Second International Summit on Human Genome Editing
NAS/NAM/RS/ASHK

“ Human Embryo Editing"

SPEAKERS AND SESSION FORMAT:

- **Kathy Niakan**
- **Paula Amato**
- **Maria Jasin**
- **Xingxu Huang**

Discussion with audience

- **Jiankui He**
- **Panel discussion: Jiankui He, Matt Porteus and Robin Lovell-Badge**

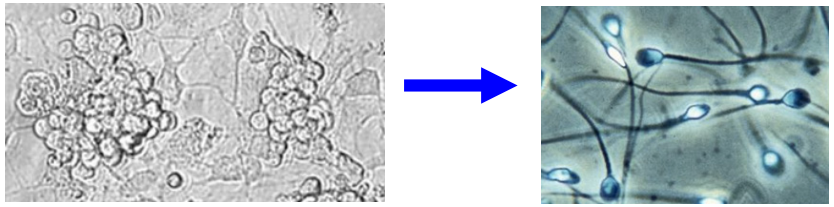
Discussion with audience

Potentially Heritable Genome Editing

POSSIBLE METHODS: 1

- Editing cells that give rise to sperm, such as spermatogonial stem cells, or perhaps via iPS cells and in vitro-derived gametes to give eggs or sperm.

- This allows verification of the edits
- before embryos are made.



This has been done using spermatogonial stem cells in mice, rats and macaques; and via ES and iPS cells in mice.

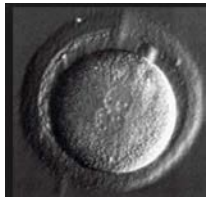
Correction of a genetic disease by CRISPR-Cas9-mediated gene editing in mouse spermatogonial stem cells. Wu et al. (2015) Cell. Res. 25, 67-79.

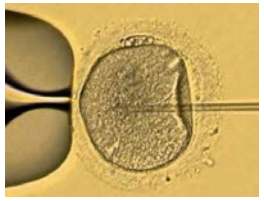
Targeted Germline Modifications in Rats Using CRISPR/Cas9 and Spermatogonial Stem Cells. Chapman et al. (2015) Cell Rep. 10, 1828-35.

N.B. Methods have been developed to go all the way in vitro from iPS cells to oocytes and to spermatogonia and perhaps sperm entirely in vitro in the mouse, and to oogonia in humans. (Notably work from Mitinori Saitou and colleagues.)

Heritable Genome Editing

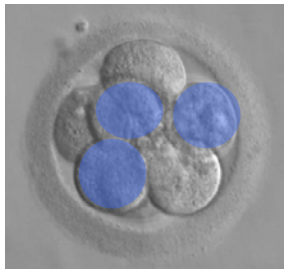
POSSIBLE METHODS: 2





Editing the fertilised egg (zygote)

- To verify the edits, for example to show that there are no unwanted on-target events (e.g. via NHEJ rather than HDR) or off-target events, requires Preimplantation Genetic Diagnosis (PGD).
- But this requires efficiencies close to 100%.
- If there mosaicism, where not all cells in the embryo carry the desired genetic alteration, then PGD becomes unreliable.



- However there are several new methods reported to allow very high efficiencies. These might approach 100%, especially if combined together, and with better understanding of DNA repair mechanisms operating in the early embryo.

These include:

- Careful choice of genome editing components
- Ways to make these more efficient, e.g. by using mechanisms that bring the DNA template to the Cas9/gRNA complex
- Choosing a specific stage in the early embryo when they are introduced.

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