CRISPR-Cas9

How targeted gene editing works, and what it can and cannot do.

Biology

Adapted from a bacterial immune system.

1. **Design a guide RNA**
   20 bases complementary to the target, next to a PAM sequence.

2. **Cas9 binds and cuts**
   A double-strand break at the target site.

3. **The cell repairs it**
   Non-homologous end joining is error-prone — this knocks the gene out.

4. **Or supply a template**
   Homology-directed repair inserts a specified sequence.

LIMITS

- Off-target cuts elsewhere in the genome
- HDR is inefficient in non-dividing cells
- Delivery into the right tissue is the main obstacle
- Germline editing raises unresolved ethical questions

The 2020 Nobel Prize in Chemistry went to Charpentier and Doudna for developing it as a genome-editing tool.