DP Biology – D1.3 (HL extension)

Editing and switching off genes

- How do mutations in genes arise?
- What effects do gene mutations have?

HL statements D1.3.8–10. Textbook pp. 643–647.



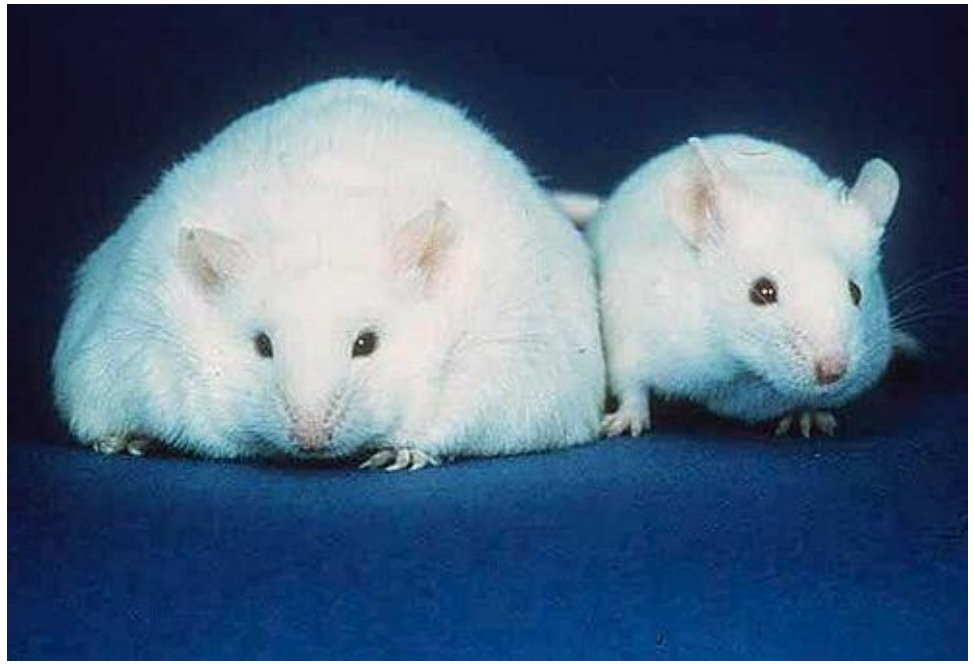
Image: a mouse lacking a gene that controls appetite (left) beside a normal mouse. Public domain.

Objectives for each class

Class	Statements	By the end of the class, you can...
1	D1.3.8–9	Explain how gene knockout reveals a gene's function, and how CRISPR-Cas9 is used to edit genes
2	D1.3.10	Evaluate two hypotheses for why some gene sequences are highly conserved

Gene knockout

D1.3.8



Knockout mouse (left) and normal mouse. Public domain.

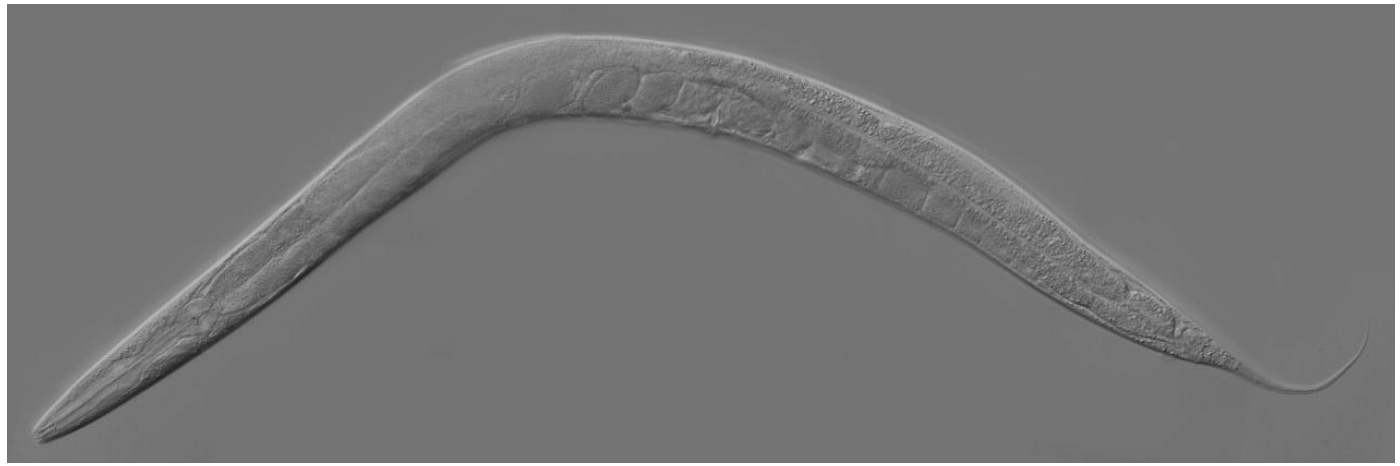
- A chosen gene is made inoperative, usually by deleting or disrupting part of it
- The phenotype of the knockout organism is compared with normal ones
- Any difference suggests what the gene does
- Libraries of knockout strains exist for model species such as mice, so researchers can order the strain they need

Examples

Mice without the p53 gene develop many tumours, showing that p53 helps prevent cancer. Mice lacking the gene for the hormone leptin overeat and become obese. Knockout techniques earned a Nobel Prize in 2007.

Why model organisms work

D1.3.8



The nematode Caenorhabditis elegans. CC BY-SA 2.5.

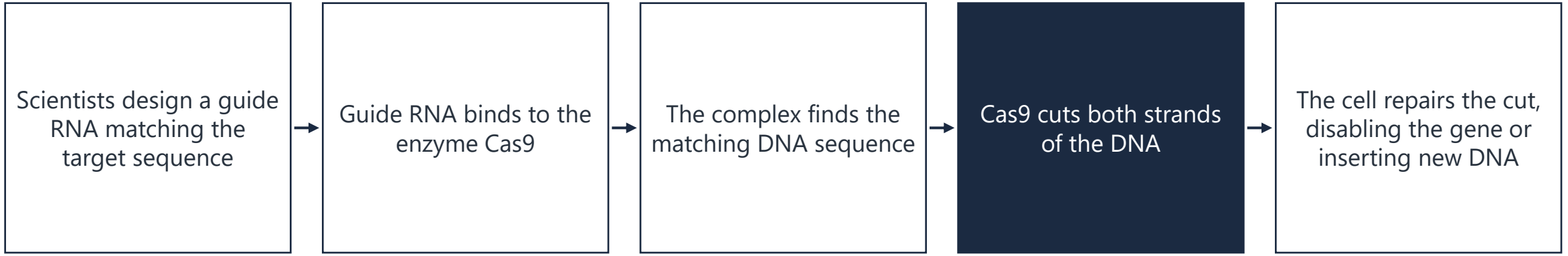
Organism	Useful because
Mouse	A mammal, so close to humans
Fruit fly	Short life cycle, many offspring
C. elegans	Transparent; every cell mapped

Evaluate

All organisms share the genetic code and many genes, so results can apply to humans. But a gene can have different roles in different species, and knocking out one gene may be covered by another. Discuss the ethics of producing animals that suffer from the knockout.

CRISPR-Cas9 gene editing

D1.3.9



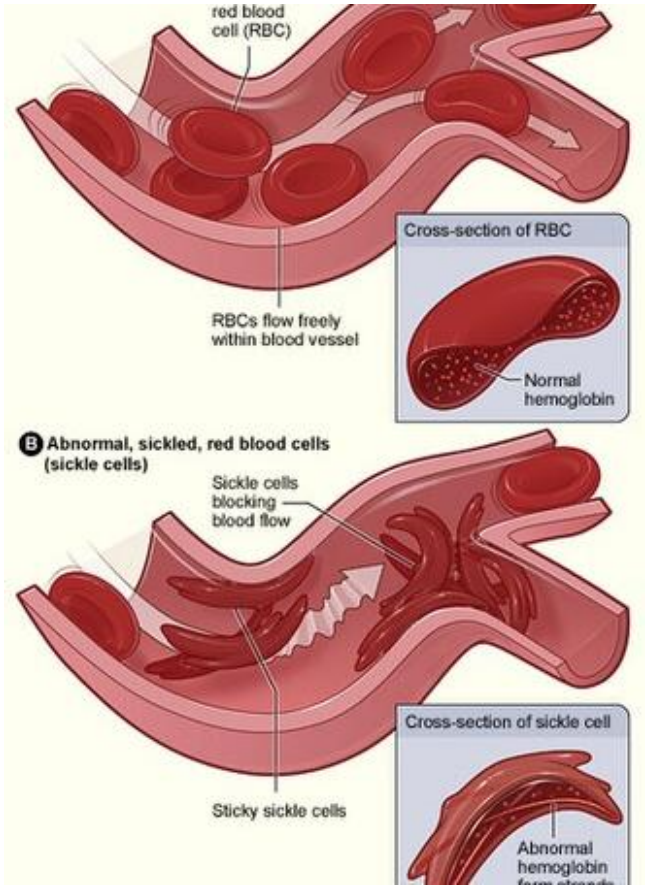
Where it came from

CRISPR sequences and Cas9 are part of a defence system in bacteria against viruses. Scientists adapted it as a tool: by changing the guide RNA, Cas9 can be sent to almost any sequence.

Why it matters

Cheaper, faster and more precise than older methods. Used in research, crops and medicine.

A successful use: sickle cell disease



Normal and sickle red blood cells. Public domain.

- Blood stem cells are taken from the patient's bone marrow
- CRISPR-Cas9 edits a gene that switches off foetal haemoglobin in adults
- The edited cells are returned; red blood cells now make foetal haemoglobin, which does not sickle
- Approved in 2023 for sickle cell disease and beta thalassaemia

Discuss

The treatment is very expensive and needs strong chemotherapy first. Who should get access?

Conserved sequences

D1.3.10

- **Conserved** sequences are identical or similar across a species or group of species
- **Highly conserved** sequences have stayed similar over long periods of evolution, for example histone and ribosomal RNA genes, shared by yeast and humans

Hypothesis	Explanation
Functional requirement	The product's function depends on its exact sequence; most changes harm it, so natural selection removes them
Slower rate of mutation	Some regions mutate less often, or are repaired more efficiently, so fewer changes arise

Evidence

Synonymous (silent) sites change faster than sites that alter the amino acid, which supports the first hypothesis.

Spot the conserved region

D1.3.10

Species	Short stretch of a protein (one letter per amino acid)
Human	S G R G K G G K G L G K G G A K R H R K
Cow	S G R G K G G K G L G K G G A K R H R K
Fruit fly	S G R G K G G K G L G K G G A K R H R K
Pea	S G R G K G G K G L G K G G A K R H R K

Activity

These are the first 20 amino acids of histone H4. How many differences can you find? Pea and human last shared an ancestor over a billion years ago. Which hypothesis best explains why so little has changed? What evidence would help you decide?

Check that you can explain

1. How gene knockout shows what a gene does
2. Why model organisms and knockout libraries are useful, and their limits
3. How CRISPR-Cas9 is used to edit a gene
4. One successful use of CRISPR-Cas9
5. What conserved and highly conserved sequences are
6. Two hypotheses for why sequences are conserved

Exit activity: 5 minutes

On your own and without notes. Hand this in as you leave.

1. State what a gene knockout is.
2. Outline the role of the guide RNA in CRISPR-Cas9 editing.
3. Give one hypothesis for why some sequences are highly conserved.

Image credits

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Adult Caenorhabditis elegans.jpg – The original uploader was Kbradnam at English Wikipedia. (Or – CC BY-SA 2.5

Sickle cell 01.jpg – The National Heart, Lung, and Blood Institute (NHLBI) – Public domain

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