TEACHER GUIDE | DEVELOPMENTAL DOMAIN | 20 LESSONS

Teach the Evidence Chain

Each lesson moves from analogy to biology to a bounded clinical decision.

Standard 45-minute lesson flow

Minutes	Teacher and student move
0-5	Carry forward the prior take-home and state today's question.
5-12	Show only the analogy panel. Ask the three observation questions.
12-18	Students write the three rules. Name where the analogy stops.
18-27	Reveal the biomedical panel. Map each rule onto the case.
27-38	Students read labeled evidence and make the concrete decision.
38-45	Reveal the strongest answer, write CER, and state the next unlock.

When Could Mateo's Cleft Have Happened?

Place the major events of human craniofacial development on a week-by-week timeline (weeks 4 to 12) and identify the time window in which a lip or palate cleft…

CARRY FORWARD

A structural finding describes what is present now; development asks when and how that structure formed.

10-YEAR TAKEAWAY

The lip and palate form in short, ordered windows, so timing narrows where a developmental change began.

Socratic launch

Show the analogy panel only: A construction calendar with locked phases. Do not name the biology yet.

- Which jobs must happen before the next phase can begin?
- What happens if one crew arrives after its phase closes?
- Which clues could identify when a finished bridge problem began?

Rules students should earn

- Development follows an ordered sequence.
- Each structure has a limited building window.
- A final defect can point back to an earlier missed step.

Biology reveal and evidence

ID	Finding supplied in the case
DEV01-E1	The upper lip normally joins during approximately weeks 4 to 7.
DEV01-E2	Secondary palate development starts near week 6 and fusion is normally complete by about week 12.
DEV01-E3	A newborn cleft is the visible result of an earlier developmental event.

Decision and answer guidance

Situation: The team asks whether the cleft started during birth, late pregnancy, or early facial development.

Strongest option: Place the origin in the early lip and palate formation windows.

Evidence required: DEV01-E1 + DEV01-E2

Claim ceiling: You may identify developmental windows. You may not identify an exact day or cause from the cleft pattern alone.

Next handoff: We answered today's question: Mateo's cleft started in a window between about week 4 and week 12. But if a cleft is a fusion…

Which Building Blocks Must Fuse to Make a Lip and Palate?

Name and locate the five facial prominences and explain which prominences must grow toward each other and fuse to build a normal upper lip.

CARRY FORWARD

The lip and palate form in short, ordered windows, so timing narrows where a developmental change began.

10-YEAR TAKEAWAY

The face forms when named tissue prominences grow into position and join specific neighbors.

Socratic launch

Show the analogy panel only: Five puzzle pieces with only certain neighbors. Do not name the biology yet.

- Which pieces can touch because their edges face one another?
- Which piece contributes to the center of the final picture?
- How could the final gap reveal which meeting failed?

Rules students should earn

- Position limits which parts can meet.
- Each part contributes specific final structures.
- A gap can identify a failed neighbor relationship.

Biology reveal and evidence

ID	Finding supplied in the case
DEV02-E1	One frontonasal, two maxillary, and two mandibular prominences surround the early mouth.
DEV02-E2	The maxillary prominence must meet the medial nasal region to build the upper lip.
DEV02-E3	The mandibular prominences mainly form lower-face structures.

Decision and answer guidance

Situation: Only three labels can be placed on the model before the family teaching visit.

Strongest option: Label the maxillary and medial nasal meeting as the key upper-lip boundary.

Evidence required: DEV02-E1 + DEV02-E2

Claim ceiling: You may name the tissue boundary involved in lip formation. You may not name the molecular cause yet.

Next handoff: We named the blocks that must fuse. But each prominence is packed with cells that grow and migrate, and we have not asked where…

Where Do the Cells That Build the Face Come From?

Describe the origin of cranial neural crest cells at the edges of the neural folds, explain delamination by epithelial-to-mesenchymal transition, and state why these cells are called multipotent.

CARRY FORWARD

The face forms when named tissue prominences grow into position and join specific neighbors.

10-YEAR TAKEAWAY

Cranial neural crest cells leave the neural folds as flexible builders that can become several craniofacial tissues.

Socratic launch

Show the analogy panel only: Students leave one school for specialized apprenticeships. Do not name the biology yet.

- What do the travelers share before they choose a workshop?
- What changes when they leave the starting building?
- Why must their options remain open during the journey?

Rules students should earn

- A starting population can share one origin.
- Cells change behavior before they move.
- Signals at the destination help narrow cell fate.

Biology reveal and evidence

ID	Finding supplied in the case
DEV03-E1	Cranial neural crest cells arise near the closing neural folds.
DEV03-E2	They undergo EMT and delamination before migration.
DEV03-E3	Their descendants form much craniofacial bone, cartilage, and connective tissue.

Decision and answer guidance

Situation: The intern claims every facial bone cell began as a mature bone cell at the neural fold.

Strongest option: Correct the claim: mobile multipotent neural crest cells specialize later.

Evidence required: DEV03-E1 + DEV03-E2

Claim ceiling: You may describe lineage potential. You may not claim that every craniofacial tissue comes only from neural crest.

Next handoff: The face-building cells are born at the top of the embryo, near the brain, and break free by delamination. But the prominences they need…

How Do the Face-Building Cells Get to the Right Place?

Describe how cranial neural crest cells migrate in organized streams from the neural folds into the frontonasal process and the pharyngeal arches, and explain why correct migration is…

CARRY FORWARD

Cranial neural crest cells leave the neural folds as flexible builders that can become several craniofacial tissues.

10-YEAR TAKEAWAY

Face-building cells must travel in organized streams to the right destination before they can build the right structure.

Socratic launch

Show the analogy panel only: Transit lines carry different crews to different stations. Do not name the biology yet.

- Why are the routes separated?
- What happens if a crew exits at the wrong station?
- What information must a route provide besides direction?

Rules students should earn

- Movement is organized, not random.
- Destination affects what a cell can build.
- Too few arrivals can leave a structure small or missing.

Biology reveal and evidence

ID	Finding supplied in the case
DEV04-E1	Cranial neural crest cells migrate in reproducible streams.
DEV04-E2	Different streams enter the frontonasal region and pharyngeal arches.
DEV04-E3	Reduced neural crest survival or migration can cause facial hypoplasia.

Decision and answer guidance

Situation: One labeled stream reaches the first pharyngeal arch, while a second group stalls near the neural tube.

Strongest option: Predict reduced tissue contribution in the stalled group's destination.

Evidence required: DEV04-E1 + DEV04-E2

Claim ceiling: You may predict a developmental consequence in the model. You may not diagnose Mateo from one animal image.

Next handoff: The face-building cells ride organized streams into the frontonasal process and the first arch, filling the prominences. But the lip is still open: the…

How and When Does the Upper Lip Close?

Explain that the upper lip closes when the medial nasal, lateral nasal, and maxillary prominences merge and fuse at about human weeks 4 to 6, forming the upper…

CARRY FORWARD

Face-building cells must travel in organized streams to the right destination before they can build the right structure.

10-YEAR TAKEAWAY

Upper-lip closure requires growth, contact, and stable fusion at the maxillary-medial nasal boundary.

Socratic launch

Show the analogy panel only: Two zipper halves must align before they close. Do not name the biology yet.

- What must happen before the zipper can close?
- How could alignment fail even if both halves exist?
- What evidence would separate missing material from failed closure?

Rules students should earn

- Parts must first grow into range.
- Correct contact must precede stable joining.
- A gap can result from failure at more than one step.

Biology reveal and evidence

ID	Finding supplied in the case
DEV05-E1	Upper-lip tissues must grow into contact during the early facial window.
DEV05-E2	The maxillary prominence meets the medial nasal region at the lip boundary.
DEV05-E3	The joined surface must remodel into continuous tissue.

Decision and answer guidance

Situation: The animation shows both tissue blocks present but never making stable contact on the left.

Strongest option: Label a failed growth/contact/fusion sequence at the left lip boundary.

Evidence required: DEV05-E1 + DEV05-E2

Claim ceiling: You may identify the failed morphologic sequence. You may not identify a gene from the animation alone.

Next handoff: The upper lip closes at about weeks 4 to 6, forming the lip and the small front triangle of palate. But that triangle is…

How the Palate Begins: Secondary Palatal Shelf Outgrowth

Explain that the secondary palate begins as two shelves that grow downward from the maxillary processes, and that their growth depends on cell proliferation driven by signals in…

CARRY FORWARD

Upper-lip closure requires growth, contact, and stable fusion at the maxillary-medial nasal boundary.

10-YEAR TAKEAWAY

The secondary palate begins as paired shelves whose cell growth must create enough tissue to reach the midline.

Socratic launch

Show the analogy panel only: Two stage platforms extend toward the center. Do not name the biology yet.

- What determines whether the platforms can meet?
- What would a short platform leave at the center?
- Why must both sides be measured?

Rules students should earn

- Growth creates the material needed for contact.
- Paired structures must reach a shared target.
- A rescue can test whether missing growth caused the gap.

Biology reveal and evidence

ID	Finding supplied in the case
DEV06-E1	Secondary palatal shelves grow from the inner sides of the maxillary regions.
DEV06-E2	Reduced mesenchymal proliferation can leave shelves too small to meet.
DEV06-E3	Directed Bmp4 expression rescued palatal growth and fusion in an Msx1-deficient mouse model.

Decision and answer guidance

Situation: Control and mutant embryos are collected before shelf elevation. You can measure only one primary outcome.

Strongest option: Measure shelf size and mesenchymal proliferation on both sides.

Evidence required: DEV06-E1 + DEV06-E2

Claim ceiling: You may test a growth mechanism in the model. You may not claim a proven human treatment.

Next handoff: The palate begins as two shelves that grow downward beside the tongue. But those shelves point straight down, with the tongue sitting between them.…

Getting Above the Tongue: Palatal Shelf Elevation

Explain how the vertical palatal shelves rotate to a horizontal position above the tongue, and identify one mechanical and one tissue cause of failed elevation.

CARRY FORWARD

The secondary palate begins as paired shelves whose cell growth must create enough tissue to reach the midline.

10-YEAR TAKEAWAY

Palatal shelves must rapidly elevate above the tongue, and jaw-tongue geometry can block that movement.

Socratic launch

Show the analogy panel only: Drawbridges rotate only after a boat clears. Do not name the biology yet.

- What blocks the bridge before the boat clears?
- Which movement changes the bridge from vertical to horizontal?
- Could intact bridge parts still fail to meet?

Rules students should earn

- A structure may need room before it can move.
- Shape change can be rapid and coordinated.
- A mechanical block can cause failure without missing parts.

Biology reveal and evidence

ID	Finding supplied in the case
DEV07-E1	Palatal shelves first grow vertically beside the tongue.
DEV07-E2	The shelves elevate to a horizontal position above the tongue.
DEV07-E3	A small jaw can keep the tongue high and mechanically block elevation.

Decision and answer guidance

Situation: Diagram A shows shelves present but vertical beside a high tongue. Diagram B shows shelves horizontal above the tongue.

Strongest option: Identify elevation failure in A and completed elevation in B.

Evidence required: DEV07-E1 + DEV07-E2

Claim ceiling: You may identify a mechanical elevation problem. You may not assign a syndrome without the full clinical pattern.

Next handoff: The shelves remodel and rise above the tongue once the tongue drops and the head widens. But now the two horizontal shelves sit almost…

Two Shelves Become One Roof: Adhesion, the Medial Edge Epithelium, and the Seam

Describe how the two elevated shelves adhere at their medial edge epithelium and form a single midline epithelial seam, and explain why a non-stick surface layer must be…

CARRY FORWARD

Palatal shelves must rapidly elevate above the tongue, and jaw-tongue geometry can block that movement.

10-YEAR TAKEAWAY

After elevation, the medial edges must recognize, adhere to, and align with one another before fusion can continue.

Socratic launch

Show the analogy panel only: A docking spacecraft needs matching ports. Do not name the biology yet.

- What must match before docking begins?
- How is touching different from locking?
- What prevents the wrong surfaces from attaching?

Rules students should earn

- Contact requires the correct surfaces.
- Alignment must come before stable adhesion.
- Surface identity can permit or prevent sticking.

Biology reveal and evidence

ID	Finding supplied in the case
DEV08-E1	Elevated shelves grow toward one another at the midline.
DEV08-E2	The medial edge epithelia make contact and adhere.
DEV08-E3	Contact creates a midline epithelial seam.

Decision and answer guidance

Situation: One pair touches but separates with gentle handling. Another pair forms a stable midline seam.

Strongest option: Score the first as contact without stable adhesion and the second as adhesion.

Evidence required: DEV08-E1 + DEV08-E2

Claim ceiling: You may score contact and adhesion. You may not call mesenchymal fusion complete while the seam remains.

Next handoff: The shelves adhere at their medial edges and form one seam down the midline. But the roof is not truly finished: a wall of…

What Happens to the Wall Between the Shelves: Seam Removal, EMT versus Apoptosis

Explain that the midline epithelial seam must be removed for the palate to become one continuous tissue, and compare the candidate mechanisms (EMT, apoptosis, cell migration, and live-cell…

CARRY FORWARD

After elevation, the medial edges must recognize, adhere to, and align with one another before fusion can continue.

10-YEAR TAKEAWAY

True palatal fusion requires removal of the midline epithelial seam so mesenchyme becomes continuous.

Socratic launch

Show the analogy panel only: Remove the temporary wall after two rooms connect. Do not name the biology yet.

- Why was the temporary wall useful at first?
- What must disappear for the rooms to become one space?
- Which observations could distinguish demolition from wall movement?

Rules students should earn

- A temporary boundary can guide joining.
- The boundary must be removed for continuity.
- Competing cell mechanisms require direct evidence.

Biology reveal and evidence

ID	Finding supplied in the case
DEV09-E1	A midline epithelial seam forms after the shelves adhere.
DEV09-E2	Seam cells are removed through processes that include apoptosis and extrusion.
DEV09-E3	Lineage labeling tests whether seam cells remain, move, or change identity.

Decision and answer guidance

Situation: A still image shows no seam at the endpoint, but the team disagrees about what happened to the seam cells.

Strongest option: Use lineage labeling plus time-resolved cell-death and extrusion markers.

Evidence required: DEV09-E1 + DEV09-E2

Claim ceiling: You may distinguish supported cell-removal mechanisms. You may not force all seam loss into one mechanism without tracking evidence.

Next handoff: The seam is removed, by mechanisms scientists are still working out, so the palate becomes one continuous tissue. But the seam cells clear at…

What Tells Tissues When and Where to Grow: The Signaling Centers SHH, BMP, FGF

Explain that palatal shelves grow on schedule because signaling molecules (SHH, BMP, FGF) are released from specific places and act as instructions for when and where tissue grows…

CARRY FORWARD

True palatal fusion requires removal of the midline epithelial seam so mesenchyme becomes continuous.

10-YEAR TAKEAWAY

Signals such as SHH, BMP, and FGF carry local instructions that coordinate growth, position, and cell fate.

Socratic launch

Show the analogy panel only: An orchestra follows several section cues. Do not name the biology yet.

- Why does each section receive a different cue?
- What happens if one cue is missing but the others continue?
- How can timing and location change the meaning of the same cue?

Rules students should earn

- Development uses multiple signals at once.
- Signals act on particular cells in particular places.
- Removing one cue can change a specific process.

Biology reveal and evidence

ID	Finding supplied in the case
DEV10-E1	SHH is produced in palatal epithelium and influences nearby mesenchyme.
DEV10-E2	BMP and FGF pathways help regulate shelf growth and regional identity.
DEV10-E3	Changing a pathway in a model can alter proliferation or shape in specific shelf regions.

Decision and answer guidance

Situation: A drug blocks SHH response only in palatal mesenchyme, and anterior shelf proliferation drops.

Strongest option: Conclude that mesenchymal SHH response supports regional growth in this model.

Evidence required: DEV10-E1 + DEV10-E2

Claim ceiling: You may infer a pathway role in the model and tissue tested. You may not erase other pathways or transfer exposure to Mateo.

Next handoff: SHH, BMP, and FGF tell the shelves how much to grow and where, and a missing signal gives a too-small or mis-grown shelf. But…

TGF-beta3, the Fusion Switch in the Medial Edge Epithelium

Explain that TGF-beta3 turns on in the medial edge epithelium and is required for the shelves to stick and dissolve the seam, and predict the cleft that results…

CARRY FORWARD

Signals such as SHH, BMP, and FGF carry local instructions that coordinate growth, position, and cell fate.

10-YEAR TAKEAWAY

TGF-beta3 makes the palatal medial edge competent to complete adhesion and seam removal.

Socratic launch

Show the analogy panel only: A temporary access code enables the final handoff. Do not name the biology yet.

- Why must the code work only at the handoff point?
- What happens if both teams arrive but the code fails?
- What result would show that arrival and fusion are separate steps?

Rules students should earn

- A late switch can control a specific transition.
- Normal arrival does not guarantee successful joining.
- A knockout can separate one step from earlier steps.

Biology reveal and evidence

ID	Finding supplied in the case
DEV11-E1	In Tgfb3-null mouse embryos, palatal shelves can reach the midline.
DEV11-E2	The shelves fail to complete normal adhesion and seam removal.
DEV11-E3	The result is cleft secondary palate in the model.

Decision and answer guidance

Situation: Both control and mutant shelves reach the midline, but only controls form continuous mesenchyme.

Strongest option: Place TGF-beta3 at the fusion and seam-removal step.

Evidence required: DEV11-E1 + DEV11-E2

Claim ceiling: You may assign a required role in mouse palatal fusion. You may not claim every human cleft palate is caused by TGFB3.

Next handoff: We found the switch that tells edge cells to fuse. But before any cell can be an edge cell, it first had to BECOME…

TEACHER PLAN 12 OF 20 | DEVELOPMENTAL BIOLOGIST (ATIT LAB COLLABORATION)

The Wnt/beta-catenin Master Switch, How a Face Cell Decides What NOT to Be

Explain that Wnt/beta-catenin signaling tells a cranial cell to become bone or skin by actively repressing the default cartilage program, and predict the fate switch when that signal…

CARRY FORWARD

TGF-beta3 makes the palatal medial edge competent to complete adhesion and seam removal.

10-YEAR TAKEAWAY

Wnt-beta-catenin signaling can steer cranial progenitors toward dermal and bone fates while repressing cartilage fate.

Socratic launch

Show the analogy panel only: A railway switch selects one track and closes another. Do not name the biology yet.

- How does opening one route affect the other route?
- What outcome would show that the switch is instructive?
- Why must the starting cells be comparable?

Rules students should earn

- Cell fate involves both activation and repression.
- Removing a signal can reveal a default or competing fate.
- Lineage labels show what the same progenitors become.

Biology reveal and evidence

ID	Finding supplied in the case
DEV12-E1	Control cranial progenitors process Wnt-beta-catenin signaling during fate selection.
DEV12-E2	Conditional beta-catenin loss removes cranial dermis and bone in the tested region.
DEV12-E3	Lineage-labeled mutant cells form cartilage in their place.

Decision and answer guidance

Situation: A classmate says the mutant has less dermis only because all labeled cells died.

Strongest option: Use labeled cartilage descendants to support a fate switch.

Evidence required: DEV12-E1 + DEV12-E2

Claim ceiling: You may support an instructive Wnt role in the tested cranial lineage. You may not generalize to every tissue or developmental stage.

Next handoff: We now see how cells choose their fate. But fusion happens at surfaces, and surfaces are dangerous: a sticky outer layer could glue the…

Periderm and IRF6, the Non-Stick Coating on the Embryo

Explain that the periderm is a non-stick protective layer made by the gene IRF6, and that losing it lets oral surfaces glue to the wrong neighbors and block…

CARRY FORWARD

Wnt-beta-catenin signaling can steer cranial progenitors toward dermal and bone fates while repressing cartilage fate.

10-YEAR TAKEAWAY

IRF6-dependent periderm acts as a temporary non-stick surface that prevents the wrong oral tissues from adhering.

Socratic launch

Show the analogy panel only: Protective film keeps stacked labels from sticking early. Do not name the biology yet.

- Why is the protective layer temporary?
- What happens if the sticky surfaces meet too early?
- When should the protection be removed?

Rules students should earn

- A temporary surface layer can prevent wrong contacts.
- Differentiation gives a cell layer a specialized function.
- Loss of protection can create a mechanical block later.

Biology reveal and evidence

ID	Finding supplied in the case
DEV13-E1	Periderm covers embryonic oral epithelial surfaces during key stages.
DEV13-E2	Irf6-deficient mouse embryos have abnormal periderm differentiation.
DEV13-E3	Abnormal oral adhesions can block palatal shelf elevation.

Decision and answer guidance

Situation: The shelves formed, but one shelf is attached to the tongue before elevation.

Strongest option: Trace the failure from periderm loss to abnormal adhesion to blocked elevation.

Evidence required: DEV13-E1 + DEV13-E2

Claim ceiling: You may explain the knockout mechanism. You may not treat all human IRF6 variants as identical to a complete mouse knockout.

Next handoff: We now know which surfaces must stay apart and which must fuse, and which gene polices that. But clefts come in different forms: some…

TEACHER PLAN 14 OF 20 | DEVELOPMENTAL BIOLOGIST (FAILURE-POINT MAPPER)

Mapping the Failure, Which Step Breaks for a Cleft Lip Versus a Cleft Palate

Map a cleft phenotype back to the exact developmental step that failed, and distinguish a single local fusion failure from a broad, multi-step patterning defect.

CARRY FORWARD

IRF6-dependent periderm acts as a temporary non-stick surface that prevents the wrong oral tissues from adhering.

10-YEAR TAKEAWAY

A cleft pattern narrows the failed developmental checkpoint, but it rarely identifies one unique cause.

Socratic launch

Show the analogy panel only: A stopped assembly line reveals a checkpoint, not the culprit. Do not name the biology yet.

- Which station is the first place unfinished work appears?
- Can several failures stop the line at the same station?
- What extra evidence is needed to identify the cause?

Rules students should earn

- Work backward to the earliest failed checkpoint.
- Different causes can create a similar endpoint.
- Phenotype localizes a process better than a molecule.

Biology reveal and evidence

ID	Finding supplied in the case
DEV14-E1	Cleft lip points to an early upper-lip growth and fusion boundary.
DEV14-E2	Cleft palate can result from failed shelf growth, elevation, adhesion, or seam removal.
DEV14-E3	Mateo has both cleft lip and palate.

Decision and answer guidance

Situation: Case A has cleft lip only. Case B has cleft palate only. Mateo has both.

Strongest option: Assign each pattern to the narrowest supported checkpoint list.

Evidence required: DEV14-E1 + DEV14-E2

Claim ceiling: You may narrow checkpoints from anatomy. You may not assign one unique molecular cause from phenotype alone.

Next handoff: We can now map which step failed and see that Mateo's looks like an isolated fusion failure. But mapping a failure is not fixing…

TEACHER PLAN 15 OF 20 | EMBRYOLOGIST (TIMING SPECIALIST)

Critical Timing Windows, When the Door Closes

Explain that each lip and palate fusion step has a narrow critical window, and that once a window closes the cleft cannot be undone by later development.

CARRY FORWARD

A cleft pattern narrows the failed developmental checkpoint, but it rarely identifies one unique cause.

10-YEAR TAKEAWAY

A developmental risk matters most when it acts during the short window for the process it can disrupt.

Socratic launch

Show the analogy panel only: A theater door closes after one scene change. Do not name the biology yet.

- Why can the scenery move only during the blackout?
- What happens if the crew arrives after the curtain opens?
- How could the same delay matter in one scene but not another?

Rules students should earn

- Some changes are possible only during a short interval.
- Timing and target process must overlap.
- After the window closes, later development builds on the existing structure.

Biology reveal and evidence

ID	Finding supplied in the case
DEV15-E1	Upper-lip fusion occurs earlier than completion of secondary-palate fusion.
DEV15-E2	A disruption must overlap a sensitive process to affect that process directly.
DEV15-E3	After a cleft is established in utero, later normal growth does not automatically fuse the gap.

Decision and answer guidance

Situation: Exposure A occurred after upper-lip closure but during palatal fusion. Exposure B occurred before both windows.

Strongest option: Prioritize A for a direct palate-window hypothesis, while keeping other explanations open.

Evidence required: DEV15-E1 + DEV15-E2

Claim ceiling: You may judge timing compatibility. You may not prove causation from timing alone.

Next handoff: We now know the face has narrow closure windows, and those windows are when it is most fragile. If the embryo is most vulnerable…

When the Outside World Reaches the Embryo

Explain how environmental exposures (folate status, smoking, valproate) change the probability that lip and palate fusion succeeds, and rank them as risk-modifiers rather than single causes.

CARRY FORWARD

A developmental risk matters most when it acts during the short window for the process it can disrupt.

10-YEAR TAKEAWAY

An environmental factor changes risk only when evidence links dose, timing, and mechanism, and risk is not destiny.

Socratic launch

Show the analogy panel only: Weather changes the chance of a delayed flight. Do not name the biology yet.

- Does a storm delay every flight?
- Why do timing and severity matter?
- What evidence separates association from a tested mechanism?

Rules students should earn

- A risk factor changes probability, not certainty.
- Dose and timing shape the effect.
- Association, animal mechanism, and human causation are different evidence levels.

Biology reveal and evidence

ID	Finding supplied in the case
DEV16-E1	Some prenatal exposures are associated with higher cleft risk in populations.
DEV16-E2	Valproate is a known teratogenic medication whose risks depend on exposure context and timing.
DEV16-E3	Most exposed pregnancies do not produce the same outcome, and many clefts occur without a known exposure.

Decision and answer guidance

Situation: A parent asks whether one action definitely caused the cleft, but the case file contains no confirmed causal exposure.

Strongest option: Explain that risk factors change probability and no single cause is established here.

Evidence required: DEV16-E1 + DEV16-E2

Claim ceiling: You may explain population risk and biological plausibility. You may not assign an unrecorded exposure or blame.

Next handoff: Yes, the environment can tip the odds during the fusion window. But here is the puzzle: the same exposure can reach two embryos with…

Same DNA, Different Outcome

Describe how DNA methylation and microRNAs change gene activity without changing the DNA sequence, and use the second hit idea to explain why two embryos with the same…

CARRY FORWARD

An environmental factor changes risk only when evidence links dose, timing, and mechanism, and risk is not destiny.

10-YEAR TAKEAWAY

The same DNA can produce different outcomes because gene activity and developmental context can differ.

Socratic launch

Show the analogy panel only: The same music score can sound different under different controls. Do not name the biology yet.

- What stays the same in both performances?
- Which controls change how the score is used?
- Why does a changed performance not mean the notes were rewritten?

Rules students should earn

- DNA sequence and gene activity are not identical.
- Regulators can change when or how strongly genes act.
- Variable outcomes can reflect multiple interacting hits.

Biology reveal and evidence

ID	Finding supplied in the case
DEV17-E1	DNA methylation can change gene activity without changing the DNA letters.
DEV17-E2	MicroRNAs can reduce how much protein is made from target messages.
DEV17-E3	Cleft penetrance can vary among people with similar genetic susceptibility.

Decision and answer guidance

Situation: Both carry the same susceptibility variant, but only one has a cleft. Their methylation profiles differ at developmental genes.

Strongest option: Propose regulation as one testable modifier while keeping other factors open.

Evidence required: DEV17-E1 + DEV17-E2

Claim ceiling: You may propose an epigenetic modifier. You may not convert an association into a single proven cause.

Next handoff: Epigenetic marks and tiny RNAs let identical DNA give different outcomes, and isolated clefting behaves like an additive, multifactorial trait. But we just reasoned…

Watching Development Happen

Explain why scientists use model organisms (mouse, zebrafish) and live imaging plus lineage labeling to watch palate fusion, and judge what each tool can and cannot tell us…

CARRY FORWARD

The same DNA can produce different outcomes because gene activity and developmental context can differ.

10-YEAR TAKEAWAY

Researchers combine lineage labels, live imaging, and model organisms to turn hidden developmental events into visible evidence.

Socratic launch

Show the analogy panel only: Replay plus colored jerseys reveals the whole play. Do not name the biology yet.

- What can the replay show that the final score cannot?
- Why do colored jerseys matter when players cross paths?
- What question would require more than one camera angle?

Rules students should earn

- Time-resolved evidence reveals sequence.
- Stable labels reveal cell lineage.
- Different models and methods answer different questions.

Biology reveal and evidence

ID	Finding supplied in the case
DEV18-E1	Lineage labels mark a cell population and its descendants.
DEV18-E2	Live imaging records movement and cell behavior over time.
DEV18-E3	Mouse and zebrafish models share important developmental mechanisms but are not identical to humans.

Decision and answer guidance

Situation: The question is whether labeled seam cells die, leave the surface, or persist during the next six hours.

Strongest option: Use stable lineage labels with live imaging and cell-state markers.

Evidence required: DEV18-E1 + DEV18-E2

Claim ceiling: You may observe mechanism in the selected model. You may not assume every human embryo follows every model detail.

Next handoff: Model organisms plus live imaging let us watch each step of fusion and pin down which one failed. So a bold question: if we…

TEACHER PLAN 19 OF 20 | DEVELOPMENTAL BIOLOGIST (RESCUE STRATEGIST)

If We Know the Window and the Signal, Could We Prevent a Cleft?

Use real mouse rescue experiments to explain rescue logic (add back the missing signal in the right place and time to restore a normal palate), and judge honestly…

CARRY FORWARD

Researchers combine lineage labels, live imaging, and model organisms to turn hidden developmental events into visible evidence.

10-YEAR TAKEAWAY

A rescue experiment supports a mechanism when restoring one step restores the outcome, but it is not yet a human treatment.

Socratic launch

Show the analogy panel only: Replace one fuse and watch one circuit return. Do not name the biology yet.

- What comparison shows that the replacement mattered?
- Why must all other conditions stay matched?
- Does restoring one circuit prove the whole building is safe?

Rules students should earn

- Compare control, disrupted, and rescued groups.
- Restore the suspected step during the relevant window.
- Mechanism evidence comes before treatment claims.

Biology reveal and evidence

ID	Finding supplied in the case
DEV19-E1	Msx1-deficient mice show reduced anterior palatal growth and cleft palate.
DEV19-E2	Directed Bmp4 expression restored growth and fusion in the reported mouse model.
DEV19-E3	The intervention was genetic and preclinical in mice.

Decision and answer guidance

Situation: A headline says the mouse rescue means cleft palate can now be prevented in human pregnancy.

Strongest option: Correct it to proof of mechanism in a specific mouse model.

Evidence required: DEV19-E1 + DEV19-E2

Claim ceiling: You may state proof of mechanism in the model. You may not claim safety, timing, delivery, or effectiveness in humans.

Next handoff: We can rescue a cleft in a mouse by adding back one signal, but only in the lab and only by editing the embryo's…

Mateo's Complete Developmental Story

Assemble the twenty-lesson evidence into one normal-versus-failed developmental account of Mateo's cleft, and conclude that it is an isolated failure of fusion in a specific window (nonsyndromic, multifactorial)…

CARRY FORWARD

A rescue experiment supports a mechanism when restoring one step restores the outcome, but it is not yet a human treatment.

10-YEAR TAKEAWAY

Mateo's cleft is best explained as a developmental pathway outcome with bounded evidence, not as one proven cause.

Socratic launch

Show the analogy panel only: An evidence board reconstructs a route without inventing a suspect. Do not name the biology yet.

- Which cards establish sequence?
- Which cards identify a failed checkpoint?
- What missing card prevents a one-cause conclusion?

Rules students should earn

- Build the story from ordered evidence.
- Separate observed phenotype, supported mechanism, and unknown cause.
- End with the strongest claim the evidence permits.

Biology reveal and evidence

ID	Finding supplied in the case
DEV20-E1	Mateo has complete unilateral left cleft lip and palate with no broader anomaly pattern established in the composite file.
DEV20-E2	Lip and palate formation require ordered growth, cell movement, signaling, adhesion, and seam removal.
DEV20-E3	The case file does not establish one causal variant, exposure, or syndrome.

Decision and answer guidance

Situation: The team must approve one paragraph for the family-facing case summary.

Strongest option: Describe the failed developmental outcomes and state that one cause is not established.

Evidence required: DEV20-E1 + DEV20-E2

Claim ceiling: You may synthesize the supported developmental pathway. You may not add a diagnosis, variant, or exposure absent from the case file.

Next handoff: Mateo's cleft is an isolated, multifactorial failure of fusion in the weeks 4 to 12 window, with the rest of development normal. The developmental…