

The CRISPR Babies:

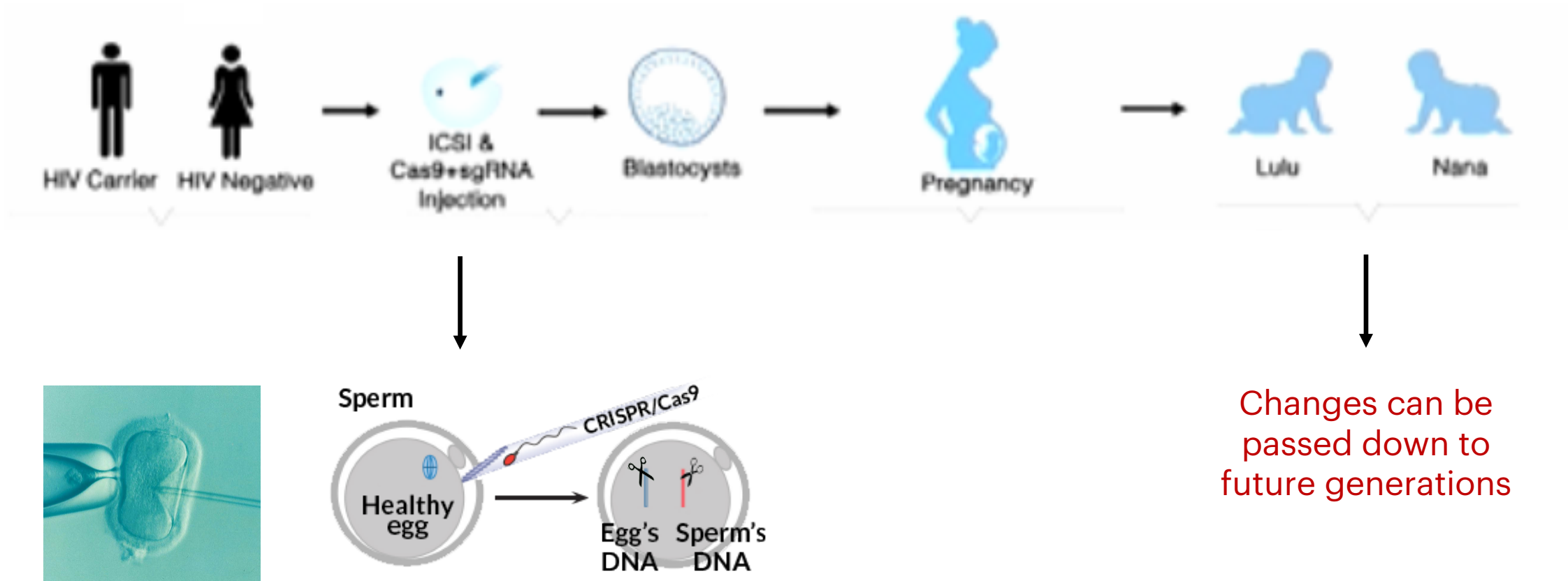
Scientific background

Megan Hochstrasser, PhD

BERGIT · 12.7.18

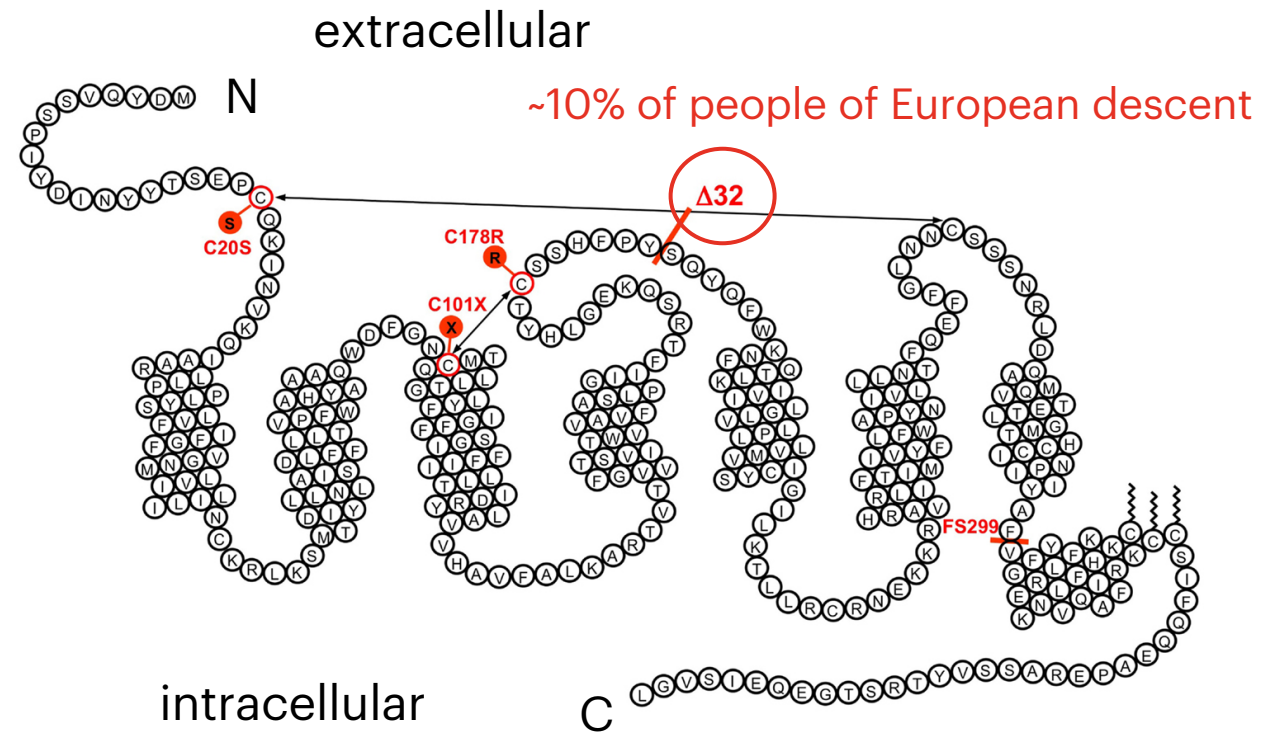
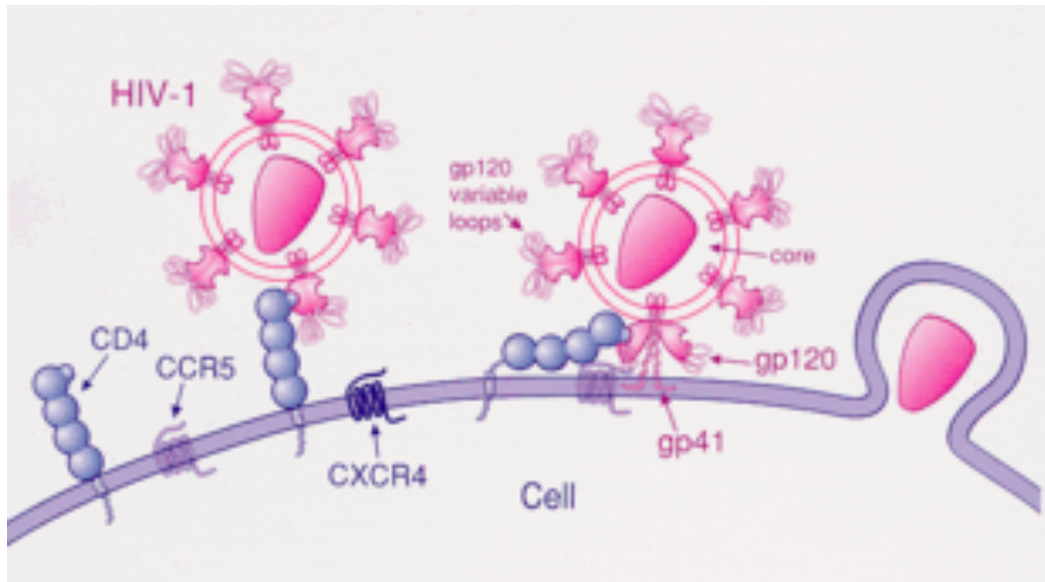


Dr. He's plan



Changes can be passed down to future generations

What is CCR5?



Only R5-tropic HIV!

Higher risk for West Nile & flu?

Goal: Mutate CCR5 gene to make babies HIV-resistant

Why?

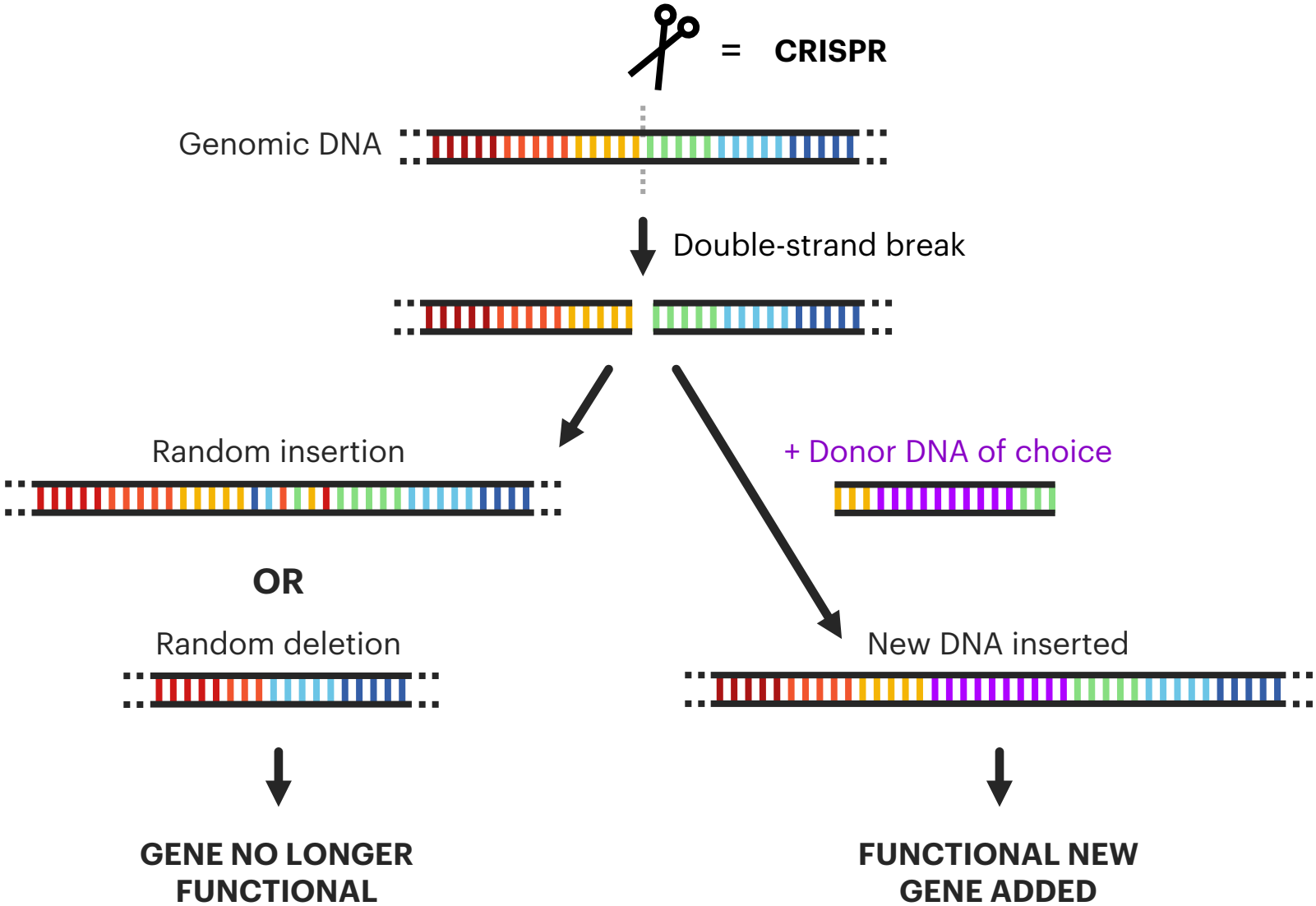


HIV+

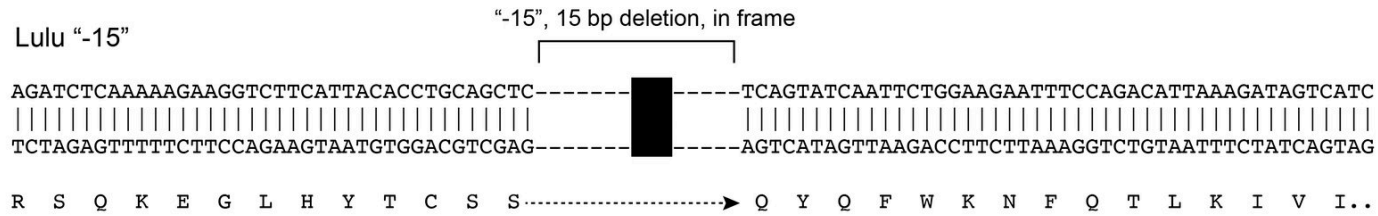


HIV-

Genome editing begins with a cut

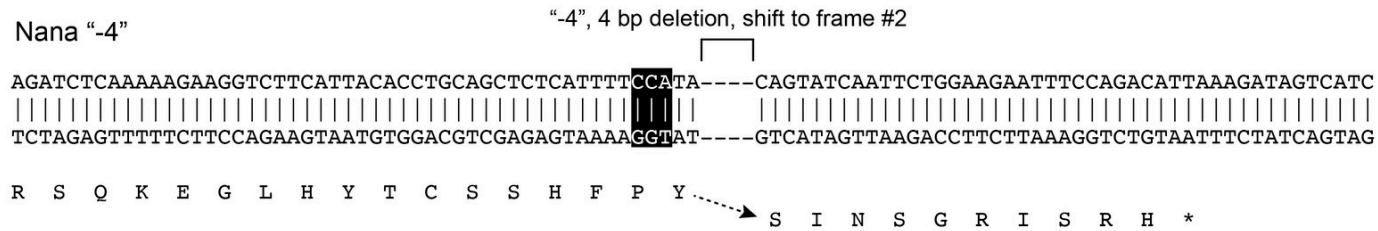


Lulu & Nana's edits



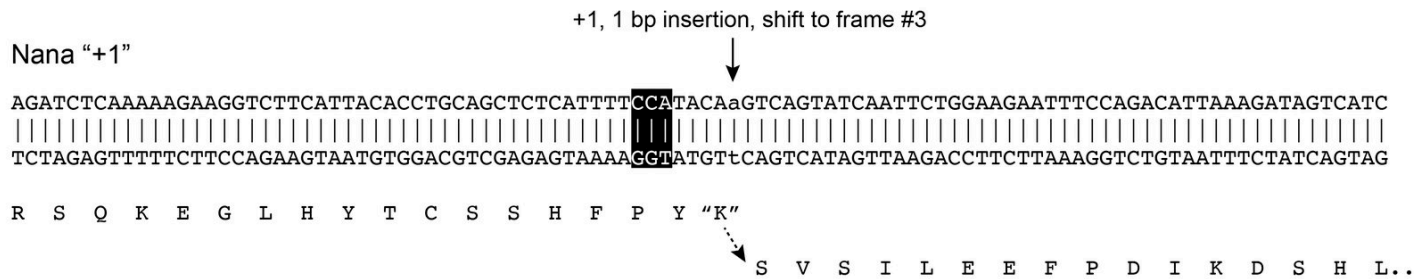
Lulu: One unchanged copy of CCR5

Other copy has 15 bp deleted



Nana: One copy w 4 bp deleted

Other copy w 1 bp inserted



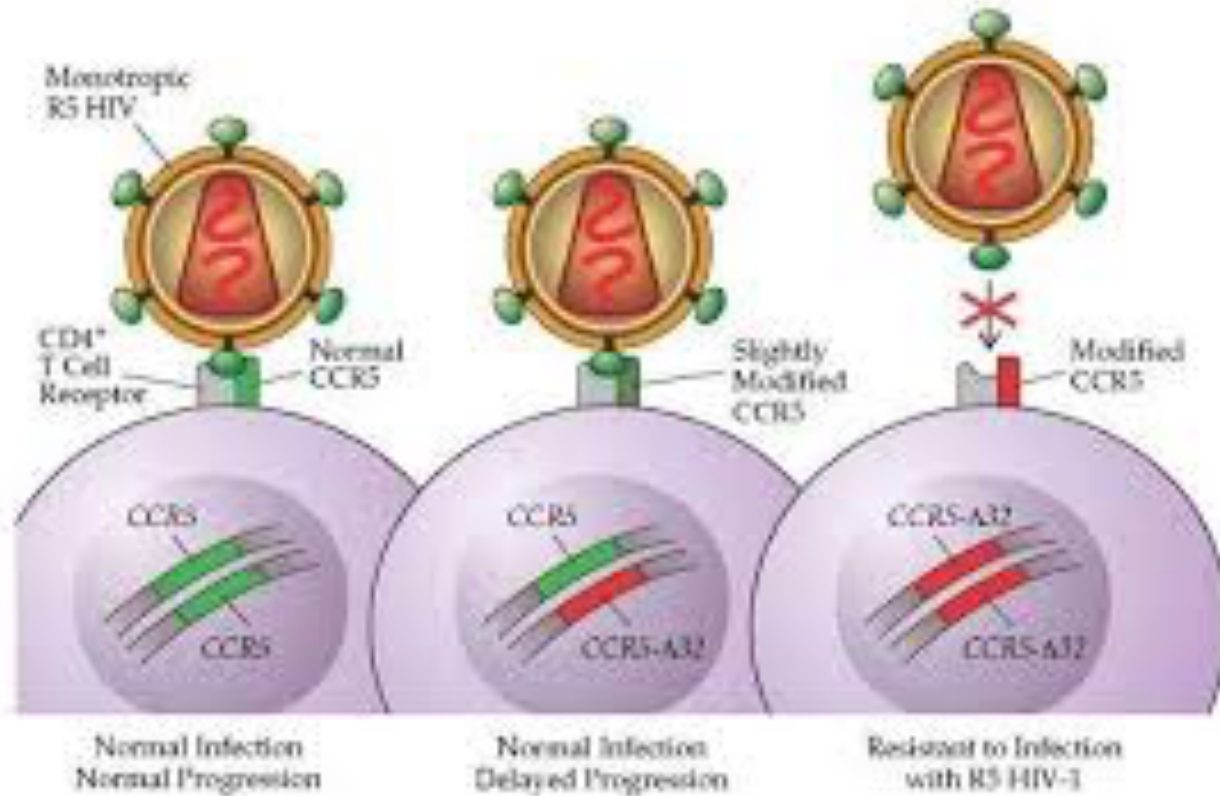
**Both cause frame shifts*

Sean Ryder



@RyderLab

What effects will these edits have?



Lulu: One unchanged copy of CCR5
Not HIV-resistant

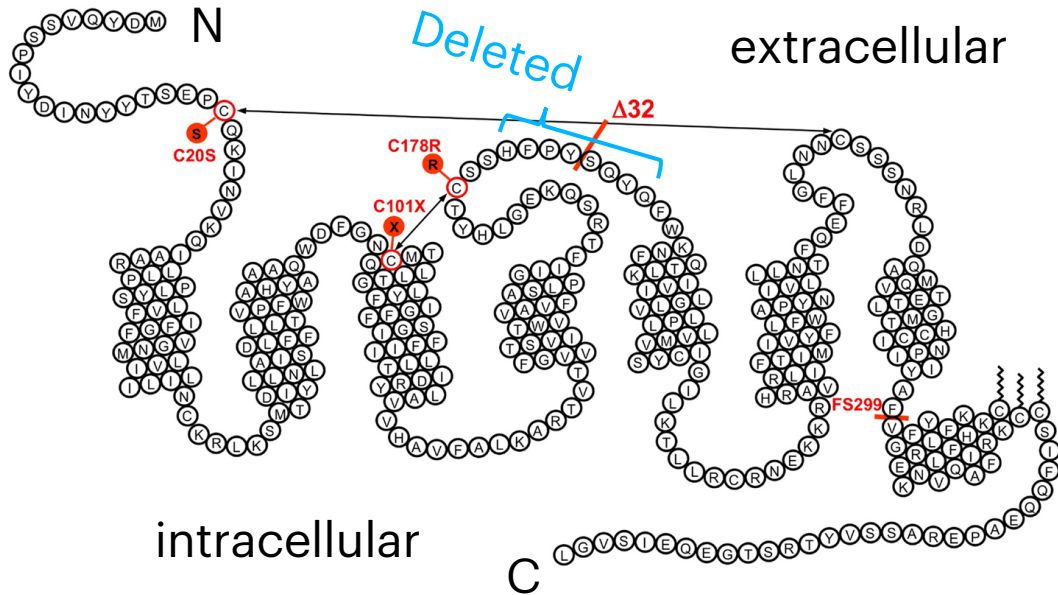
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What effects will these edits have?



Lulu 15 bp del

Lulu: One unchanged copy of CCR5
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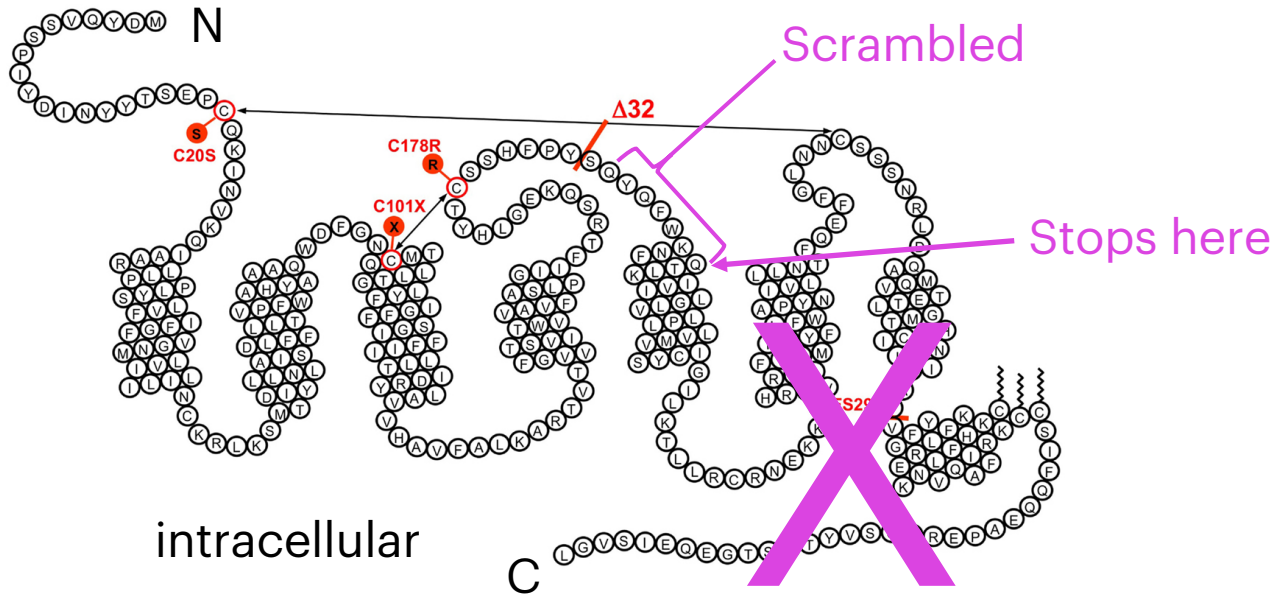
Other copy has 15 bp deleted
Unknown effect

Nana: One copy w 4 bp deleted

Other copy w 1 bp inserted

**Both cause frame shifts*

What effects will these edits have?



Nana 4 bp del

Lulu: One unchanged copy of CCR5
Not HIV-resistant

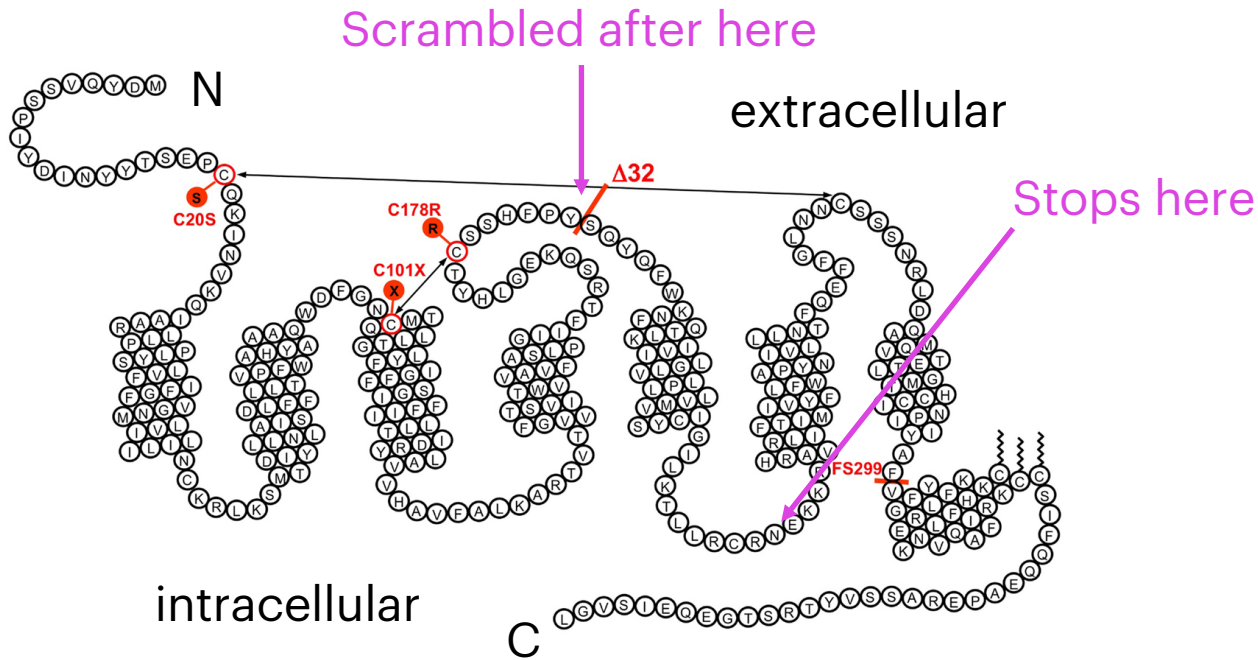
Other copy has 15 bp deleted
Unknown effect

Nana: One copy w 4 bp deleted
Unknown effect

Other copy w 1 bp inserted

**Both cause frame shifts*

What effects will these edits have?



Nana 1 bp ins

Lulu: One unchanged copy of CCR5
Not HIV-resistant

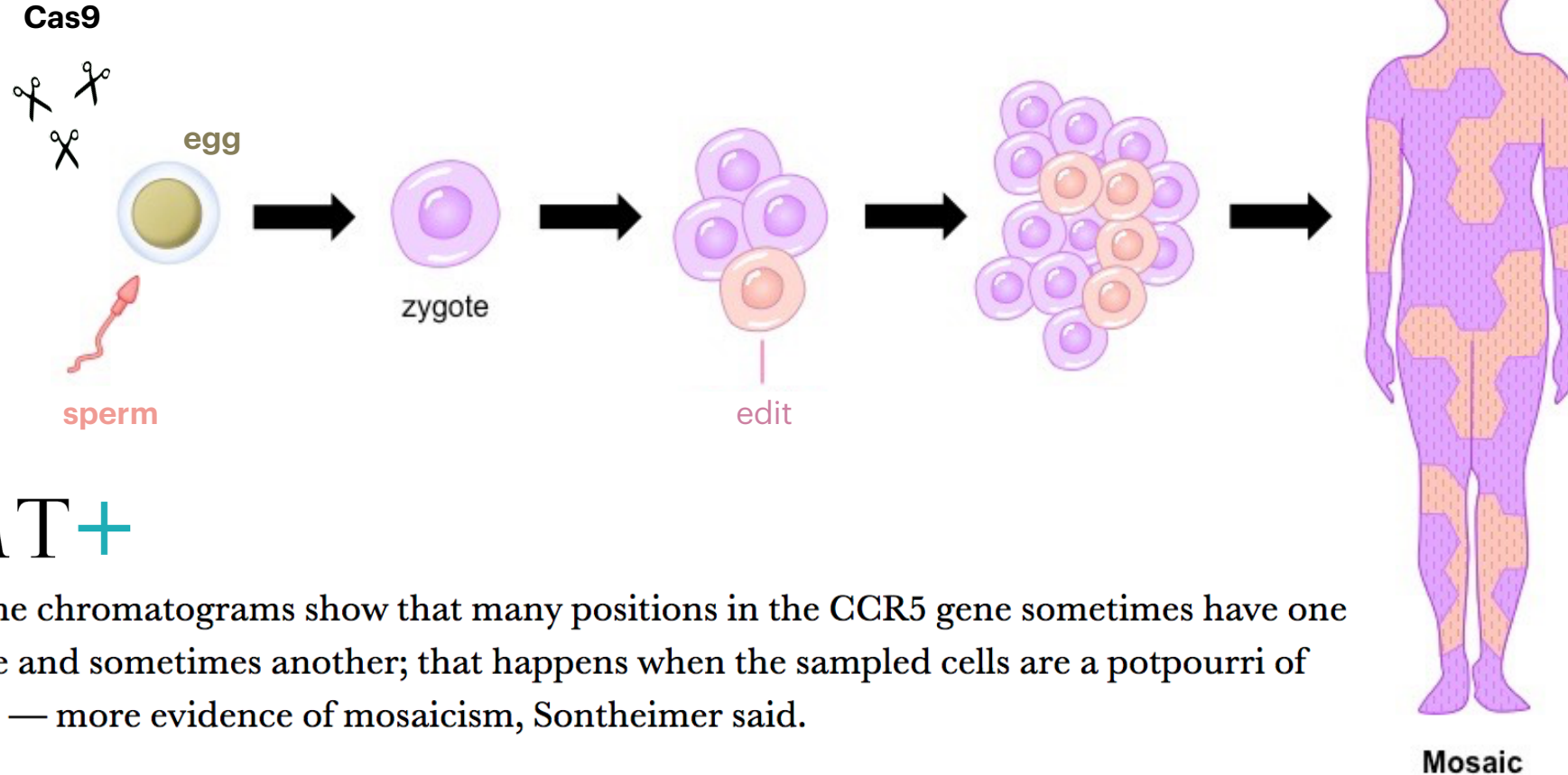
Other copy has 15 bp deleted
Unknown effect

Nana: One copy w 4 bp deleted
Unknown effect

Other copy w 1 bp inserted
Unknown effect

**Both cause frame shifts*
Likely to inhibit function

What is mosaicism?



STAT+

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?

A Hypocritical Oath

The CRISPR Journal, Ahead of Print | Perspective

 Open Access | 

Draft Ethical Principles for Therapeutic Assisted Reproductive Technologies

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

Published Online: 28 Nov 2018 | <https://doi.org/10.1089/crispr.2018.0051>

1. **Mercy for families in need (怜悯之心)**

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 (有所为更有所不为)**

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.



