

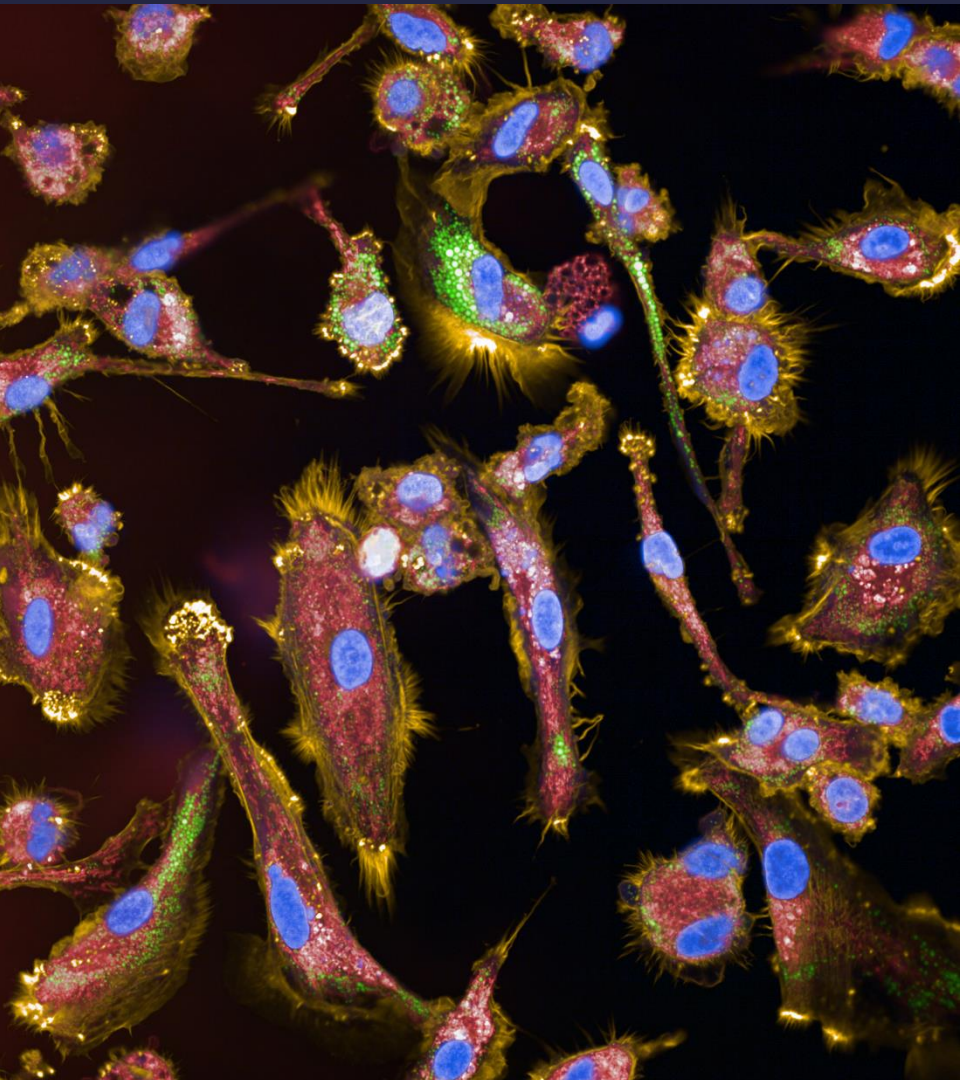


At The Cutting Edge: Applications of CRISPR

Dr Sam Washer

Postdoctoral Research Fellow

Gene Editing Research and Development



1. CRISPR

2. Editing Cell Lines

3. Research

4. Treating Human Disease

5. Next Gen CRISPR

Why?

20p

Britain's first and only concise **quality** newspaper

SPORT

Dortmund 0 Arsenal 1
Ramsey rifles
Gunners to brink of last 16

Champions League
Celtic fall as Chelsea fly high

League United
Lewis Moody writes for

What if JFK had lived?
By Stephen King

Genetic revolution that can eradicate disease

■ 'Jaw-dropping' breakthrough lets scientists delete faulty parts of the human genome

■ Discovery has potential for treating cancer, HIV, Down's syndrome and Huntington's

■ 'A triumph with huge implications for science,' declares Nobel Prize winner

New NHS drugs deal to save billions

An end to 800 years of Portsmouth shipbuilding

Killer pet bulldog was stray found in the park

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THURSDAY
7 NOVEMBER 2013
Number 311

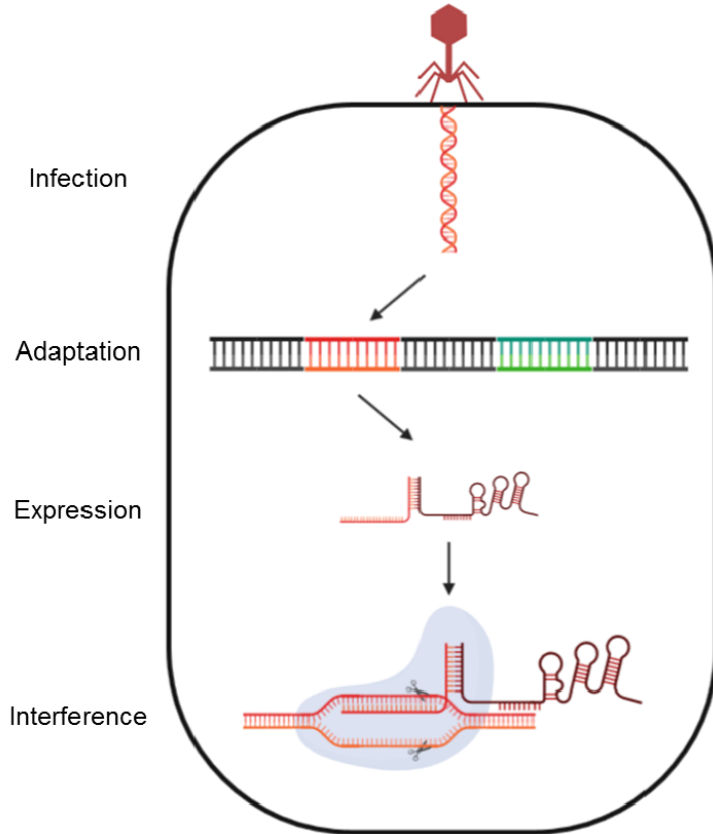
COMMENT
Grace Dent
Boyd Tonkin
Jane Merrick

Thursday 07 November 2013

CRISPR

The molecular scissors transforming genetics

CRISPR - bacterial immune system



Clustered Regularly Interspaced Short Palindromic Repeats

Bacterial immune response to viruses

Three components:

- crRNA
- tracrRNA
- Cas9

Sequence is 20bp

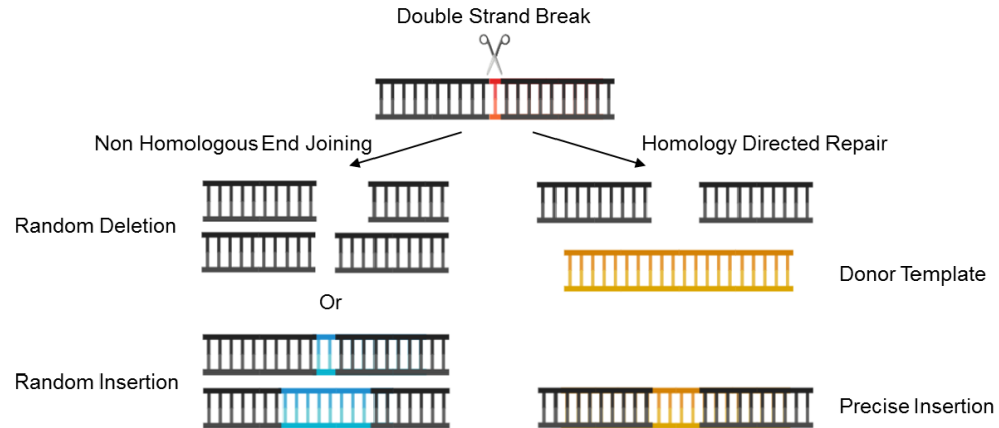
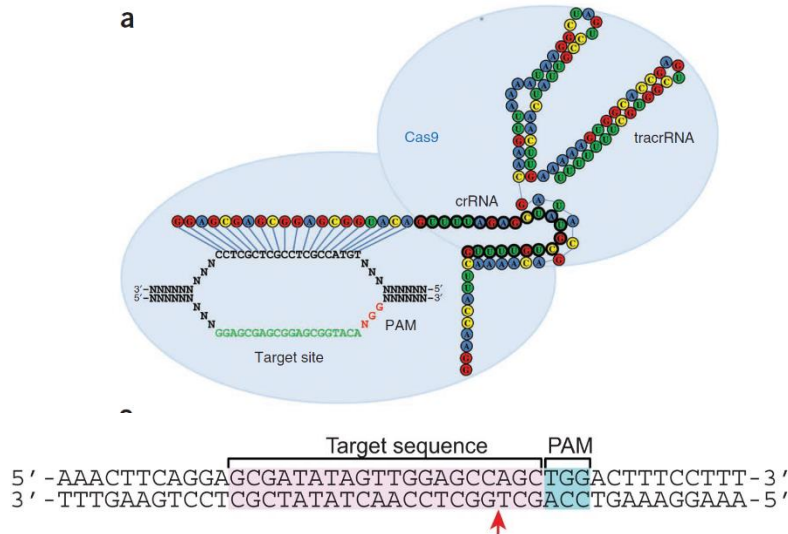
Requires a PAM (Protospacer Adjacent Motif)

Induces a double strand break

Jennifer Doudna and Emmanuelle Charpentier – Nobel Prize

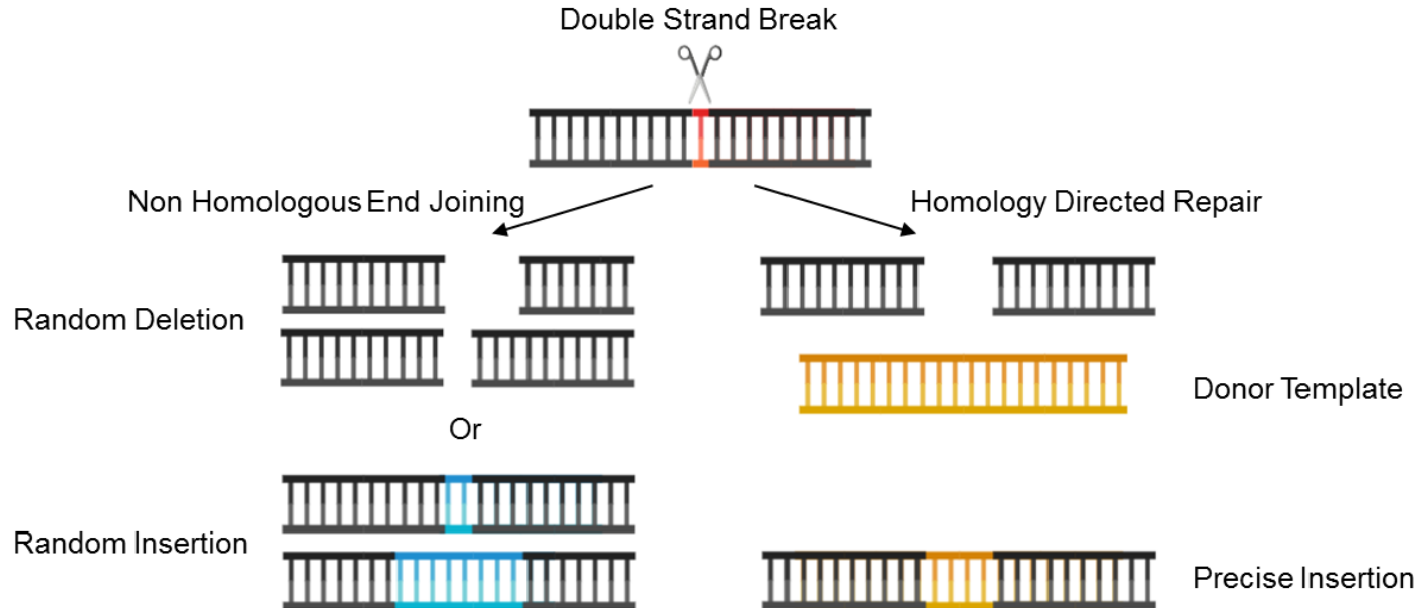
Chemistry 2020

Cas9 causes a double strand break at precise locations



Non Homologous End Joining can result in a frameshift mutation and can stop protein translation
OR
Homology directed repair can correct mutated DNA back to healthy DNA

Editing Cells



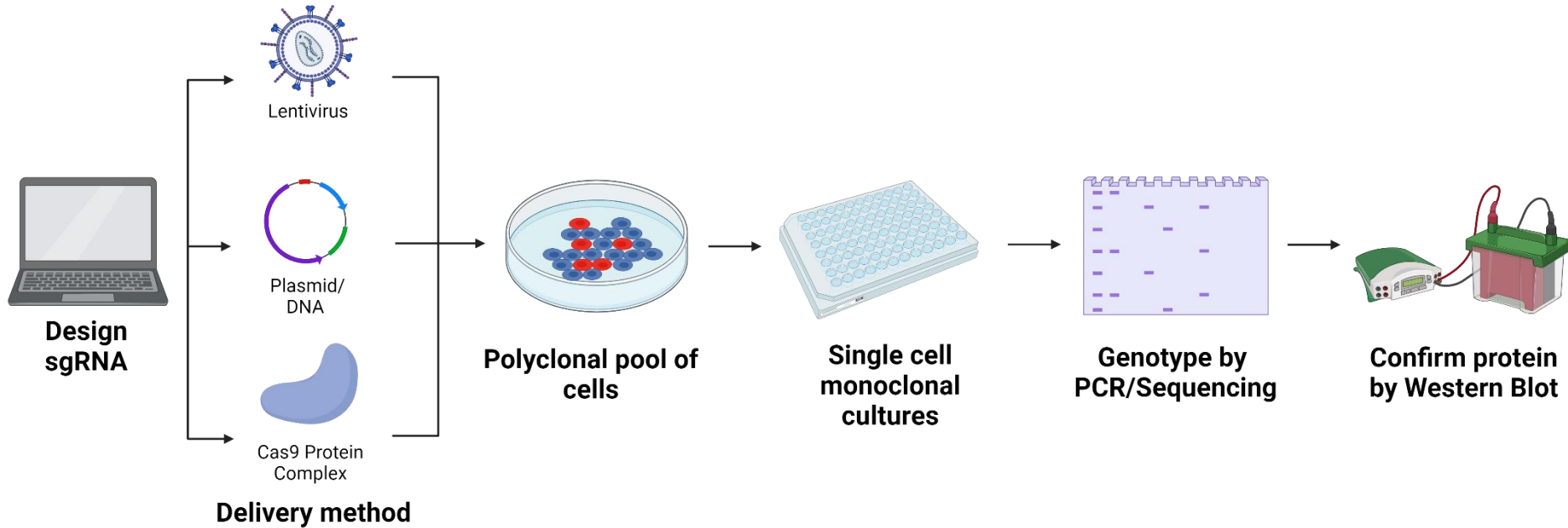
Genetic Knockout –

- What does the gene do?
- Removing disease causing alleles

Genetic Knock-in –

- Correcting disease causing mutations
- Generating reporter cell lines/models

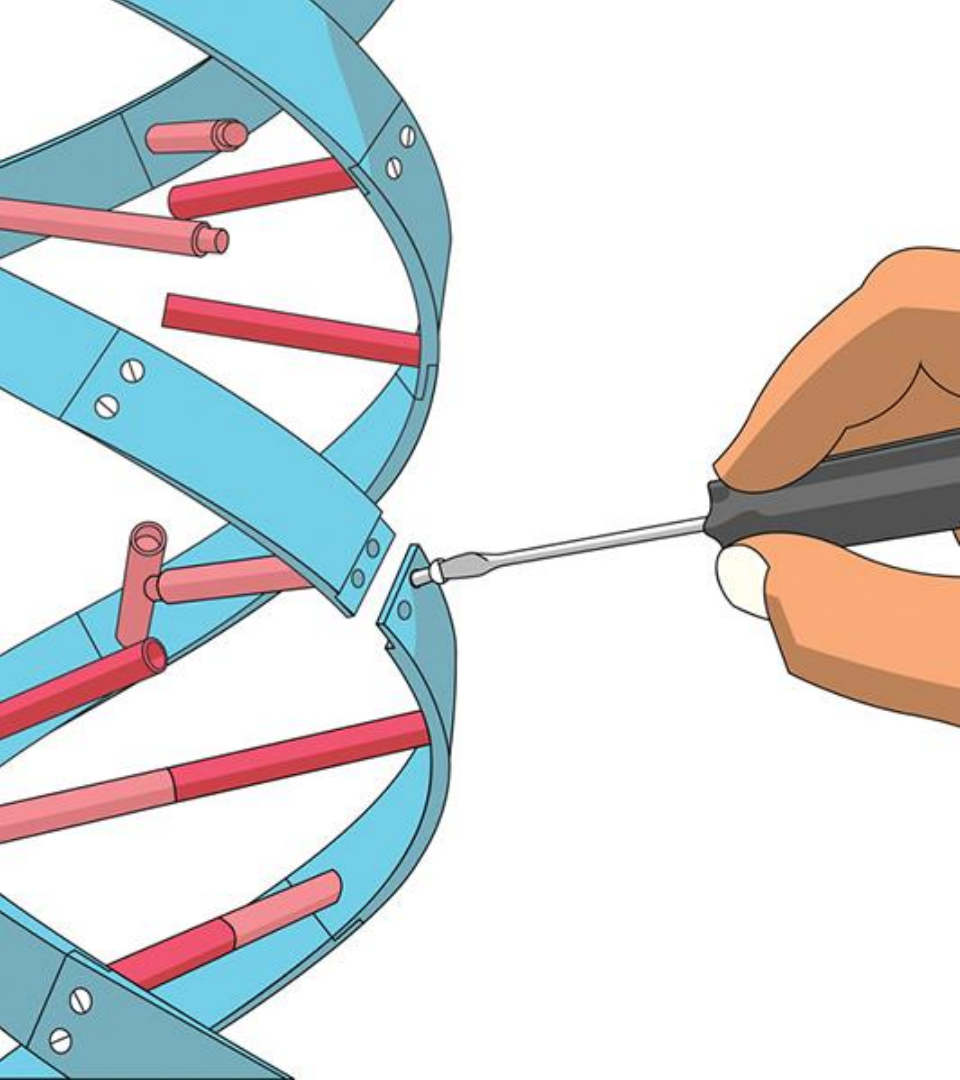
How do we edit a cell?



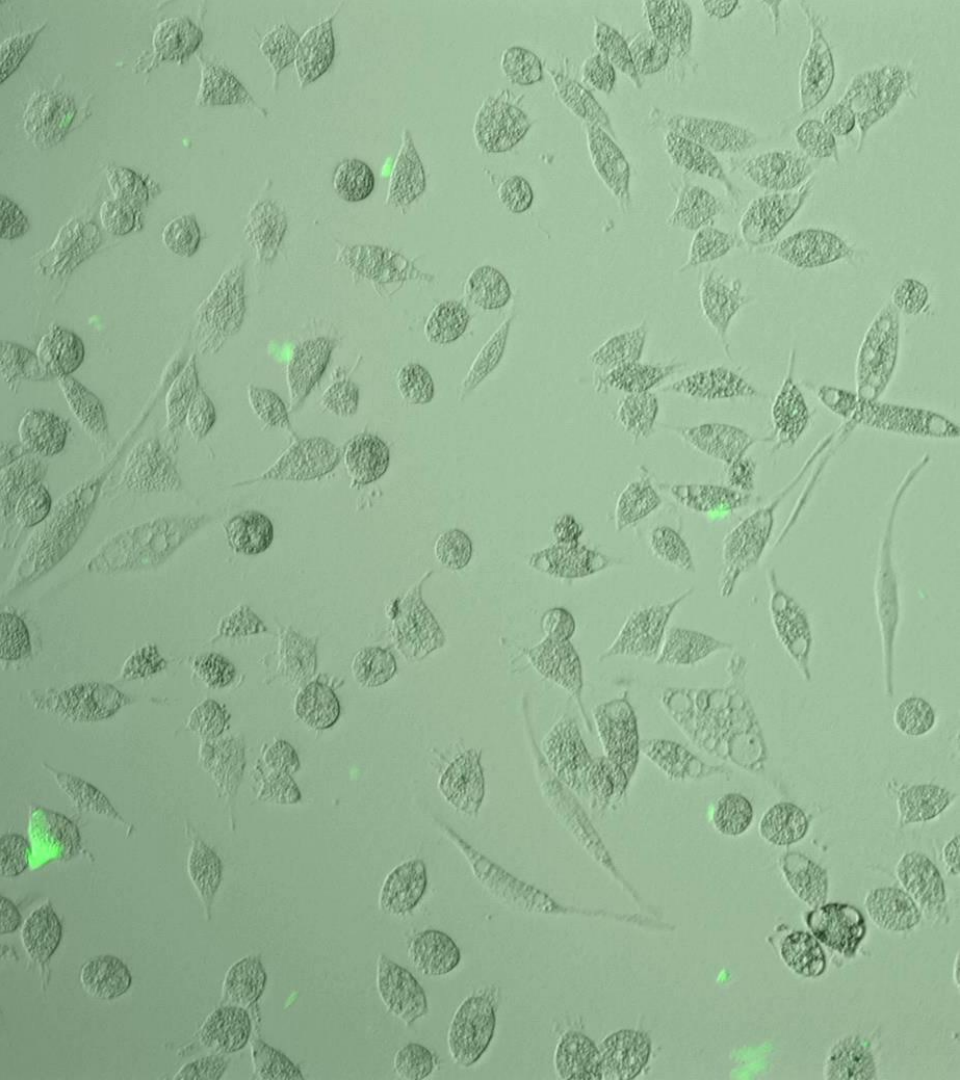
What research can we do with edited human cells?







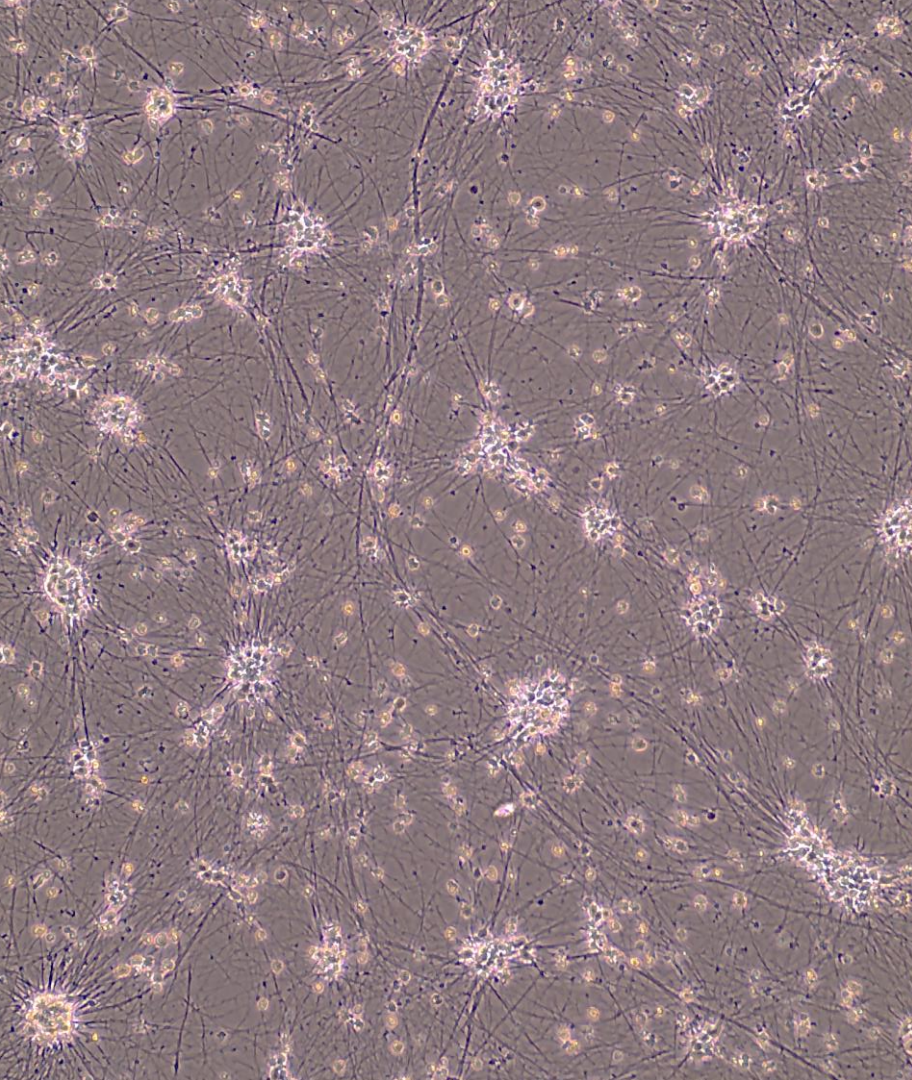
Basic biological understanding



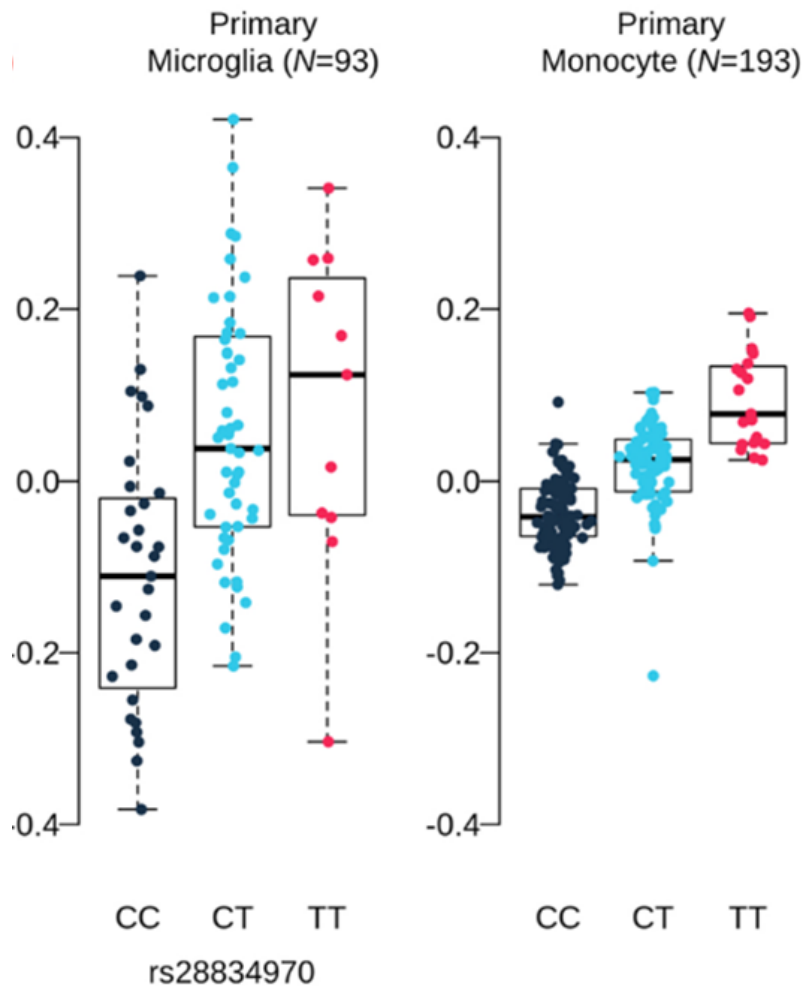
Discover what genes do



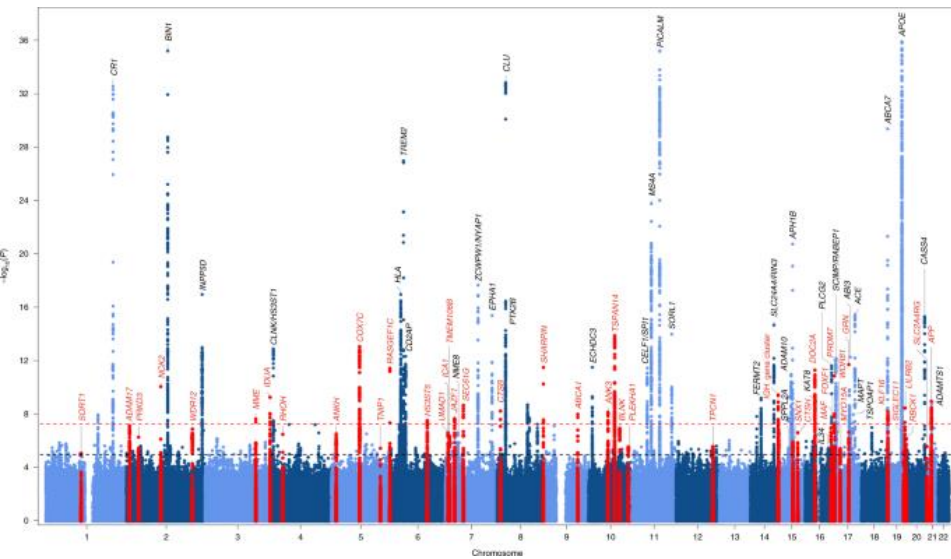
Discover what genes do



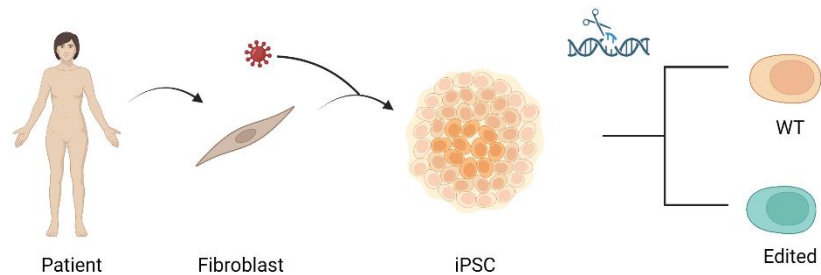
Discover what genes do

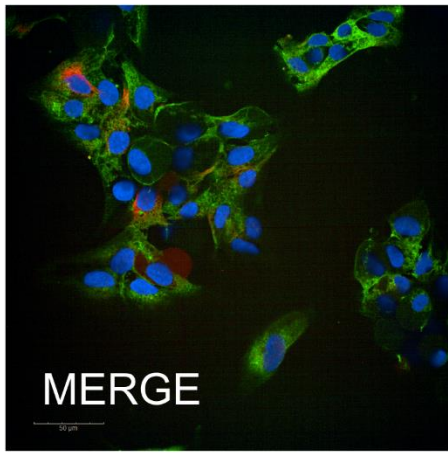
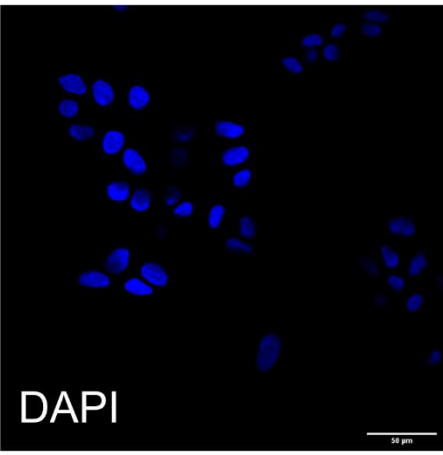
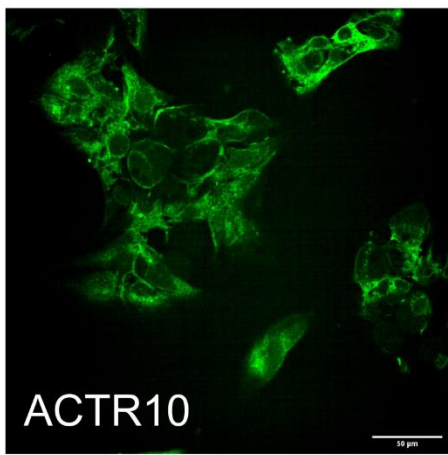
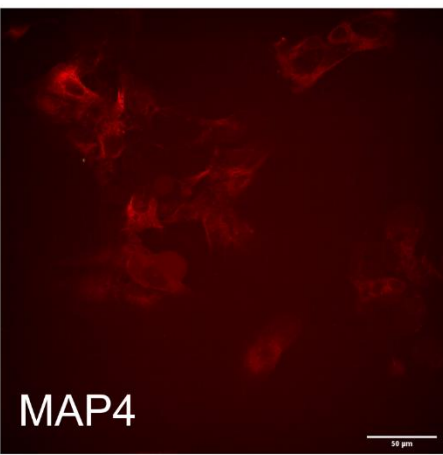


Explore genetic variation



Explore genetic variation

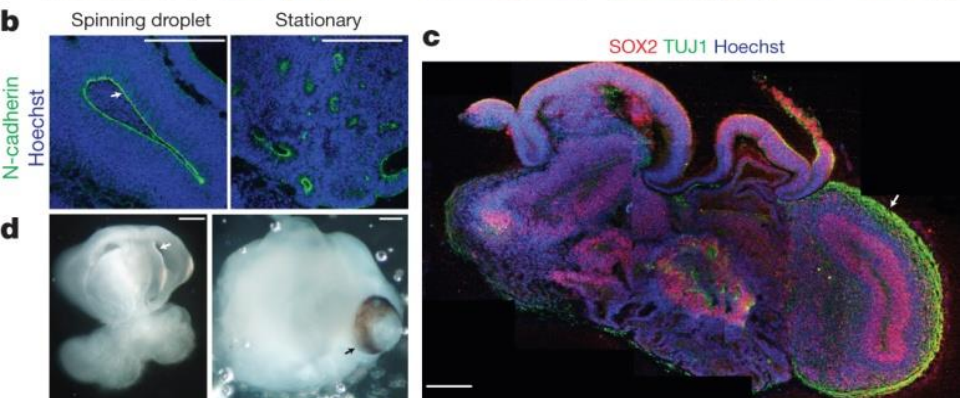
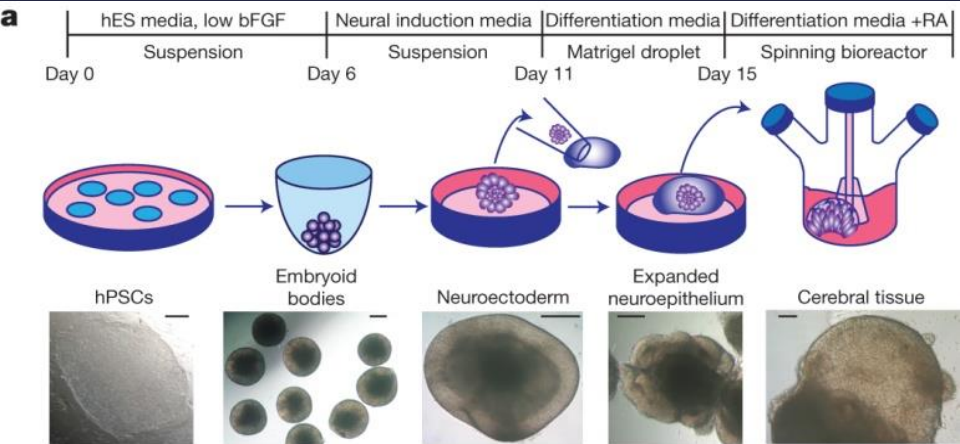




Generate reporter lines



Farming/Agriculture



Dive into the unknown

How can CRISPR treat disease?



Case Study: Sickle Cell Anaemia

The first CRISPR treatment for a genetic disease

Treatments for Sickle cell

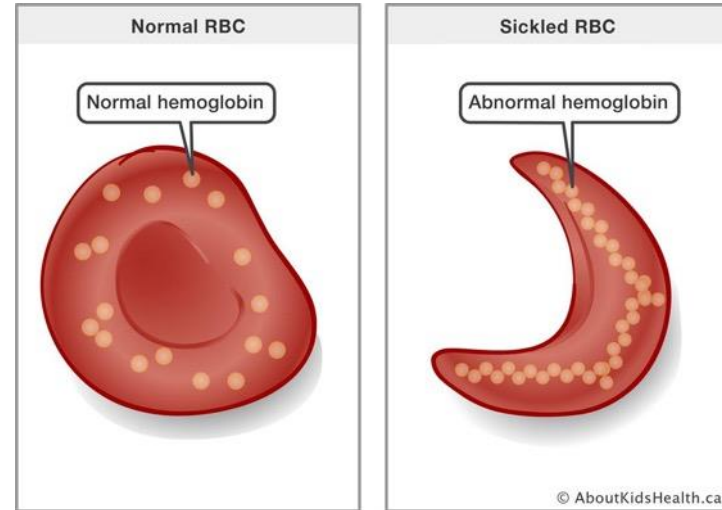
Genetic Disease – Autosomal Recessive

1 DNA base change causes haemoglobin to aggregate

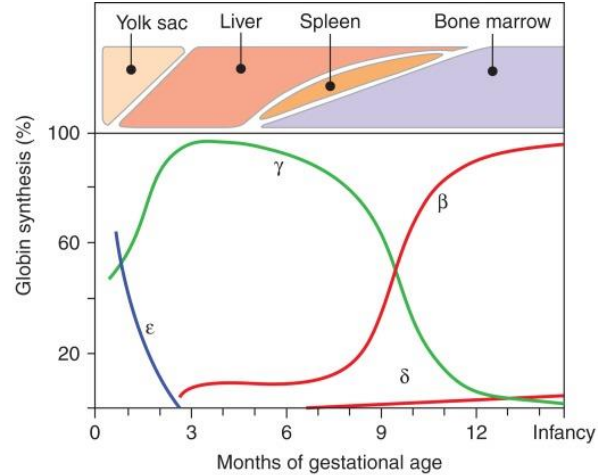
GAG -> GTG

Glu -> Val

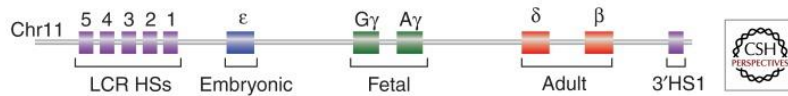
Blockages by sickled red blood cells can cause pain and strokes



Treatments for Sick cell



β -Globin locus



BCL11A^{+/+} Stem Cells



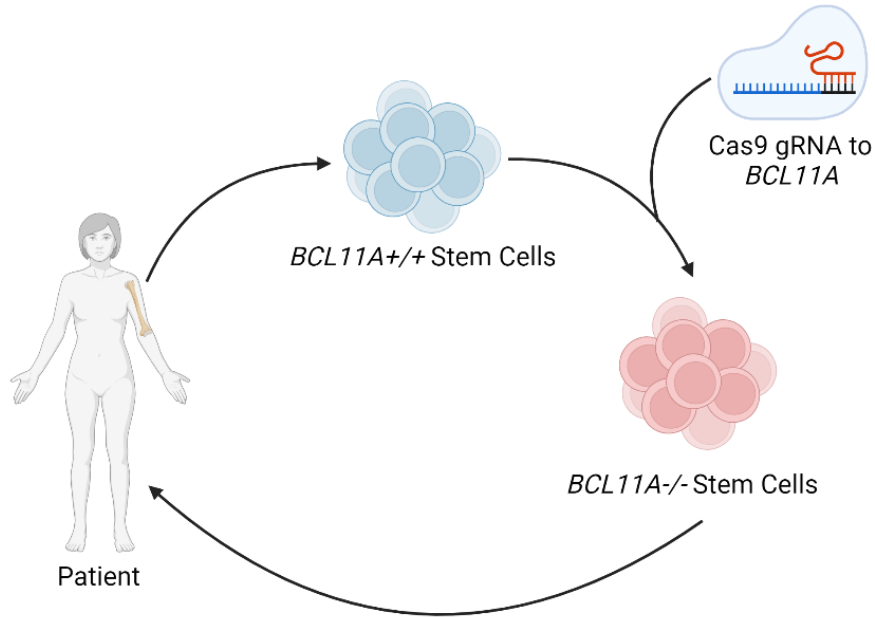
Adult β -Haemoglobin
(Sickled RBC)

BCL11A^{-/-} Stem Cells



Foetal γ -Haemoglobin
(Normal RBC)

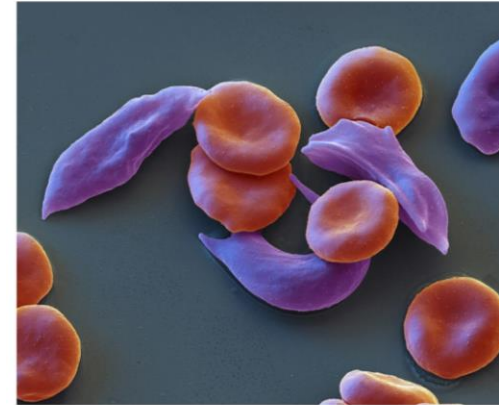
Treatments for Sick cell



UK first to approve CRISPR treatment for diseases: what you need to know

The landmark decision could transform the treatment of sickle-cell disease and β -thalassaemia – but the technology is expensive.

By [Carissa Wong](#)



Sickle-cell anaemia is marked by red blood cells that are misshapen and sticky, affecting blood flow. Credit: Eye Of Science/SPL

28/29 patients treated were “cured”

Other genetic treatments?

Monogenic Disease

- Cystic Fibrosis
- Huntingtons
- Fragile X
- Duchenne Muscular Dystrophy

Polygenic Disease

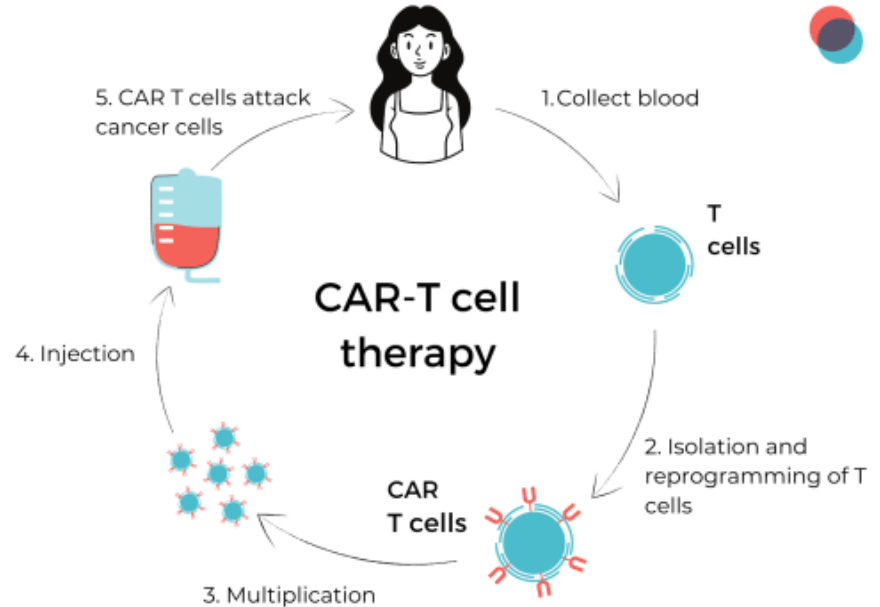
- Diabetes Type 1
- Cardiovascular disease

Infectious Disease

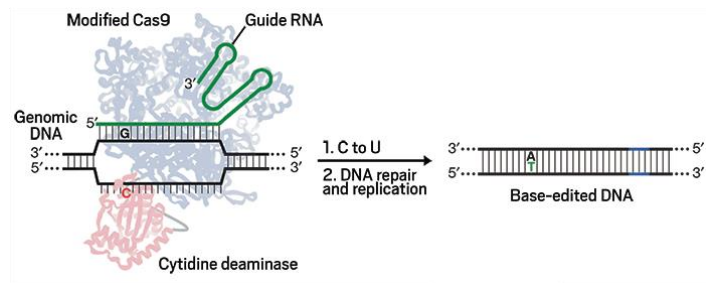
- HIV
- Hep B

Cancers

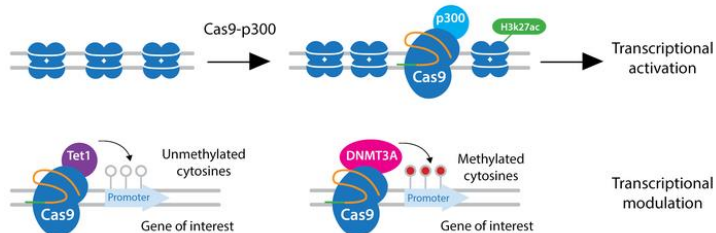
- **CAR-T Therapy**



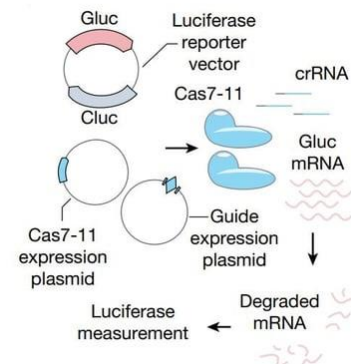
New CRISPR methods



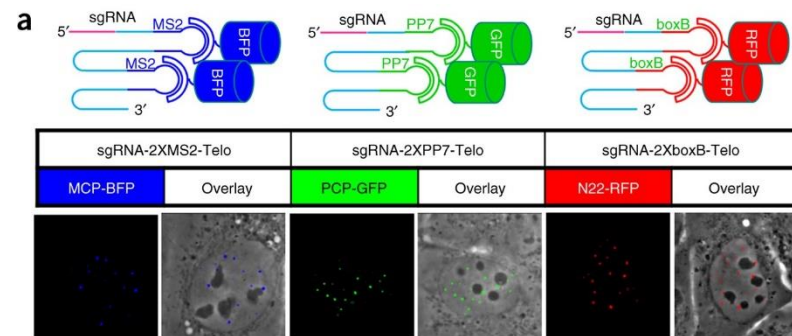
Base editors



Epigenetic editors

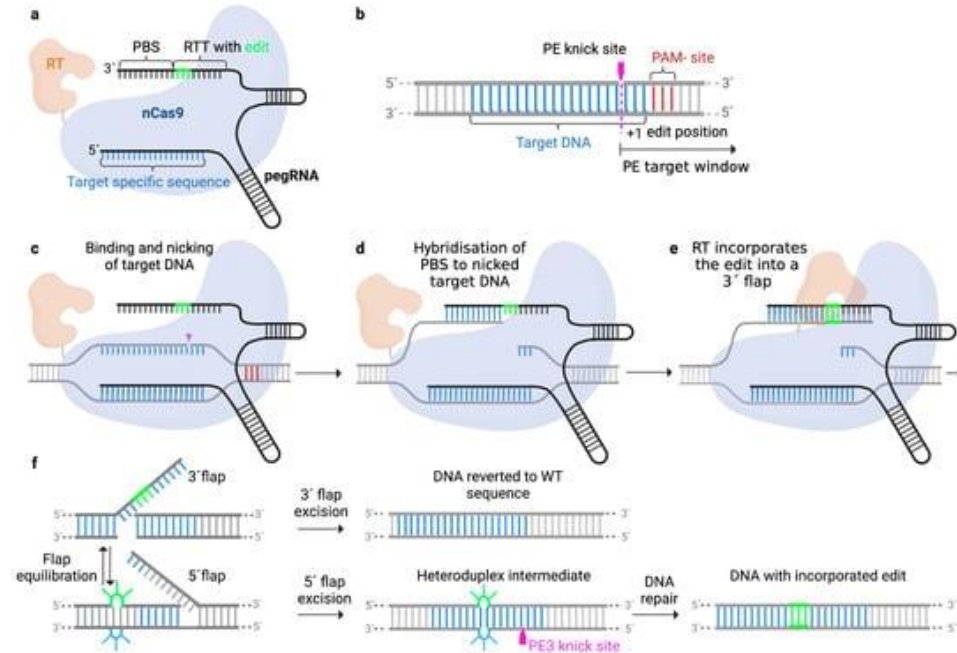


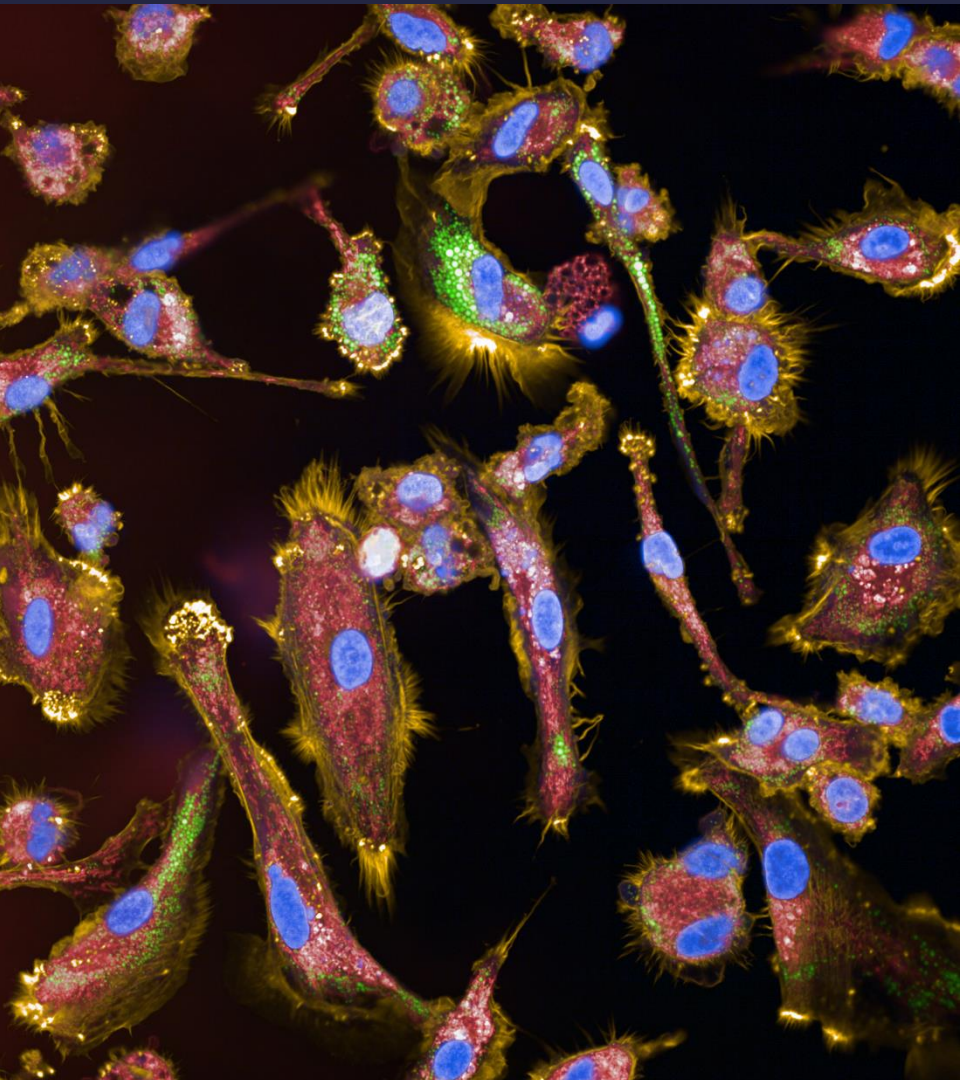
RNA editors



Visualisation

Prime Editing – The future?





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3. Research

4. Treating Human Disease

5. Next Gen CRISPR