Hunting the Exemplar Cleft Gene: Linkage to 1q32

How do you hunt a gene when you have no address for it?

CARRY FORWARD

Most isolated clefts fit a multifactorial threshold model in which many small influences add to risk.

10-YEAR TAKEAWAY

Linkage follows inherited chromosome markers to narrow a gene's address before sequencing names the gene.

1. Observe the analogy before naming the biology

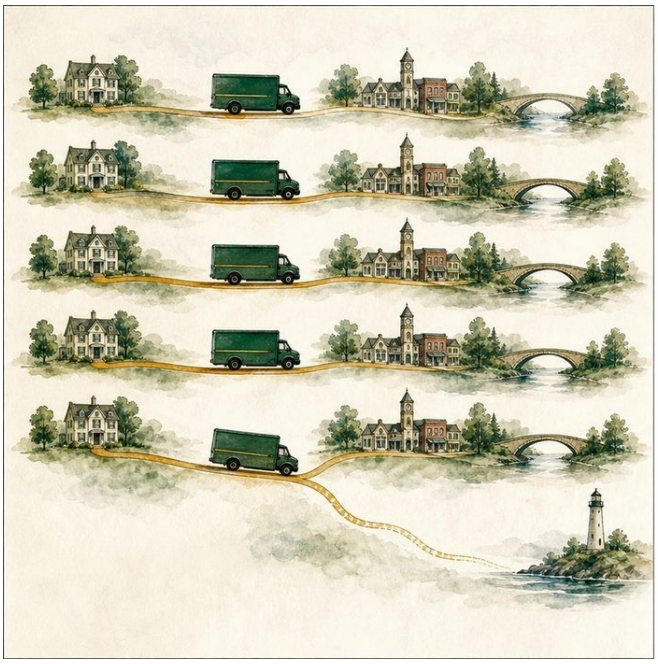


Illustration: Track a delivery truck by the landmarks it passes

1. Which landmark stays with the truck most often?

2. What would a route change separate?

3. How close must a landmark be to remain useful?

2. Turn observations into rules

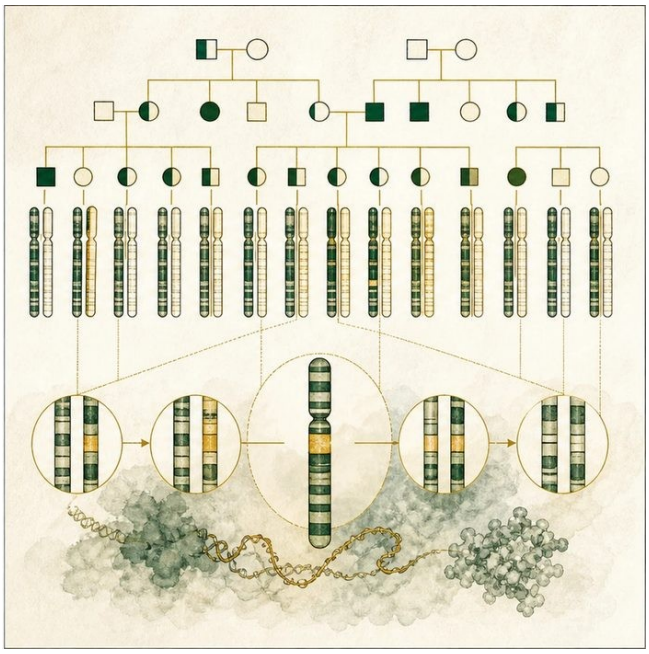
1. Rule 1: Track co-inheritance across relatives. Explain it in your own words.

2. Rule 2: Recombination can separate distant markers. Explain it in your own words.

3. Rule 3: Strong linkage narrows a region, not one final gene. Explain it in your own words.

Where the analogy stops: Chromosomes recombine biologically; they do not follow roads.

3. Map the rules onto the biomedical example



Biomedical teaching illustration: Follow a linked marker to chromosome 1q32

Analogy step	Biology step	How the relationship stays the same
Truck	Disease-associated chromosome segment	_____
Nearby landmark	DNA marker	_____
Route change	Meiotic recombination	_____

4. Use the case evidence

ID	Finding supplied in the case	Why it matters
GEN04-E1	In large Van der Woude families, certain chromosome 1 markers co-segregated with the phenotype.	The disease locus was linked to that region.
GEN04-E2	Recombination events narrowed the shared interval to 1q32.	Family crossovers set region boundaries.
GEN04-E3	The interval still contained more than one possible gene.	Linkage gives an address range, not a gene name.

5. Make the clinical decision

You are the linkage analyst for a historical gene hunt. A marker travels with the syndrome in nearly every informative relative, but several genes lie nearby.

A. Prioritize the linked interval for sequencing.

B. Declare the marker itself the causal gene.

C. Ignore recombination boundaries.

Decision. Choose the next step and cite what linkage can and cannot locate.

Claim ceiling: You may prioritize a locus. You may not call a marker causal or name IRF6 before sequence evidence.

Claim. State the choice you can defend.

Evidence. Use these labeled IDs: GEN04-E1 + GEN04-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. Linkage follows inherited chromosome markers to narrow a gene's address before sequencing names the gene.

1. What does co-segregation mean?

2. Why is a linked marker not automatically causal?

Glossary

Term	Plain-English definition
DNA marker	A known, variable spot in the genome used as a trackable signpost near a gene, even though the marker itself is not the disease gene.
linkage	The tendency of two spots close together on a chromosome to be inherited together.
co-segregation	When a marker version and a disease are inherited together in every affected family member, evidence that the responsible gene sits nearby.
recombination	The shuffling of chromosome pieces during egg and sperm formation, which can occasionally separate a marker from a nearby gene.
locus	The specific address of a gene or marker on a chromosome, such as the band 1q32.

Next lesson unlock

We have an address, chromosome 1q32, but an address is not a name. What is the actual gene sitting there, and what does it make?

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.