STUDENT READING PACK | DEVELOPMENTAL DOMAIN | NINTH-GRADE TARGET

The Developmental Domain Explainer

Short readings that supply every idea needed for each lesson decision.

REQUIRED	OPTIONAL
Read the three short paragraphs and use the labeled case evidence.	**Open the publication links only if you want to go deeper.**

How every reading is structured

- Why it matters
- The question
- Prior takeaway
- Analogy and rules
- Biomedical example
- Case evidence
- Decision
- Take-home
- Glossary
- Optional sources

READING 1 OF 20 | DEVELOPMENT SCULPTS

When Could Mateo's Cleft Have Happened?

During which weeks of development does the face form, and when could a cleft like Mateo's have started?

START WITH

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

REMEMBER

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

Why this matters

Timing turns a visible structure into a testable developmental question.

The biology in plain English

The face changes quickly during the first trimester. Separate tissue blocks grow toward one another and join.

The upper lip forms before the secondary palate finishes. Their windows overlap, but they are not identical.

A cleft seen at birth records an earlier missed developmental step. It does not prove when, why, or which gene changed.

Biomedical teaching illustration: Place lip and palate formation on the human timeline

Check your understanding

- Which window is earlier, lip closure or completion of palatal fusion?
- Why can the newborn exam not reveal one exact developmental day?

READING 1 OF 20 | EVIDENCE, DECISION, AND GLOSSARY

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV01-E1	The upper lip normally joins during approximately weeks 4 to 7.	Mateo's cleft lip began during an early facial fusion window.
DEV01-E2	Secondary palate development starts near week 6 and fusion is normally complete by about week 12.	Mateo's cleft palate began during a later, overlapping window.
DEV01-E3	A newborn cleft is the visible result of an earlier developmental event.	The delivery-room appearance does not give the exact day or cause.

Concrete decision

You are the developmental biologist at Mateo's case conference. The team asks whether the cleft started during birth, late pregnancy, or early facial development.

A. Place the origin in the early lip and palate formation windows.

B. Place the origin during delivery.

C. Claim one exact day from appearance alone.

Decision prompt: Choose the timeline statement and cite the two evidence cards that set its limits.

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

Glossary

Term	Plain-English definition
embryo	The developing human from about week 3 to week 8, when most organs and the face first take shape.
craniofacial development	The set of steps in the embryo that shape the skull and face, including how facial swellings grow and fuse into lips, palate, and jaw.
gestational week	A way of counting how far along a pregnancy is, measured in weeks from the start of the mother's last menstrual period.
fusion	When two growing tissue edges meet at the midline and join into one continuous structure, as the lip and palate do during development.
critical window	A lesson term defined by the surrounding model and case evidence.

READING 2 OF 20 | DEVELOPMENT SCULPTS

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

What are the building blocks of the face, and which ones must fuse to form a normal upper lip?

START WITH

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

REMEMBER

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

Why this matters

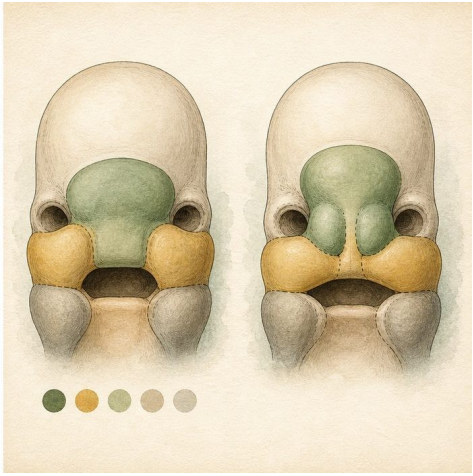
Accurate maps prevent students and clinicians from treating the face as one undivided sheet.

The biology in plain English

Early in development, the face is arranged as five swellings called facial prominences around the early mouth.

The center and sides do not make the same structures. The medial nasal regions help form the middle upper lip, while maxillary prominences contribute the sides.

Normal upper-lip formation requires growth, contact, and stable joining at the correct boundary.



Biomedical teaching illustration: Map the five prominences to the upper lip

Check your understanding

- Which two named regions meet to form the upper lip?
- Why are the mandibular prominences not the best answer for Mateo's upper-lip cleft?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV02-E1	One frontonasal, two maxillary, and two mandibular prominences surround the early mouth.	The five prominences are the starting blocks of the face.
DEV02-E2	The maxillary prominence must meet the medial nasal region to build the upper lip.	A failed meeting at this boundary can produce cleft lip.
DEV02-E3	The mandibular prominences mainly form lower-face structures.	They are not the direct lip-fusion boundary in Mateo's cleft.

Concrete decision

You are labeling a surgical teaching model for the cleft team. Only three labels can be placed on the model before the family teaching visit.

A. Label the maxillary and medial nasal meeting as the key upper-lip boundary.

B. Label the mandibular midline as Mateo's upper-lip failure.

C. Label every prominence as making the same structure.

Decision prompt: Choose the useful label set and defend it with two evidence cards.

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

Glossary

Term	Plain-English definition
facial prominence	One of the five swellings of tissue (one frontonasal, two maxillary, two mandibular) that grow toward the midline and fuse to build the face.
frontonasal prominence	A bulge of tissue in the early embryo's face that gives rise to the forehead, bridge of the nose, and middle of the upper lip.
maxillary process	A paired bulge of embryo tissue that grows toward the midline to form the upper jaw, cheeks, and sides of the upper lip.
mandibular process	The paired early facial swellings below the mouth that grow toward each other to form the lower jaw and chin.
medial nasal process	A pair of inner embryonic tissue bulges that merge to form the center of the upper lip, the philtrum, and the tip of the nose.
lateral nasal process	A swelling on each side of the developing face that forms the outer wing of the nostril during early facial growth.
stomodeum	The shallow pit on the front of the early embryo that becomes the opening of the mouth as the face takes shape.

READING 3 OF 20 | CELLS DIFFERENTIATE

Where Do the Cells That Build the Face Come From?

Where in the early embryo are the face-building cells born, and how do they get free to start their journey?

START WITH

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

REMEMBER

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

Why this matters

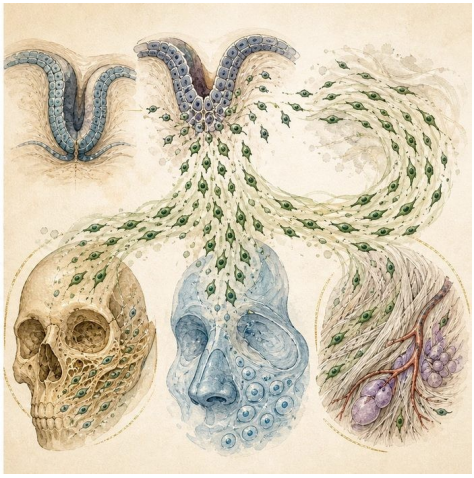
Cell origin and cell fate are different questions, and development connects them over time.

The biology in plain English

Cranial neural crest cells begin near the neural folds. They are not mature bone or cartilage cells at that stage.

Before moving, they change from a tightly attached epithelial state to a more mobile mesenchymal state. This is called EMT.

After migration, local signals help their descendants become specialized craniofacial tissues.



Biomedical teaching illustration: Follow cranial neural crest cells from neural fold to facial mesenchyme

Check your understanding

- What changes during EMT?
- Why is multipotent more accurate than mature bone cell for an early neural crest cell?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV03-E1	Cranial neural crest cells arise near the closing neural folds.	They share an early origin before entering the face.
DEV03-E2	They undergo EMT and delamination before migration.	They must loosen epithelial attachments and become mobile.
DEV03-E3	Their descendants form much craniofacial bone, cartilage, and connective tissue.	Their early state supports several later fates.

Concrete decision

You are explaining lineage tracing to a new lab intern. The intern claims every facial bone cell began as a mature bone cell at the neural fold.

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

B. Agree that mature bone cells migrate from the neural fold.

C. Claim all facial tissues come from one mature cell type.

Decision prompt: Choose the correction and cite evidence for both mobility and later specialization.

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

Glossary

Term	Plain-English definition
neural crest cell	A migrating embryonic cell type that leaves the forming spinal cord and builds much of the face, skull, and many other tissues.
neural fold	The two raised ridges of the early embryo that rise up and fuse along the midline to form the neural tube, source of the brain and spinal cord.
delamination	When a cell loosens from a sheet of connected cells and leaves to crawl on its own.
epithelial-to-mesenchymal transition (EMT)	A change where a settled, sheet-bound epithelial cell loosens its bonds and becomes a mobile, crawling mesenchymal cell.
multipotent	Able to become several different cell types, but not every type in the body.
mesenchyme	Loose, unsettled cells in a watery matrix that can crawl and later become bone, cartilage, or connective tissue.

READING 4 OF 20 | CELLS MOVE

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

How do cranial neural crest cells travel from the neural folds to the right facial blocks, and why does taking the correct route matter?

START WITH

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

REMEMBER

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

Why this matters

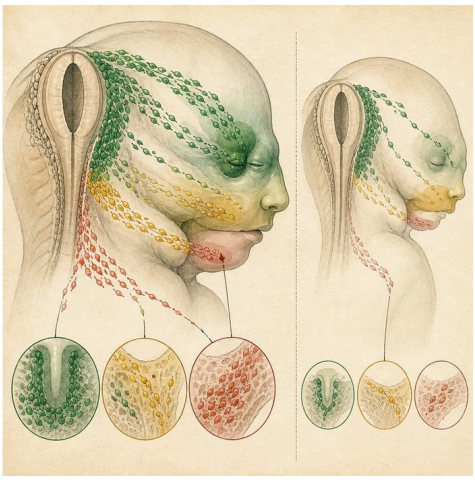
A cell with the right fate potential still fails the system if it never reaches the correct place.

The biology in plain English

Cranial neural crest cells travel along organized pathways. Scientists can label the cells and follow the streams in model organisms.

Some streams enter the frontonasal region. Others enter pharyngeal arches that contribute to jaws and related structures.

If too few cells arrive, the target tissue may be smaller than expected. This is called hypoplasia.



Biomedical teaching illustration: Trace neural crest streams into facial regions

Check your understanding

- How is an organized stream different from random movement?
- What could happen if too few cells reach a facial destination?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV04-E1	Cranial neural crest cells migrate in reproducible streams.	Their movement has spatial organization.
DEV04-E2	Different streams enter the frontonasal region and pharyngeal arches.	Route and destination are linked.
DEV04-E3	Reduced neural crest survival or migration can cause facial hypoplasia.	Cell number at the destination affects growth.

Concrete decision

You are reviewing a lineage-tracing image from a mouse embryo. One labeled stream reaches the first pharyngeal arch, while a second group stalls near the neural tube.

A. Predict reduced tissue contribution in the stalled group's destination.

B. Predict no effect because cell position never matters.

C. Claim the image proves a specific human diagnosis.

Decision prompt: Choose the defensible prediction and cite the route and cell-number evidence.

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

Glossary

Term	Plain-English definition
migration	The active movement of cells from one location to another, essential during development, wound healing, and the spread of cancer.
pharyngeal arch (branchial arch)	One of the ridged blocks of embryo tissue along the future neck that give rise to the jaw, face, and throat structures.
frontonasal process	An early facial swelling above the mouth that grows into the forehead, the bridge and tip of the nose, and the middle of the upper lip.
migratory stream	An organized flow of cells, such as neural crest cells, traveling together along a set path to where they will build a structure.
mesenchyme	Loose, unsettled cells in a watery matrix that can crawl and later become bone, cartilage, or connective tissue.
hypoplasia	Underdevelopment of a tissue or organ from too few cells, leaving it smaller or less complete than normal.

READING 5 OF 20 | DEVELOPMENT SCULPTS

How and When Does the Upper Lip Close?

Which blocks must merge and fuse to close the upper lip, and when does this happen?

START WITH

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

REMEMBER

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

Why this matters

Breaking fusion into steps prevents students from treating the word fusion as a single unexplained event.

The biology in plain English

The upper lip does not appear all at once. Tissue prominences enlarge, approach the right neighbors, contact, and remodel.

The important boundary is between a maxillary prominence and a medial nasal region.

A cleft lip can result when growth, contact, or stable joining does not complete during the window.

Biomedical teaching illustration: Name the three steps in upper-lip closure

Check your understanding

- What three steps must occur before the lip is continuous?
- Why does contact alone not prove successful fusion?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV05-E1	Upper-lip tissues must grow into contact during the early facial window.	Distance is a developmental variable.
DEV05-E2	The maxillary prominence meets the medial nasal region at the lip boundary.	The contact must occur at the correct neighbor.
DEV05-E3	The joined surface must remodel into continuous tissue.	Touching alone is not the completed lip.

Concrete decision

You are annotating a developmental animation for the family conference. The animation shows both tissue blocks present but never making stable contact on the left.

A. Label a failed growth/contact/fusion sequence at the left lip boundary.

B. Label a secondary palate elevation failure only.

C. Claim the tissue blocks were never present.

Decision prompt: Choose the label that fits the animation and cite the boundary evidence.

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

Glossary

Term	Plain-English definition
fusion	When two growing tissue edges meet at the midline and join into one continuous structure, as the lip and palate do during development.
primary palate	A lesson term defined by the surrounding model and case evidence.
intermaxillary segment	The central facial block formed in the embryo that gives rise to the philtrum of the lip, the front gum, and the primary palate.
philtrum	The vertical groove in the middle of the upper lip, bordered by two ridges, that forms where facial parts fuse during development.
incisive foramen	A small opening in the roof of the mouth just behind the front teeth that marks the boundary between the primary and secondary palate.
cleft lip	A birth difference where the upper lip does not fully fuse before birth, leaving a gap or split that can reach toward the nose.

READING 6 OF 20 | DEVELOPMENT SCULPTS

How the Palate Begins: Secondary Palatal Shelf Outgrowth

Where does the back of the palate come from, and what makes it grow?

START WITH

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

REMEMBER

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

Why this matters

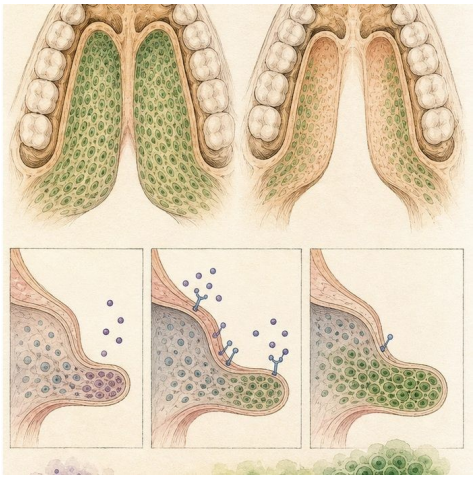
A shelf cannot fuse if it never grows enough tissue to reach its partner.

The biology in plain English

The secondary palate starts as two shelves growing inward from the maxillary regions.

Cells in the shelf mesenchyme divide and add tissue. Too little growth can leave the shelves short.

Mouse rescue experiments can test a mechanism. They do not by themselves prove that the same intervention is safe or effective in humans.



Biomedical teaching illustration: Connect cell proliferation to palatal shelf length

Check your understanding

- How can lower proliferation change shelf contact?
- What does the Bmp4 rescue support, and what does it not prove?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV06-E1	Secondary palatal shelves grow from the inner sides of the maxillary regions.	The palate begins as paired outgrowths.
DEV06-E2	Reduced mesenchymal proliferation can leave shelves too small to meet.	Cell number and shelf size are connected.
DEV06-E3	Directed Bmp4 expression rescued palatal growth and fusion in an Msx1-deficient mouse model.	The experiment supports a growth mechanism in that model.

Concrete decision

You are choosing the readout for a palatal-growth experiment. Control and mutant embryos are collected before shelf elevation. You can measure only one primary outcome.

A. Measure shelf size and mesenchymal proliferation on both sides.

B. Measure newborn speech before fusion occurs.

C. Claim human prevention from the mouse embryos.

Decision prompt: Choose the primary outcome and cite the evidence linking cell growth to shelf size.

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

Glossary

Term	Plain-English definition
secondary palate	A lesson term defined by the surrounding model and case evidence.
palatal shelf	One of two tissue ledges in the embryo that swing up from beside the tongue to horizontal and meet at the midline to form the roof of the mouth.
maxillary process	A paired bulge of embryo tissue that grows toward the midline to form the upper jaw, cheeks, and sides of the upper lip.
mesenchyme	Loose, unsettled cells in a watery matrix that can crawl and later become bone, cartilage, or connective tissue.
proliferation	The rapid increase in cell number as cells repeatedly grow and divide, building or repairing tissue.

READING 7 OF 20 | CELLS MOVE

Getting Above the Tongue: Palatal Shelf Elevation

How do two downward-pointing shelves move to a horizontal position above the tongue, and what can stop them?

START WITH

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

REMEMBER

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

Why this matters

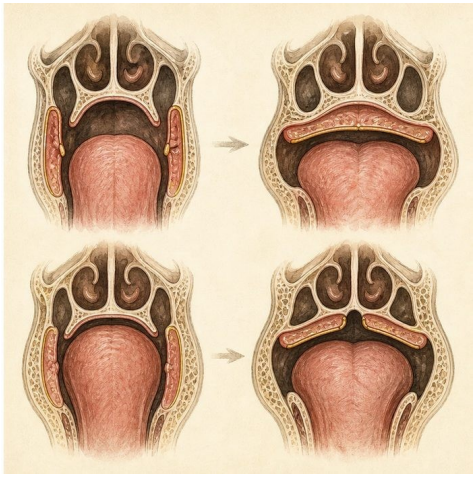
Development depends on moving structures, not only on making the correct parts.

The biology in plain English

At first, palatal shelves point downward beside the tongue. They must change to a horizontal position above it.

Jaw growth and tongue descent help create room. The shelves also generate forces within their own tissue.

If the tongue remains high because the jaw is very small, the shelves may be blocked even though they formed.



Biomedical teaching illustration: Use jaw and tongue position to explain shelf elevation

Check your understanding

- What changes between the vertical and horizontal shelf stages?
- How can jaw size affect the palate without removing shelf tissue?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV07-E1	Palatal shelves first grow vertically beside the tongue.	Their early position is not the final roof position.
DEV07-E2	The shelves elevate to a horizontal position above the tongue.	Movement is required before midline contact.
DEV07-E3	A small jaw can keep the tongue high and mechanically block elevation.	Geometry can cause cleft palate even when shelves exist.

Concrete decision

You are reviewing two fetal MRI teaching diagrams. Diagram A shows shelves present but vertical beside a high tongue. Diagram B shows shelves horizontal above the tongue.

A. Identify elevation failure in A and completed elevation in B.

B. Call both diagrams identical because shelves are present.

C. Diagnose a named syndrome from shelf position alone.

Decision prompt: Choose the comparison and cite the evidence that separates presence from position.

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

Glossary

Term	Plain-English definition
elevation	The developmental step where the palatal shelves lift from a downward position up to horizontal so they can meet above the tongue.
horizontal	Lying flat and level, side to side; the palatal shelves must swing into a horizontal position above the tongue before they can fuse.
vertical	Running up and down, along the head-to-foot direction, as opposed to side to side or front to back.
hyaluronan	A large sugar molecule of the extracellular matrix that holds water and gives tissues like the developing palate their springy, hydrated structure.
Pierre Robin sequence	A chain of features starting with a small lower jaw, which pushes the tongue back and blocks the airway and often comes with a cleft palate.

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

How do the touching edges of two separate shelves become a single, joined roof?

START WITH

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

REMEMBER

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

Why this matters

Scientists need separate words for steps that occur minutes or hours apart.

The biology in plain English

Once the shelves are above the tongue, their inner edges approach the midline. These edges are covered by medial edge epithelium.

Touching is apposition. Stable sticking is adhesion. The two are related but not identical.

The first stable connection forms a midline epithelial seam that must later be removed.

Biomedical teaching illustration: Zoom in on the medial edge epithelium

Check your understanding

- How is apposition different from adhesion?
- Why is a midline seam not yet the final continuous palate?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV08-E1	Elevated shelves grow toward one another at the midline.	Correct position creates the opportunity for contact.
DEV08-E2	The medial edge epithelia make contact and adhere.	A specific surface interaction begins fusion.
DEV08-E3	Contact creates a midline epithelial seam.	The first joined state still contains an epithelial wall.

Concrete decision

You are scoring palate explants after 24 hours in culture. One pair touches but separates with gentle handling. Another pair forms a stable midline seam.

A. Score the first as contact without stable adhesion and the second as adhesion.

B. Score both as complete fusion.

C. Ignore the seam because touching is always enough.

Decision prompt: Choose the scoring rule and cite the evidence that separates contact from adhesion.

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

Glossary

Term	Plain-English definition
adhesion	The way cells stick to each other and to the matrix around them using surface proteins, holding tissues together and guiding how they move.
medial edge epithelium (MEE)	The cell layer on the inner edge of each palatal shelf, which must be removed for the shelves to fuse into a single palate.
midline epithelial seam (MES)	The thin line of surface cells formed when the two palate shelves meet, which must break down so the palate can fully fuse.
periderm	A thin temporary outer cell layer of the embryo; if it sticks where it should not, the growing edges cannot fuse.
midline	The imaginary center line of the body; many facial structures form by growing toward and meeting at it.

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

What happens to the wall of seam cells so the palate becomes one continuous tissue, and how sure are scientists about the answer?

START WITH

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

REMEMBER

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

Why this matters

The final shape can hide the cell behaviors that produced it.

The biology in plain English

The midline epithelial seam is useful during initial joining, but it separates the mesenchyme on the two sides.

Seam cells are removed. Studies support apoptosis and extrusion, while the importance of EMT has been debated.

Lineage labeling marks cells so researchers can follow their descendants and avoid guessing from an endpoint.

Biomedical teaching illustration: Test what happens to midline seam cells

Check your understanding

- What final tissue state shows true fusion?
- Why is lineage labeling stronger than one endpoint image for testing seam-cell fate?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV09-E1	A midline epithelial seam forms after the shelves adhere.	The seam is a normal temporary stage.
DEV09-E2	Seam cells are removed through processes that include apoptosis and extrusion.	Cell loss helps eliminate the barrier.
DEV09-E3	Lineage labeling tests whether seam cells remain, move, or change identity.	Mechanism requires tracking, not appearance alone.

Concrete decision

You are choosing an experiment to test seam removal. A still image shows no seam at the endpoint, but the team disagrees about what happened to the seam cells.

A. Use lineage labeling plus time-resolved cell-death and extrusion markers.

B. Use the endpoint image alone to prove one mechanism.

C. Assume all seam cells became bone.

Decision prompt: Choose the experiment and explain why the endpoint image is not enough.

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

Glossary

Term	Plain-English definition
midline epithelial seam (MES)	The thin line of surface cells formed when the two palate shelves meet, which must break down so the palate can fully fuse.
epithelial-to-mesenchymal transition (EMT)	A change where a settled, sheet-bound epithelial cell loosens its bonds and becomes a mobile, crawling mesenchymal cell.
apoptosis	Programmed, controlled cell death that the body uses on purpose, including to clear the seam between two tissues during palate fusion.
cell extrusion	A process where a sheet of cells squeezes out and removes one of its own cells, sealing the gap to keep the layer intact.
lineage labeling	A method that tags a starting cell with a permanent marker so all of its descendant cells can be tracked over time.

READING 10 OF 20 | CELLS DIFFERENTIATE

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

What signals tell the palatal shelves how much to grow and where, and what happens to a shelf if a signal is missing?

START WITH

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

REMEMBER

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

Why this matters

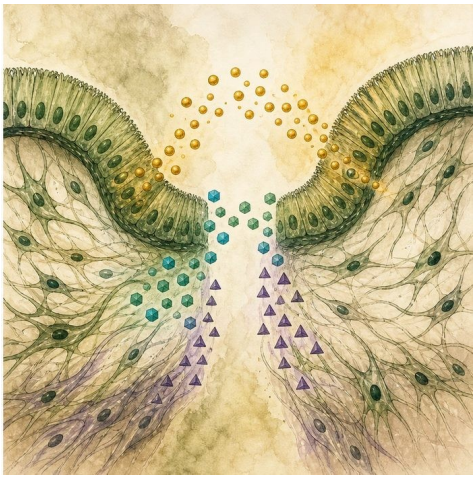
Signals explain how neighboring tissues coordinate rather than developing as isolated parts.

The biology in plain English

Cells send protein signals to nearby cells. A signal only matters when the target cell can receive and respond to it.

SHH, BMP, and FGF pathways help coordinate growth and pattern in the developing palate.

Because signals interact, blocking one pathway tests one part of a network rather than proving a single master cause.



Biomedical teaching illustration: Map epithelial-mesenchymal cross-talk

Check your understanding

- What are the source and target in epithelial-mesenchymal cross-talk?
- Why does one inhibitor result not prove that only one signal matters?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV10-E1	SHH is produced in palatal epithelium and influences nearby mesenchyme.	Signal source and target can be different tissues.
DEV10-E2	BMP and FGF pathways help regulate shelf growth and regional identity.	Several pathways coordinate the process.
DEV10-E3	Changing a pathway in a model can alter proliferation or shape in specific shelf regions.	Signal effects depend on place and time.

Concrete decision

You are interpreting a pathway-inhibition experiment. A drug blocks SHH response only in palatal mesenchyme, and anterior shelf proliferation drops.

A. Conclude that mesenchymal SHH response supports regional growth in this model.

B. Conclude that SHH is the only signal in palate development.

C. Conclude that Mateo received the same drug.

Decision prompt: Choose the bounded conclusion and cite source-target and growth evidence.

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.

Glossary

Term	Plain-English definition
signaling molecule	A chemical messenger released by one cell that travels to another cell and triggers a specific response.
signaling center	A small group of cells in a developing embryo that releases signals telling nearby cells how to grow and what to become.
SHH (Sonic hedgehog)	A signaling molecule that tells cells their position during development and helps pattern the face, limbs, and brain.
BMP	Bone morphogenetic protein, a signaling molecule that tells cells where to form bone, cartilage, and other tissues during development.
FGF	Fibroblast growth factor, a signaling molecule that drives cells to grow and divide while shaping developing tissues.
epithelial-mesenchymal cross-talk	Back-and-forth chemical signaling between surface epithelial cells and underlying mesenchyme cells that guides how tissues grow and form.

READING 11 OF 20 | DEVELOPMENT CAN GO WRONG

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

What is the master switch that lets two palate shelves fuse into one roof, and what happens if it never turns on?

START WITH

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

REMEMBER

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

Why this matters

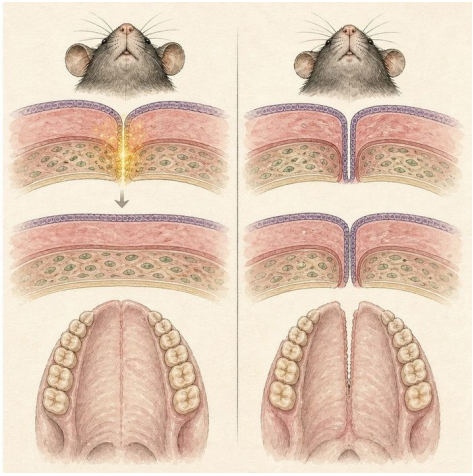
A knockout is most useful when the normal and mutant tissues are compared at the same developmental step.

The biology in plain English

TGF-beta3 is strongly involved at the medial edge of the palatal shelves during fusion.

Mouse embryos without Tgfb3 can bring shelves to the midline, but the epithelial seam is not removed normally.

This separates shelf arrival from final fusion. It does not make TGFB3 the cause of every human cleft.



Biomedical teaching illustration: Read the Tgfb3 knockout result step by step

Check your understanding

- Which earlier step still occurs in the knockout?
- What claim about human clefts would go beyond this mouse result?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV11-E1	In Tgfb3-null mouse embryos, palatal shelves can reach the midline.	Earlier growth and elevation can still occur.
DEV11-E2	The shelves fail to complete normal adhesion and seam removal.	The defect is concentrated at the fusion transition.
DEV11-E3	The result is cleft secondary palate in the model.	Failure of a late step can preserve a gap despite shelf contact.

Concrete decision

You are presenting a knockout figure at lab meeting. Both control and mutant shelves reach the midline, but only controls form continuous mesenchyme.

A. Place TGF-beta3 at the fusion and seam-removal step.

B. Place TGF-beta3 only at neural crest birth.

C. Claim the mutant shelves never formed.

Decision prompt: Choose the step assignment and cite the matched contact evidence.

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

Glossary

Term	Plain-English definition
TGF-beta3	A signaling protein essential for palate fusion; it drives the edge cells between the two palatal shelves to disappear so they can join.
medial edge epithelium (MEE)	The cell layer on the inner edge of each palatal shelf, which must be removed for the shelves to fuse into a single palate.
knockout	An organism or cell engineered to have a specific gene switched off, used to reveal what that gene normally does.
fusion competence	The readiness of two developing facial parts to join properly, including the right timing, signals, and surface cells, so they can merge into one.

READING 12 OF 20 | CELLS DIFFERENTIATE

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

How does a single cranial cell decide whether to become bone, skin, or cartilage, and what is the off choice it has to actively avoid?

START WITH

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

REMEMBER

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

Why this matters

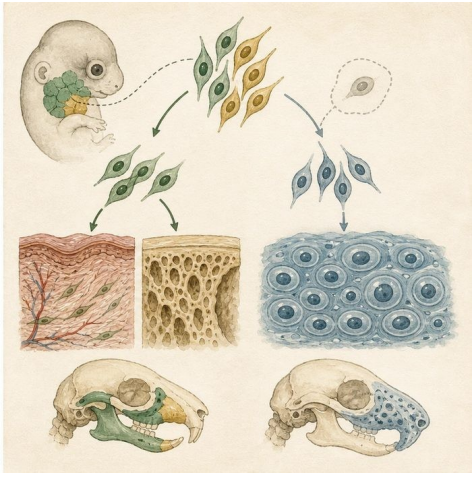
This experiment makes the foundation 'cells differentiate' visible as a decision with competing outcomes.

The biology in plain English

Wnt signaling can stabilize beta-catenin, which then helps change gene activity in responding cells.

Atit Lab lineage experiments tested cranial progenitors during a short fate-selection window.

Without beta-catenin, labeled cells formed cartilage where dermis and bone should have formed. That result supports a fate switch, not only cell death.



Biomedical teaching illustration: Map the Atit Lab beta-catenin experiment

Check your understanding

- Which observation supports a fate switch?
- Why must the conclusion stay limited to the lineage and region tested?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV12-E1	Control cranial progenitors process Wnt-beta-catenin signaling during fate selection.	The pathway is active during the decision window.
DEV12-E2	Conditional beta-catenin loss removes cranial dermis and bone in the tested region.	The pathway is required for those fates in that model.
DEV12-E3	Lineage-labeled mutant cells form cartilage in their place.	The same progenitor population changed fate rather than simply disappearing.

Concrete decision

You are the student lead for an Atit Lab figure discussion. A classmate says the mutant has less dermis only because all labeled cells died.

A. Use labeled cartilage descendants to support a fate switch.

B. Agree that lineage labels cannot show descendants.

C. Claim Wnt controls every cell fate in the embryo.

Decision prompt: Choose the strongest response and cite the evidence that rules against simple cell loss.

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

Glossary

Term	Plain-English definition
cell fate	A lesson term defined by the surrounding model and case evidence.
Wnt/beta-catenin	A lesson term defined by the surrounding model and case evidence.
default fate	The cell type or outcome a cell becomes automatically unless a specific signal redirects it onto a different path.
repression	The turning down or shutting off of a gene's activity so that less of its protein is made.

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

What keeps the surfaces inside the mouth from sticking to the wrong neighbor, and what happens when that protection is missing?

START WITH

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

REMEMBER

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

Why this matters

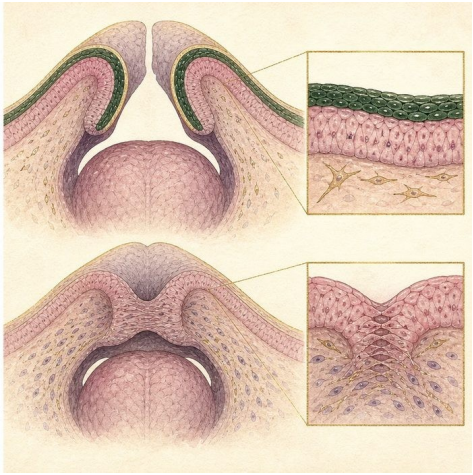
A differentiated surface cell can protect an entire moving structure from the wrong neighbor.

The biology in plain English

Periderm is a temporary outer cell layer on embryonic epithelial surfaces. It helps prevent tissues inside the mouth from sticking to the wrong neighbor.

IRF6 helps oral epithelial cells complete this protective differentiation program.

In Irf6-deficient mouse embryos, abnormal adhesions can tie the tongue and palate together and block later shelf elevation.



Biomedical teaching illustration: Connect IRF6, periderm, and oral adhesion

Check your understanding

- What specialized job does periderm perform?
- How can a surface defect become a movement defect?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV13-E1	Periderm covers embryonic oral epithelial surfaces during key stages.	It provides a temporary specialized surface.
DEV13-E2	Irf6-deficient mouse embryos have abnormal periderm differentiation.	IRF6 is required for normal protection in the model.
DEV13-E3	Abnormal oral adhesions can block palatal shelf elevation.	A surface defect can create a later movement defect.

Concrete decision

You are explaining an Irf6 mutant image to a clinical genetics group. The shelves formed, but one shelf is attached to the tongue before elevation.

A. Trace the failure from periderm loss to abnormal adhesion to blocked elevation.

B. Say the shelf failed because it never existed.

C. Call every IRF6 variant a complete gene knockout.

Decision prompt: Choose the causal sequence and cite the surface and movement evidence.

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

Glossary

Term	Plain-English definition
periderm	A thin temporary outer cell layer of the embryo; if it sticks where it should not, the growing edges cannot fuse.
IRF6	Interferon Regulatory Factor 6, a transcription factor needed by the skin-like cells that let the lip and palate fuse; a leading cleft gene.
intraoral adhesion	An abnormal band of tissue that connects structures inside the mouth that should be separate, sometimes seen with cleft conditions.
cell-autonomous	Describing an effect that plays out inside the very cell carrying the change, rather than in its neighbors.

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

If you are handed a specific cleft, can you read it backward to the one developmental step that failed?

START WITH

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

REMEMBER

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

Why this matters

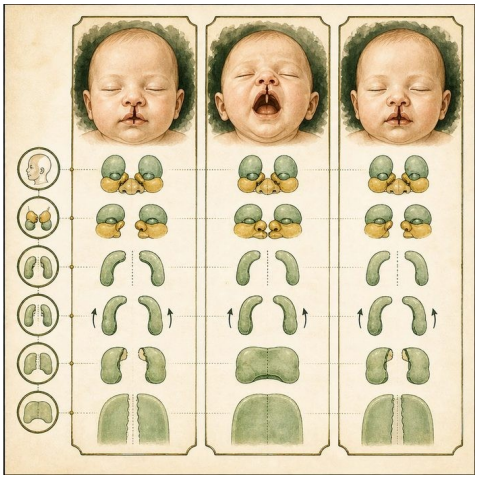
Backward reasoning is useful only when students keep the difference between process and cause.

The biology in plain English

A phenotype is an observable outcome. Researchers can use it to reason backward toward a failed developmental step.

Cleft lip most directly points to an upper-lip boundary. Cleft palate has several possible checkpoints because shelves must grow, move, adhere, and remove a seam.

The pattern narrows the investigation but usually does not name one gene or exposure.



Biomedical teaching illustration: Read three cleft patterns backward

Check your understanding

- Why does cleft palate have several possible checkpoints?
- What can phenotype support more strongly than it supports a specific gene?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV14-E1	Cleft lip points to an early upper-lip growth and fusion boundary.	The phenotype localizes an early facial checkpoint.
DEV14-E2	Cleft palate can result from failed shelf growth, elevation, adhesion, or seam removal.	Several mechanisms share the palate endpoint.
DEV14-E3	Mateo has both cleft lip and palate.	His pattern spans connected but distinguishable developmental events.

Concrete decision

You are triaging three cases for a developmental review board. Case A has cleft lip only. Case B has cleft palate only. Mateo has both.

A. Assign each pattern to the narrowest supported checkpoint list.

B. Assign one gene to each pattern from anatomy alone.

C. Treat all three patterns as the same developmental event.

Decision prompt: Choose the triage method and explain why the palate list remains broader.

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

Glossary

Term	Plain-English definition
phenotype	The observable traits of an organism, such as appearance or function, that result from its genotype combined with environmental influences.
fusion failure	When tissue layers that should join during development do not merge, leaving a gap such as a cleft lip or palate.
patterning defect	A mistake in the body plan set early in development, where signals place or shape parts wrongly so a structure forms in the wrong arrangement.
isolated defect	A birth difference that occurs on its own, without other linked malformations or a broader syndrome accompanying it.

Critical Timing Windows, When the Door Closes

Is there a moment after which a cleft can no longer be prevented, and the open structure stays open for good?

START WITH

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

REMEMBER

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

Why this matters

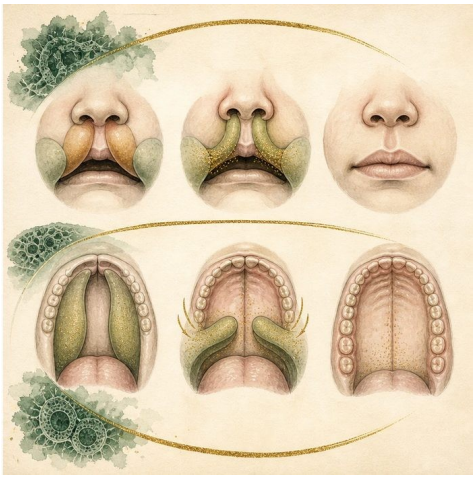
A risk factor without compatible timing is a weak developmental explanation.

The biology in plain English

A critical window is a period when a structure or process is especially sensitive because it is actively changing.

The upper lip closes before the secondary palate finishes. An event after lip closure is less compatible with directly causing cleft lip.

Compatible timing is necessary for many causal claims, but it is not sufficient proof by itself.



Biomedical teaching illustration: Compare lip and palate critical windows

Check your understanding

- What makes an exposure timing compatible with a developmental outcome?
- Why does compatible timing not prove causation?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV15-E1	Upper-lip fusion occurs earlier than completion of secondary-palate fusion.	The two structures have different timing windows.
DEV15-E2	A disruption must overlap a sensitive process to affect that process directly.	Exposure timing is part of causal reasoning.
DEV15-E3	After a cleft is established in utero, later normal growth does not automatically fuse the gap.	Subsequent development builds around the open structure.

Concrete decision

You are reviewing an exposure timeline without naming the exposure. Exposure A occurred after upper-lip closure but during palatal fusion. Exposure B occurred before both windows.

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

B. Claim A directly caused Mateo's cleft lip.

C. Claim timing never matters.

Decision prompt: Choose the timing hypothesis and cite the window evidence.

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

Glossary

Term	Plain-English definition
critical window	A lesson term defined by the surrounding model and case evidence.
lip fusion window	The brief stretch of early development when the facial processes must join to form the upper lip, around weeks four to seven.
palate fusion window	The limited stretch of embryo development when the palate shelves must rise and join; missing this window leaves a cleft palate.
irreversible	Describing a change or step that cannot be undone once it has happened, locking the outcome in place.

READING 16 OF 20 | DEVELOPMENT CAN GO WRONG

When the Outside World Reaches the Embryo

Can the outside world change how the face forms, and if so, how strongly?

START WITH

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

REMEMBER

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

Why this matters

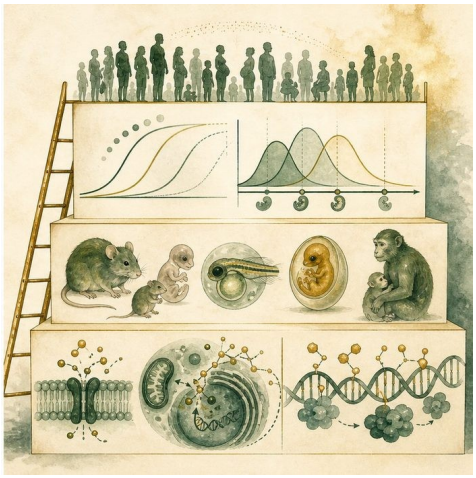
Plain language about probability protects both scientific accuracy and families.

The biology in plain English

A teratogen is an exposure that can disrupt development under some conditions. Effects depend on dose, timing, and the developing tissue.

Population studies can find associations. Animal and cell studies can test possible mechanisms.

A risk factor does not guarantee an outcome. Mateo's composite case does not include evidence that one exposure caused his cleft.



Biomedical teaching illustration: Grade evidence for folate, valproate, and other exposures

Check your understanding

- What three features make exposure evidence stronger?
- Why is risk factor more accurate than guaranteed cause?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV16-E1	Some prenatal exposures are associated with higher cleft risk in populations.	Association can identify a factor worth studying.
DEV16-E2	Valproate is a known teratogenic medication whose risks depend on exposure context and timing.	A specific factor can have biologically important prenatal effects.
DEV16-E3	Most exposed pregnancies do not produce the same outcome, and many clefts occur without a known exposure.	Risk is probabilistic and multifactorial.

Concrete decision

You are writing a family-facing explanation for Mateo's chart. A parent asks whether one action definitely caused the cleft, but the case file contains no confirmed causal exposure.

A. Explain that risk factors change probability and no single cause is established here.

B. Assign blame without exposure evidence.

C. Say environmental factors can never affect development.

Decision prompt: Choose the explanation and cite evidence about probability and case limits.

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

Glossary

Term	Plain-English definition
teratogen	An agent such as a drug, chemical, or infection that can disrupt development and cause birth differences if exposure happens during pregnancy.
critical window	A lesson term defined by the surrounding model and case evidence.
folate	A B vitamin the body needs to build DNA and new cells; taking enough before and in early pregnancy lowers the risk of cleft and neural tube defects.
valproate	A medication used for seizures and mood that raises the risk of birth defects, including cleft palate, when taken during pregnancy.
risk factor	Anything that raises a person's chance of developing a disease, such as smoking, family history, or high blood pressure, without guaranteeing it.

READING 17 OF 20 | DEVELOPMENT CAN GO WRONG

Same DNA, Different Outcome

How can identical DNA give two different outcomes, a fused palate or a cleft?

START WITH

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

REMEMBER

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

Why this matters

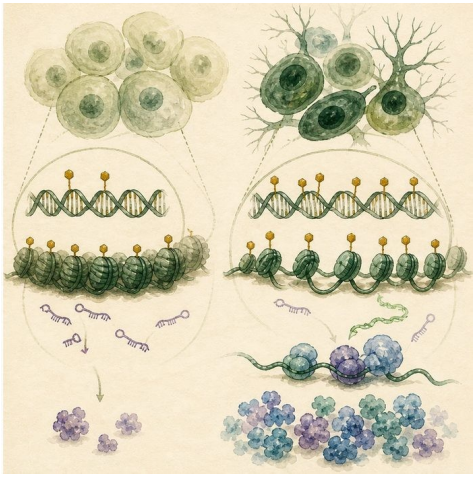
Variable penetrance is easier to understand when students separate the genome from its use.

The biology in plain English

DNA sequence stores genetic information, but cells also control which genes are used, when they are used, and how strongly.

Methylation can affect gene activity. MicroRNAs can reduce protein production from messages.

These controls may help explain variable penetrance, but human epigenetic associations still require careful testing for cause and timing.



Biomedical teaching illustration: Separate DNA sequence from epigenetic regulation

Check your understanding

- What can change without changing DNA letters?
- Why does a methylation difference not automatically prove cause?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV17-E1	DNA methylation can change gene activity without changing the DNA letters.	Sequence and regulation are separate layers.
DEV17-E2	MicroRNAs can reduce how much protein is made from target messages.	Post-transcriptional regulation can alter pathway output.
DEV17-E3	Cleft penetrance can vary among people with similar genetic susceptibility.	A susceptibility variant does not force one outcome.

Concrete decision

You are comparing two siblings in a research model. Both carry the same susceptibility variant, but only one has a cleft. Their methylation profiles differ at developmental genes.

A. Propose regulation as one testable modifier while keeping other factors open.

B. Claim the methylation profile proves the only cause.

C. Claim identical variants must always produce identical anatomy.

Decision prompt: Choose the testable explanation and cite sequence-versus-regulation evidence.

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

Glossary

Term	Plain-English definition
epigenetics	The study of chemical tags on DNA and its packaging that switch genes on or off without changing the underlying DNA sequence itself.
DNA methylation	A chemical tag added to DNA that can quiet a gene without changing its underlying sequence.
microRNA	A tiny RNA molecule that fine-tunes gene activity by binding messenger RNA and blocking it from being made into protein.
second hit	A second damaging change needed on top of an inherited one before a trait or disease appears, explaining why some carriers stay healthy.
penetrance	The fraction of people carrying a disease-linked genotype who actually show the trait.

READING 18 OF 20 | CELLS MOVE

Watching Development Happen

How do we actually watch development go right or wrong?

START WITH

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

REMEMBER

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

Why this matters

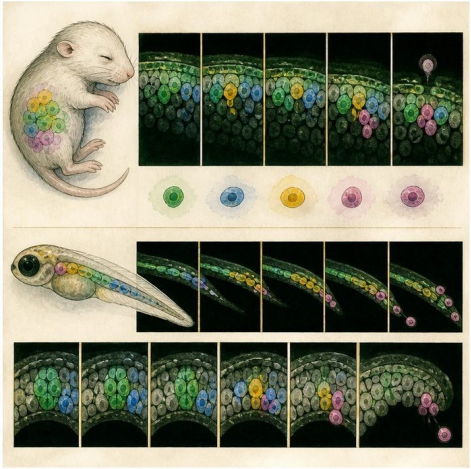
A good method makes the needed event observable instead of asking students to imagine it.

The biology in plain English

Lineage labeling marks cells and their descendants. It helps researchers track identity through movement and differentiation.

Live imaging adds time, so scientists can see which event happens first and how cells behave.

Model organisms make early development observable, but every conclusion must state which species, tissue, and stage were tested.



Biomedical teaching illustration: Choose a method to watch development

Check your understanding

- Which method adds cell identity?
- Which method adds sequence over time?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV18-E1	Lineage labels mark a cell population and its descendants.	They answer where cells came from and what they became.
DEV18-E2	Live imaging records movement and cell behavior over time.	It can reveal order and timing.
DEV18-E3	Mouse and zebrafish models share important developmental mechanisms but are not identical to humans.	Model choice sets a limit on transfer.

Concrete decision

You are choosing a method for a seam-removal study. The question is whether labeled seam cells die, leave the surface, or persist during the next six hours.

A. Use stable lineage labels with live imaging and cell-state markers.

B. Use only the adult skull endpoint.

C. Use one unlabeled still image.

Decision prompt: Choose the method set and cite the evidence for both time and identity.

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

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.
lineage labeling	A method that tags a starting cell with a permanent marker so all of its descendant cells can be tracked over time.
live imaging	Watching cells or tissues under a microscope as they move and change over time, instead of viewing a single fixed snapshot.
cell extrusion	A process where a sheet of cells squeezes out and removes one of its own cells, sealing the gap to keep the layer intact.
homology	Similarity between genes or structures in different species because they were inherited from a shared common ancestor.

READING 19 OF 20 | DEVELOPMENT CAN GO WRONG

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

If we know the window and the missing signal, can we add it back and rescue a normal palate, and what does that result really promise for a human baby?

START WITH

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

REMEMBER

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

Why this matters

Rescue experiments are powerful precisely because their claims can be specific and testable.

The biology in plain English

A rescue experiment first creates or studies a developmental defect, then restores a suspected missing step.

In an Msx1-deficient mouse model, directed Bmp4 expression restored palatal growth and fusion. That supports the pathway relationship in the model.

Human treatment would still require safe delivery, correct timing, dose control, and strong evidence that benefits exceed risks.

Biomedical teaching illustration: Interpret the Msx1-Bmp4 mouse rescue

Check your understanding

- What three groups make a rescue comparison strong?
- What human-treatment questions remain unanswered?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV19-E1	Msx1-deficient mice show reduced anterior palatal growth and cleft palate.	The mutant provides a defined disrupted pathway.
DEV19-E2	Directed Bmp4 expression restored growth and fusion in the reported mouse model.	Restoring a downstream signal rescued the phenotype.
DEV19-E3	The intervention was genetic and preclinical in mice.	The experiment is not a tested prenatal therapy for humans.

Concrete decision

You are briefing a translational research committee. A headline says the mouse rescue means cleft palate can now be prevented in human pregnancy.

A. Correct it to proof of mechanism in a specific mouse model.

B. Approve the human-treatment claim.

C. Reject the experiment as useless because it used mice.

Decision prompt: Choose the accurate headline and cite both the rescue and translation-limit evidence.

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

Glossary

Term	Plain-English definition
rescue experiment	Adding a working gene back into a mutant to see if it restores the normal trait, which proves that gene was responsible.
gain-of-function	A mutation that gives a protein a new or stronger activity rather than weakening it, sometimes causing harm.
critical window	A lesson term defined by the surrounding model and case evidence.
preclinical	Research done in cells and animals to test safety and effect before a treatment is ever tried in people.
proof of mechanism	Evidence that a treatment actually acts on the biological target the way it was designed to, not just that it works.

Mateo's Complete Developmental Story

Assembling everything we learned, what is the complete developmental story of Mateo's cleft, and what kind of cleft is it?

START WITH

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

REMEMBER

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

Why this matters

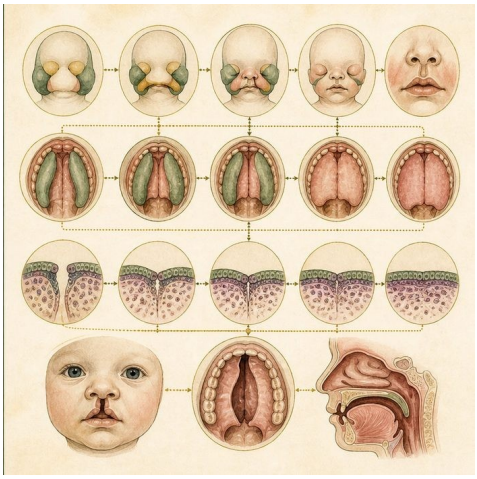
The final lesson teaches scientific restraint as part of expertise, not as a weakness.

The biology in plain English

Mateo's lip and palate pattern records missed joining across connected early developmental windows.

The unit shows several necessary processes: cell origin and fate, migration, tissue growth, shelf elevation, adhesion, signaling, and seam removal.

The composite case does not prove one cause. The strongest conclusion is a bounded developmental story that guides the next genetics and anatomy questions.



Biomedical teaching illustration: Assemble Mateo's complete developmental story

Check your understanding

- Which parts of Mateo's developmental story are supported?
- Which causal claim must remain open for the next domain?

Case evidence supplied for this lesson

ID	Finding supplied in the case	Why it matters
DEV20-E1	Mateo has complete unilateral left cleft lip and palate with no broader anomaly pattern established in the composite file.	The phenotype is specific while the cause remains open.
DEV20-E2	Lip and palate formation require ordered growth, cell movement, signaling, adhesion, and seam removal.	Several developmental checkpoints can contribute to the final pattern.
DEV20-E3	The case file does not establish one causal variant, exposure, or syndrome.	The final explanation must remain multifactorial and bounded.

Concrete decision

You are the lead developmental biologist at the final case conference. The team must approve one paragraph for the family-facing case summary.

A. Describe the failed developmental outcomes and state that one cause is not established.

B. Name one gene as proven without a case result.

C. Say development offers no useful explanation.

Decision prompt: Choose the summary and cite the phenotype evidence plus the uncertainty evidence.

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

Glossary

Term	Plain-English definition
synthesis	Building a molecule in the cell, as in protein synthesis (making a protein from mRNA).
isolated (nonsyndromic)	A cleft that occurs on its own, without other birth differences or a named syndrome accompanying it.
fusion failure	When tissue layers that should join during development do not merge, leaving a gap such as a cleft lip or palate.
multifactorial	Caused by several genes acting together with environmental factors, not by a single gene alone.
developmental story	The step-by-step account of how a structure forms over time, linking each early event to the final feature it produces.