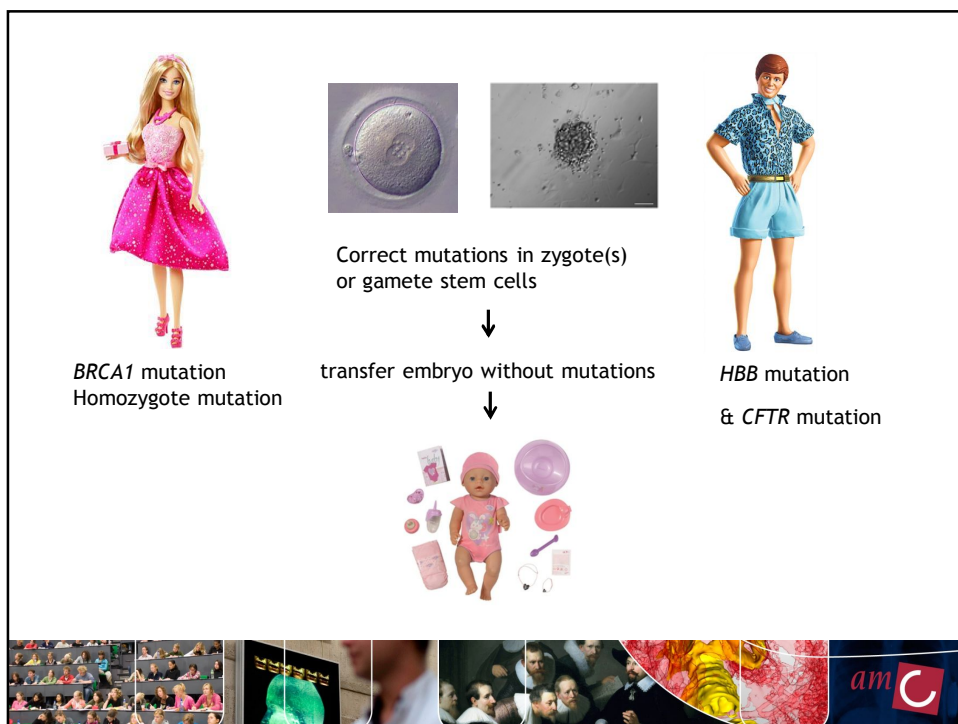


Correction of a genetic disease by CRISPR-Cas9-mediated gene editing in mouse spermatogonial stem cells

Yuxuan Wu^{1,2,*}, Hai Zhou^{1,2,3,*}, Xiaoying Fan^{4,*}, Ying Zhang^{2,5,*}, Man Zhang^{1,2,*}, Yinghua Wang^{1,2}, Zhenfei Xie^{1,2}, Meizhu Bai^{1,2,6}, Qi Yin^{1,2}, Dan Liang^{1,2}, Wei Tang¹, Jiaoyang Liao^{1,2}, Chikai Zhou^{1,2}, Wujuan Liu^{1,2}, Ping Zhu¹, Hongshan Guo¹, Hong Pan^{1,2}, Chunlian Wu¹, Huijuan Shi¹, Ligang Wu^{2,5}, Fuchou Tang⁴, Jinsong Li^{1,2,6}



But we will of course solve all these problems





Complete Meiosis from Embryonic Stem Cell-Derived Germ Cells In Vitro

Quan Zhou,^{1,2,8} Mei Wang,^{2,3,8} Yan Yuan,^{1,2,8} Xuepeng Wang,^{2,4} Rui Fu,² Haifeng Wan,² Mingming Xie,^{2,5} Mingxi Liu,¹ Xuejiang Guo,¹ Ying Zheng,⁶ Guihai Feng,² Qinghua Shi,⁷ Xiao-Yang Zhao,^{2,8,*} Jiahao Sha,^{1,*} and Qi Zhou^{2,8}

¹State Key Laboratory of Reproductive Medicine, Department of Histology and Embryology, Nanjing Medical University, Nanjing 210029, China

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⁶Department of Histology and Embryology, Medical College of Yangzhou University, Yangzhou 225001, Jiangsu, China

⁷Molecular and Cell Genetics Laboratory, Chinese Academy of Sciences Key Laboratory of Innate Immunity and Chronic Disease, Hefei National Laboratory for Physical Sciences at Microscale and School of Life Sciences, University of Science and Technology of China, Hefei 230027, China

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*Correspondence: qzhou@ioz.ac.cn (Q.Z.), shajh@njmu.edu.cn (J.S.), zhaoxiaoyang@smu.edu.cn (X.-Y.Z.)
<http://dx.doi.org/10.1016/j.stem.2016.01.017>

LETTER

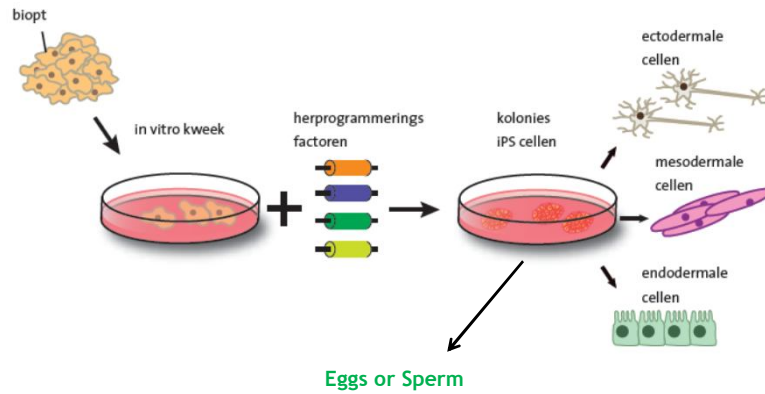
doi:10.1038/nature20104

Reconstitution *in vitro* of the entire cycle of the mouse female germ line

Orie Hikabe^{1,*}, Nobuhiko Hamazaki¹, Go Nagamatsu¹, Yayoi Obata², Yuji Hirao³, Norio Hamada^{1,4}, So Shimamoto¹, Takuya Imamura¹, Kinichi Nakashima¹, Mitinori Saitou^{5,6,7,8} & Katsuhiko Hayashi^{1,9,*}



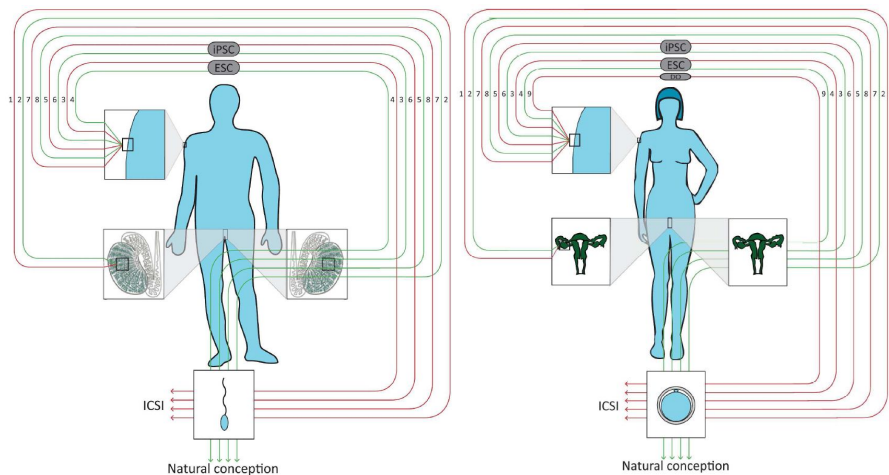
Induced Pluripotent Stem Cells



Bernard Roelen (2016) cahier "Stamcellen", published by Biowetenschappen en Maatschappij.



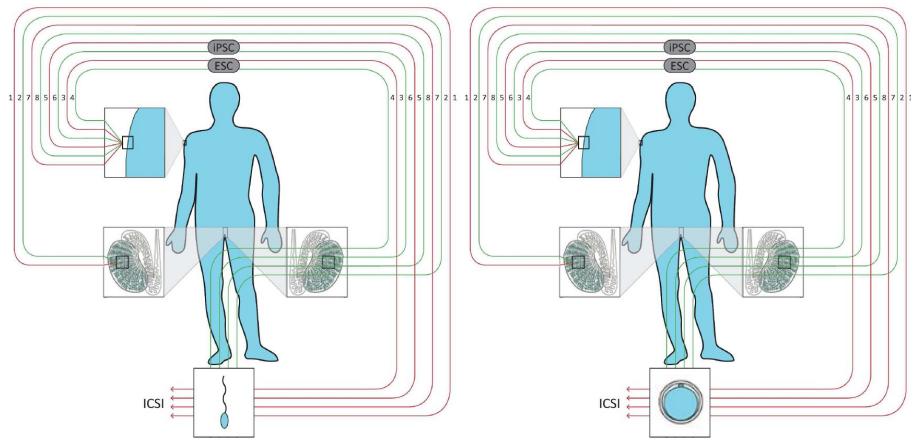
Artificial gametes



Hendriks S, Dancet EA, van Pelt AM, Hamer G and Repping S (2015) Artificial Gametes: a systematic review of biological progress. *Human Reproduction Update* 3, 285-296.



Artificial gametes



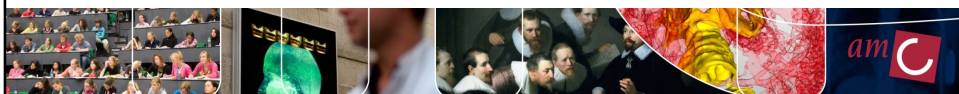
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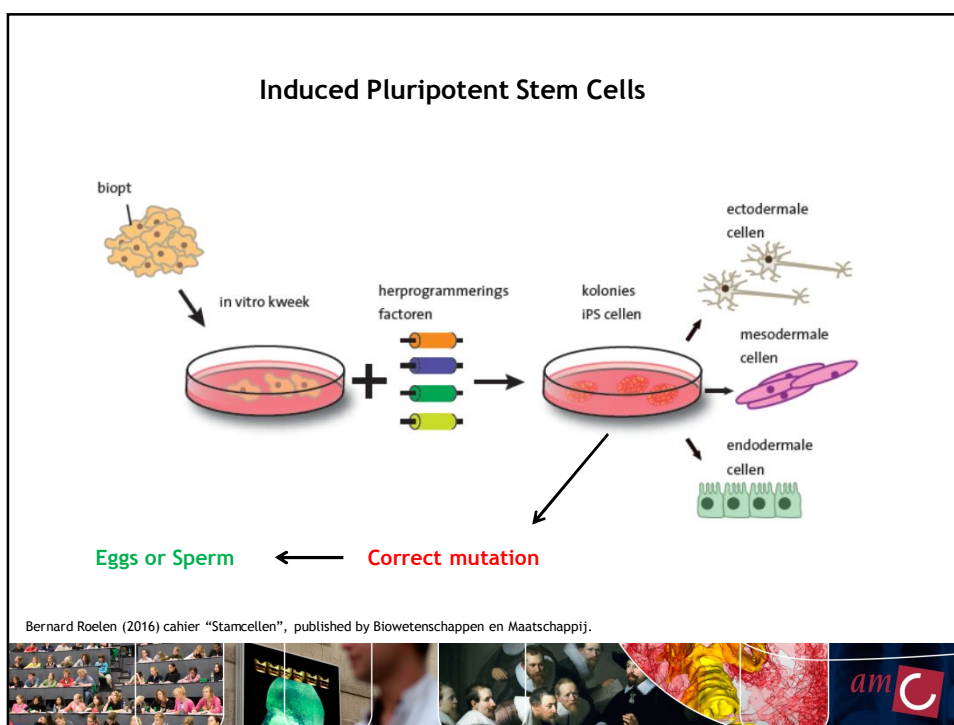


Take skin biopsy
Make iPSCs
Transform into oocyte



Sperm







Sperm





HBB mutation

Take skin biopsy
Make iPSCs
Correct mutation
Transform into oocyte





Take skin biopsy
Make iPSCs
Correct mutation(s)
Transform into oocyte

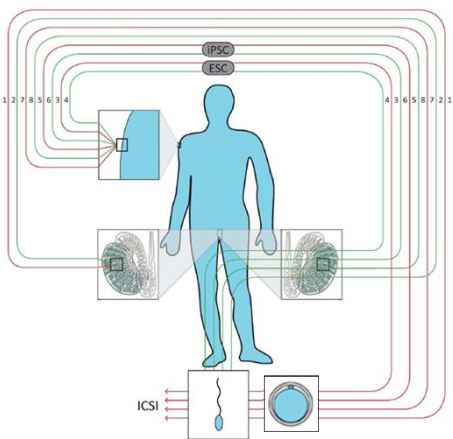




Take skin biopsy
Make iPSCs
Correct mutation(s)
Transform into sperm cell



Self fertilization?



Take skin biopsy
Make iPSCs

Correct mutation(s)

Transform half into oocytes

Other half into sperm



The diagram illustrates a self-fertilization process. A human figure is shown with a skin biopsy taken from the arm. This leads to the creation of iPSCs (Induced Pluripotent Stem Cells) and ESCs (Embryonic Stem Cells). The process involves correcting mutations and then transforming half of the cells into oocytes and the other half into sperm. The sperm is shown using ICSI (Intracytoplasmic Sperm Injection) to fertilize an oocyte. The final result is a male doll.

Designer baby ?






The image shows a female doll on the left and a male doll on the right. In the center, there is a baby doll surrounded by various accessories including a bottle, a pacifier, a blanket, and a stroller. This represents the concept of a 'designer baby'.

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Center for Reproductive Medicine



All authors of used pictures and illustrations

Barbie & Ken

