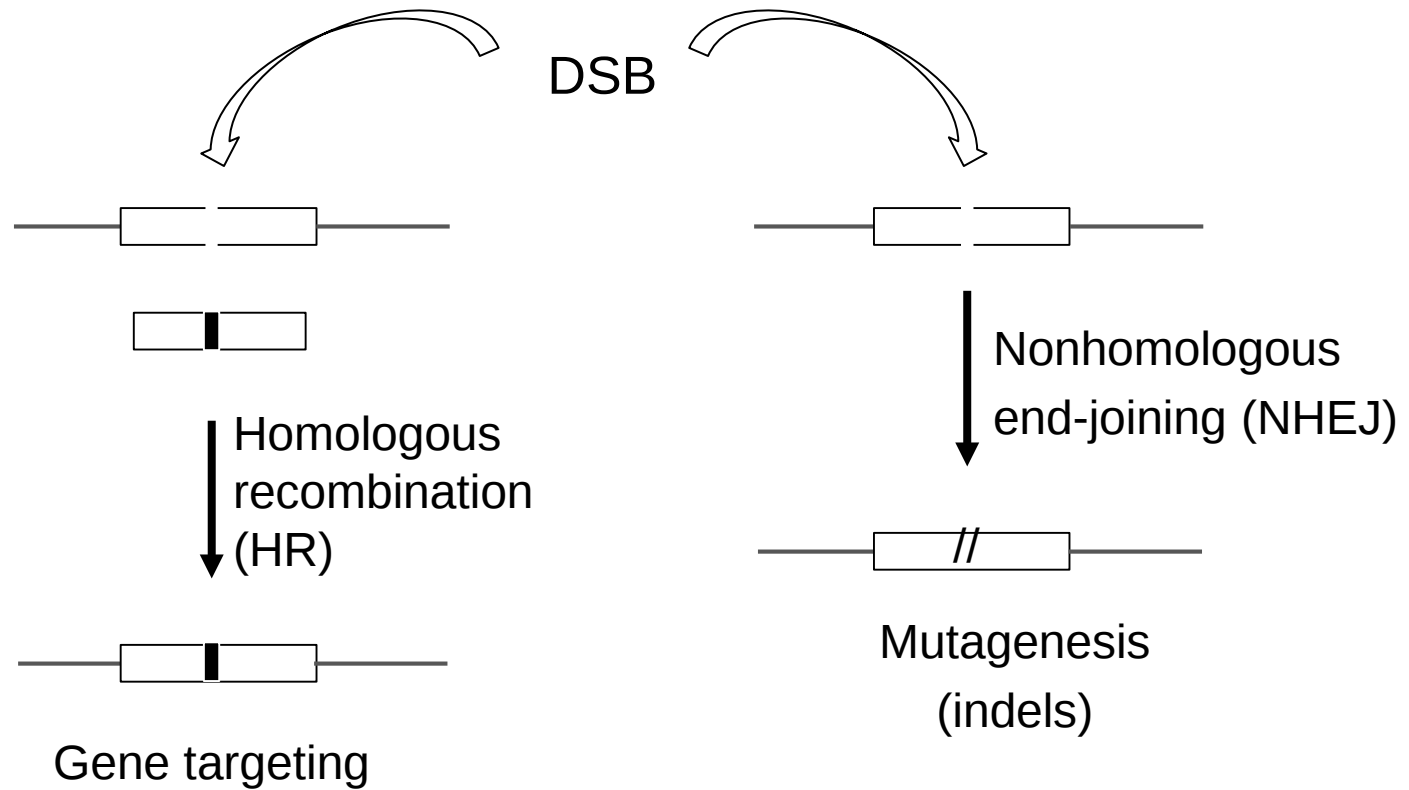


Trust in science, scientists and the role of journals

Maria Jasin, PhD

Memorial Sloan Kettering Cancer Center

Gene editing – 1994 and onward



Correction of a pathogenic gene mutation in human embryos

Hong Ma^{1*}, Nuria Marti-Gutierrez^{1*}, Sang-Wook Park^{2*}, Jun Wu^{3*}, Yeonmi Lee¹, Keiichiro Suzuki³, Amy Koski¹, Dongmei Ji¹, Tomonari Hayama¹, Riffat Ahmed¹, Hayley Darby¹, Crystal Van Dyken¹, Ying Li¹, Eunju Kang¹, A.-Reum Park², Daesik Kim⁴, Sang-Tae Kim², Jianhui Gong^{5,6,7,8}, Ying Gu^{5,6,7}, Xun Xu^{5,6,7}, David Battaglia^{1,9}, Sacha A. Krieg⁹, David M. Lee⁹, Diana H. Wu⁹, Don P. Wolf¹, Stephen B. Heitner¹⁰, Juan Carlos Izpisua Belmonte^{3§}, Paula Amato^{1,9§}, Jin-Soo Kim^{2,4§}, Sanjiv Kaul^{10§} & Shoukhrat Mitalipov^{1,10§}

Online Aug 2 2017

QUARTZ

EMAILS EDITIONS BECOM

Two independent experts Quartz contacted—Dieter Egli of Columbia University and Maria Jasin of the Memorial Sloan Kettering Cancer Center—weren't sure Mitalipov's claims were water tight. Based on the information provided in the study, Egli couldn't confidently say for sure that the tests used to detect mosaicism caught all mosaics. In other words, it's possible that results appear to be more positive than they actually are. Jasin pointed out that more evidence was needed to back up the claim that it was the more accurate method of DNA repair that the embryo used. She acknowledged that working with human embryos has extra constraints because researchers need to justify the use of every extra embryo, but still felt there were some gaps in the study.



nature

Brief Communications Arising

Critical comments on recent *Nature* papers may, after peer review, be published online as Brief Communications Arising, usually alongside a reply from the criticized *Nature* authors. If the submission only serves to identify an important error in the published paper, it is published in the form of a clarification statement (corrigendum or retraction, for example) by the *Nature* authors (see Complaints and corrections, below). Alternatively, readers may post comments on *Nature* papers at the journal's website, under the full-text online version of the paper.

- Comments should be sent to the authors of the paper under discussion before submission to *Nature*, so that disputes can be resolved directly whenever possible and points where both parties agree removed from the submitted contribution. If after 2 weeks the original authors have not responded, this should be indicated at submission.

If the *Nature* authors do not respond within 10 days of receipt of the comment, the editor will proceed without the response. Late Replies may not be considered for publication.

Presentation of new data and of Supplementary Information is not permitted in Replies.

Timeline:

2017

Aug: *Nature* press conference

Aug 2nd: Ma et al publication in *Nature*

Aug 26th: Egli et al BCA submission to *Nature*
BCA post on *bioRxiv*

Oct 2nd: Editorial note

02 October 2017 Editorial Note: Readers are alerted that some of the conclusions of this paper are subject to critiques that are being considered by editors. Some of these critiques have been publicly deposited in preprint form. A further editorial response will follow the resolution of these issues.

2018

Aug 8th: Egli et al BCA published,
Ma et al Reply published

BRIEF COMMUNICATIONS ARISING

Inter-homologue repair in fertilized human eggs?

ARISING FROM H. Ma et al. *Nature* **548**, 413–419 (2017); <https://doi.org/10.1038/nature23305>

Issues:

Length to publication of criticism (BCA):

- Concern that results will be taken at face value and applied in a “rogue” clinic
- Oocyte donation (ovarian stimulation of healthy women): how did the home institution IRB board respond?

Controlled ovarian stimulation. Research oocyte donors were evaluated before study inclusion as previously reported; standard IVF protocols and procedures for ovarian stimulation were described previously⁴⁴. Oocyte donation cycles were managed by OHSU Fertility physicians. Immediately following oocyte retrieval, recovered gametes were transferred to the research laboratory. All study-related procedures took place at the OHSU Center for Embryonic Cell and Gene Therapy. Following oocyte retrieval, cumulus-oocyte complexes (COCs) were treated with hyaluronidase to disaggregate cumulus and granulosa cells. Mature metaphase II (MII) oocytes were placed in Global Medium (LifeGlobal, IVFonline) supplemented with 10% serum substitute supplement (Global 10% medium) at 37°C in 6% CO₂ and covered with tissue culture oil (Sage IVF, Cooper Surgical).

Compensation. All research donors were compensated for their time, effort, and discomfort associated with the donation process at rates similar to those used for gamete donation for fertility purposes.

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- Oocyte donation (ovarian stimulation of healthy women): how did the home institution IRB board respond?
- Financial donations solicited by author
- ? Transparency about questions raised about research findings, desperate families

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By giving much needed resources to the most creative minds in biomedical research you will accelerate scientific discovery and development of novel therapeutic approaches involving stem cells and gene therapy. Much of our lab's success can be attributed to gifts from individual donors who supported our research projects not yet eligible for Federal funding.

Philanthropic gifts from corporations and foundations provide critical money for our new research initiatives on human embryo and stem cell research. These partnerships will pave the way for some of the most exciting and fruitful advances in biomedical research - from using stem cells in regenerative medicine to novel gene therapy approaches for the treatment of inherited human conditions.

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- Makes clear that original paper cannot stand on its own
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Concern about for-profit journals

- was timeline (or original publication) influenced by the for-profit status of the journal

What can be done:

Self regulation of publication?

- separate journal

- community insistence on publication of reviews

- prior review by an international committee

Email from student in US

An important reason why I'm writing to you is that I believe the fight for the rights and proper care of Lulu, Nana and their family will definitely require efforts of the international scientific and medical community. Furthermore, this could be a great opportunity to introduce to the Chinese society the importance of the social work system, legitimate ethics committee in science and medicine, and proper caregiving. With more information being revealed to the global community, the incidence might be dealt as an internal or domestic affair, rendering the family more isolated from potential help.