

How Do We Prove the Gene Causes It?

How can a scientist prove that losing IRF6 causes clefting, instead of just appearing alongside it?

CARRY FORWARD

The IRF6 network helps oral epithelial cells form periderm, preventing wrong adhesions before correct fusion.

10-YEAR TAKEAWAY

Knockout and rescue experiments strengthen causation when loss creates a defect and restoration reverses part of it.

Cells differentiate	Development sculpts	Cells move	Development can go wrong
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1. Observe the analogy before naming the biology

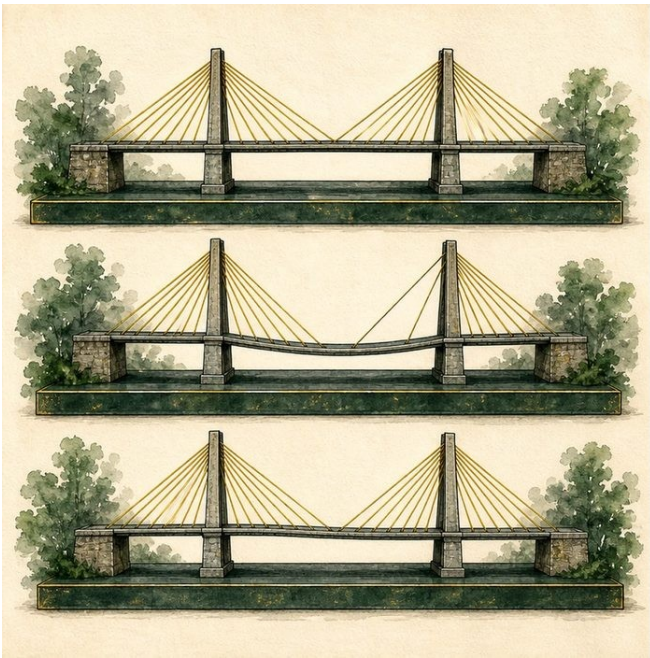


Illustration: Remove one bridge cable, then restore it

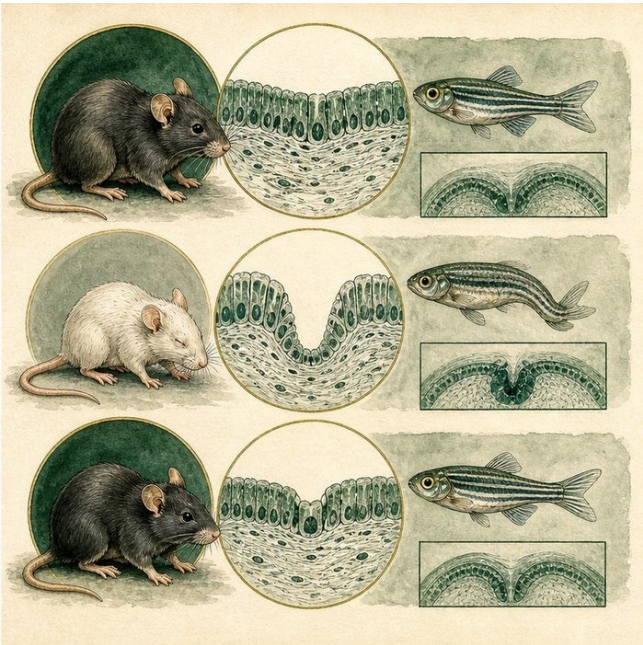
- 1. Which comparison shows necessity?
- 2. Which comparison tests sufficiency or rescue?
- 3. Why might a partial rescue still teach mechanism?

2. Turn observations into rules

- 1. Rule 1: Compare matched control and knockout groups. Explain it in your own words.
- 2. Rule 2: Restore the suspected function in a defined tissue or time. Explain it in your own words.
- 3. Rule 3: Measure both rescue and remaining defects. Explain it in your own words.

Where the analogy stops: Genes act in networks and tissues, so restoration can be incomplete.

3. Map the rules onto the biomedical example



Biomedical teaching illustration: Read IRF6 knockout and partial-rescue evidence

Analogy step	Biology step	How the relationship stays the same
Intact bridge	Wild-type control	_____
Cable removed	Irf6 knockout	_____
Cable restored	Tissue-specific or mRNA rescue	_____

4. Use the case evidence

ID	Finding supplied in the case	Why it matters
GEN15-E1	Irf6 knockout models develop abnormal epithelium, oral adhesions, and cleft palate.	Loss of function produces the predicted phenotype.
GEN15-E2	Restoring epithelial IRF6 reduces some adhesions but does not fully rescue every defect.	The rescue supports an epithelial role and reveals limits.
GEN15-E3	Zebrafish rescue experiments add evidence in a second model.	Cross-model replication strengthens the mechanism while remaining preclinical.

5. Make the clinical decision

You are judging whether the rescue proves complete correction. The rescue group has fewer adhesions but still has cleft palate in several regions.

- A. Call it a partial mechanistic rescue.
- B. Call it a complete cure.
- C. Ignore the improvement because it was incomplete.

Decision. Choose the verdict and cite both improvement and remaining phenotype.

Claim ceiling: You may support causation and a tissue role. You may not claim complete rescue or human treatment.

Claim. State the choice you can defend.

Evidence. Use these labeled IDs: GEN15-E1 + GEN15-E2.

Reasoning. Explain why the evidence supports the claim and stays inside the claim ceiling.

6. Reduce the lesson to one lasting idea

Take-home. Knockout and rescue experiments strengthen causation when loss creates a defect and restoration reverses part of it.

1. What does knockout test?
2. Why is a partial rescue still informative?

Glossary

Term	Plain-English definition
model organism	A species, such as zebrafish or mouse, studied because its biology is similar enough to ours to teach us about human development and disease.
knockout	An organism or cell engineered to have a specific gene switched off, used to reveal what that gene normally does.
rescue experiment	Adding a working gene back into a mutant to see if it restores the normal trait, which proves that gene was responsible.
causation	When one factor actually brings about another, shown by controlled evidence rather than by the two simply appearing together.
correlation	Two things tending to occur together, which does not by itself prove that one causes the other.

Next lesson unlock

We proved IRF6 loss causes clefting using knockout and rescue in mouse and zebrafish, so we now understand how the cleft happens in one embryo. But why is cleft lip and palate far more common in some human populations than in others? We chase that next, when the population geneticist takes the seat.

The journal links on the lesson page are optional. Everything required for this guided-notes set is already supplied here and in the case file.