The CRISPR Babies: Scientific background

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Dr. He’s plan

Changes can be passed down to future generations
What is CCR5?

Goal: Mutate CCR5 gene to make babies HIV-resistant

Only R5-tropic HIV!
Higher risk for West Nile & flu?

Why?
~10% of people of European descent

extracellular

intracellular

HIV-

HIV+
Genome editing begins with a cut

1. **Genomic DNA**
   - Random insertion
   - Random deletion

2. **Double-strand break**
3. **OR**
   - Random insertion + Donor DNA of choice
   - Random deletion + Donor DNA of choice

4. **New DNA inserted**
   - Functional new gene added

5. **GENE NO LONGER FUNCTIONAL**

CRISPR = CRISPR-Cas9 system

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**Diagram Explanation:**
- CRISPR enzymes create double-strand breaks in DNA.
- These breaks can lead to random insertions or deletions.
- Alternatively, a donor DNA of choice can be used to insert new DNA sequences.
- Depending on the process, the gene may remain non-functional or a new gene is added.
Lulu: One unchanged copy of CCR5

Other copy has 15 bp deleted

Nana: One copy w 4 bp deleted

Other copy w 1 bp inserted

*Both cause frame shifts

Sean Ryder

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  - Likely to inhibit function
What is mosaicism?

Instead, the chromatograms show that many positions in the CCR5 gene sometimes have one nucleotide and sometimes another; that happens when the sampled cells are a potpourri of genotypes — more evidence of mosaicism, Sontheimer said.
Scientific summary

Lulu

One normal copy of CCR5, one missing 5 amino acids (unknown effect)
HIV resistance unlikely – at best, slower AIDS progression
Mosaic (unknown effect)  *Parents informed about Lulu’s edit, mosaicism, possible off-target – chose to implant anyway

Nana

4 bp deletion in one copy, 1 bp insertion in other; both causes truncations
Could be HIV-resistant but not proven
Mosaic?

2nd pregnancy established – no info  Off-targets?

Large on-target deletions?
Draft Ethical Principles for Therapeutic Assisted Reproductive Technologies

He Jiankui, Ryan Ferrell, Chen Yuanlin, Qin Jinzhou, and Chen Yangran

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1. Mercy for families in need (悲悯之心)
A broken gene, infertility, or a preventable disease should not extinguish life or undermine a loving couple’s union.
For a few families, early gene surgery may be the only viable way to heal a heritable disease and save a child from a lifetime of suffering.

2. Only for serious disease, never vanity (有所为有所不为)
Gene surgery is a serious medical procedure that should never be used for aesthetics, enhancement, or sex selection purposes — or in any way that would compromise a child’s welfare, joy, or free will. No one has a right to determine a child’s genetics except to prevent disease.
Gene surgery exposes a child to potential safety risks that can be permanent. Performing gene surgery is only permissible when the risks of the procedure are outweighed by a serious medical need.

3. Respect a child’s autonomy (探索你自由)
A life is more than our physical body and its DNA. After gene surgery, a child has equal rights to live life freely, to choose his or her occupation, to citizenship, and to privacy. No obligations exist to his or her parents or any organization, including paying for the procedure.

4. Genes do not define you (生活需要奋斗)
Our DNA does not predetermine our purpose or what we could achieve. We flourish from our own hard work, nutrition, and support from society and our loved ones. Whatever our genes may be, we are equal in dignity and potential.

5. Everyone deserves freedom from genetic disease (促进普惠的健康权)
Wealth should not determine health. Organizations developing genetic cures have a deep moral obligation to serve families of every background.