

Pancreatoblastoma

A malignant pediatric pancreatic tumor defined by acinar and squamoid differentiation

Morphology • Wnt biology • diagnosis • management

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Learning objectives

- Identify the clinicopathologic profile of pancreatoblastoma
- Recognize diagnostic squamoid corpuscles in acinar-pattern tumors
- Construct a defensible differential and multidisciplinary work-up
- Relate molecular features and extent of disease to clinical decisions

Four anchors

01

Predominantly affects children aged 1–15 years

02

Squamous islands intermingle with acinar cells

03

Malignant behavior, but outcomes exceed pancreatic ductal adenocarcinoma

04

Frequent activation of the Wnt signaling pathway

Cell lineage frames the differential

- Exocrine acinar cells synthesize digestive enzymes
- Ductal epithelium forms the pancreatic drainage network
- Endocrine islet cells produce peptide hormones

Acinar

Digestive enzymes

Ductal

Drainage epithelium

Endocrine

Hormone production

Which pancreatic masses occur in children?

Entity	Useful diagnostic orientation
Pancreatoblastoma	Acinar differentiation + squamoid corpuscles
Solid pseudopapillary neoplasm	Solid/cystic, pseudopapillary architecture
Neuroendocrine tumor	Neuroendocrine morphology and markers
Ductal carcinoma	Malignant ductal glands with desmoplasia

Rare overall, important in young children

- Pediatric pancreatic malignancies are uncommon
- Pancreatoblastoma accounts for a meaningful share of childhood pancreatic tumors
- Relative frequency within pediatric pancreatic tumors is not population incidence

10–20%

Of childhood pancreatic tumors in the NCI PDQ summary; Denominator matters.

Age is a powerful clinical clue

- Presentation from 1 to 15 years
- Contemporary pediatric series show a median diagnosis age around 4–5 years
- Occurrence in adults is documented, so age alone cannot establish or exclude the diagnosis

Infancy



Early childhood



Adolescence



Rare adult cases

The Beckwith–Wiedemann association

- Beckwith–Wiedemann syndrome increases pancreaticoblastoma risk
- Syndromic context is particularly relevant in very early-onset tumors
- Constitutional predisposition should prompt genetics input when indicated

Overgrowth syndrome



Cancer predisposition



Early pancreatic mass



Genetic evaluation

Familial adenomatous polyposis is another clue

- Association with familial adenomatous polyposis has been reported
- The APC pathway links this association biologically to Wnt signaling
- This is an association—not evidence that most cases are hereditary

APC dysfunction



Wnt dysregulation



Pancreatoblastoma association

Embryonal differentiation: A working model

- Pancreatoblastoma has an embryonal/fetal-acinar phenotype
- Tumor cells can display acinar, solid, and trabecular organization
- Normal developmental identity may be altered rather than simply retained

Embryonal phenotype

Acinar features

Heterogeneous patterns

The molecular theme is Wnt activation

- Recurrent Wnt-pathway activating alterations
- CTNNB1 encodes β -catenin, a transcriptional co-regulator
- Abnormal β -catenin signaling is mechanistically relevant, not a stand-alone diagnosis

Wnt-pathway alteration



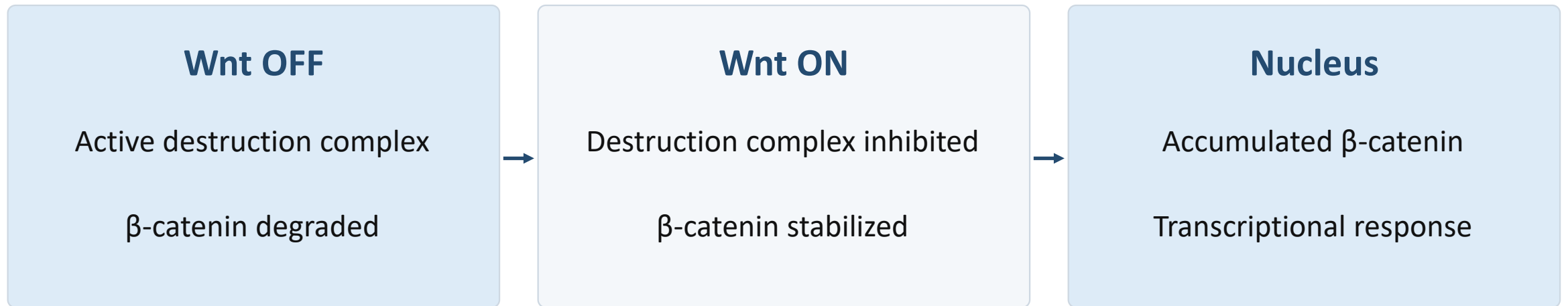
β -catenin stabilization



Transcriptional effects

Canonical Wnt signaling: An overview

- With low Wnt activity, the destruction complex limits β -catenin accumulation
- Wnt receptor signaling suppresses β -catenin destruction
- Stabilized β -catenin can enter the nucleus and alter target transcription



CTNNB1 alterations

- Somatic CTNNB1 variants can stabilize β -catenin signaling
- NCI PDQ identifies CTNNB1 as a common mechanism of Wnt activation in pancreaticoblastoma
- A pathway alteration does not uniquely identify a pancreatic tumor subtype

CTNNB1 activating variant



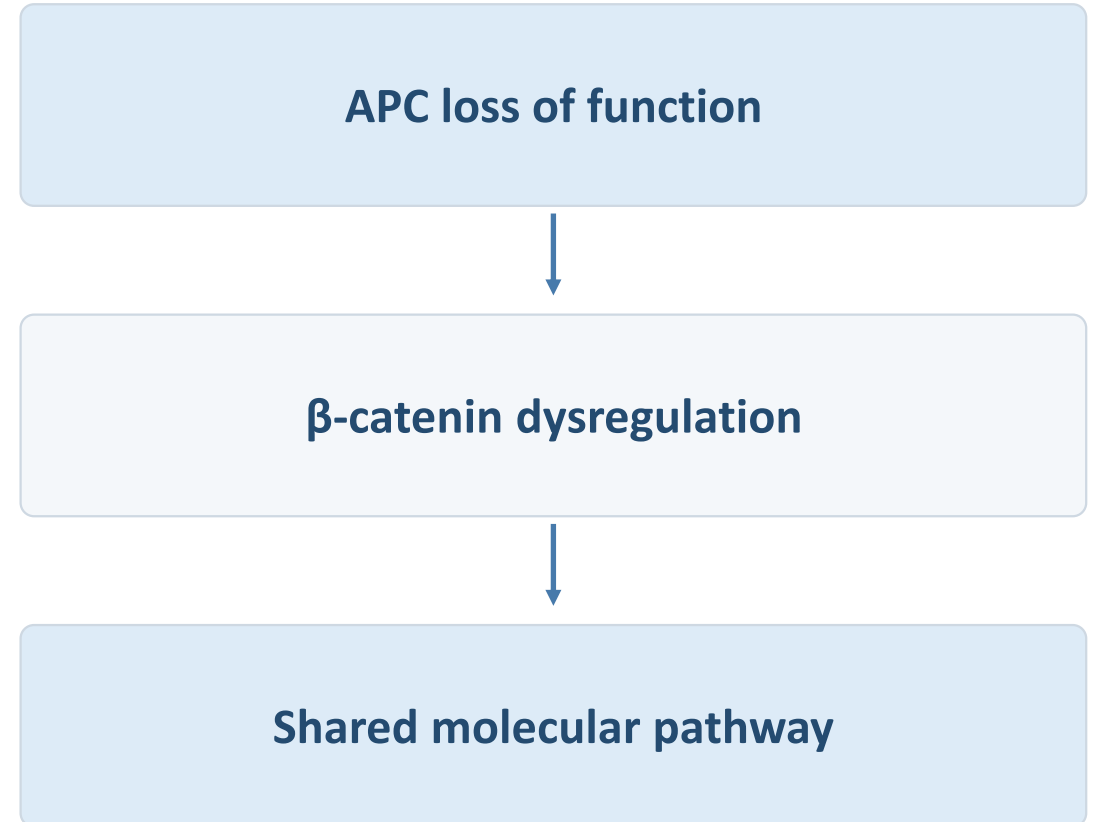
Reduced β -catenin turnover



Wnt target-gene signaling

APC connects genotype with pathway

- APC is part of the β -catenin destruction machinery
- Loss of its suppressive function can raise β -catenin pathway activity
- Robbins also describes APC or CTNNB1 alterations in acinar cell carcinoma



IGF2 alterations are another recurrent finding

- NCI PDQ describes frequent IGF2 gene alterations
- These alterations coexist with a proposed disturbance of pancreas differentiation
- Avoid translating this observation into an unproven clinical treatment target

Wnt signaling

IGF2 alteration

Cell differentiation

Molecular overlap is not diagnostic identity

Finding	Interpretation
Wnt-pathway alteration	Supports pathway biology, not unique identity
Acinar marker positivity	Supports exocrine acinar differentiation
Squamoid corpuscles	Strong morphologic clue to pancreatoblastoma

Clinical presentation may be deceptively bland

- A large palpable abdominal mass can be the presenting finding
- Abdominal pain or fullness is nonspecific
- Some children have little symptom burden despite a sizable neoplasm

Expanding mass



Abdominal enlargement



Clinical detection

Common symptoms arise from local mass effect

- Abdominal pain, vomiting, anorexia, and weight change may occur
- Symptoms depend on size, location, and surrounding anatomy
- None of these features is specific for pancreatoblastoma

Compression

Displacement

Variable symptoms

Jaundice is surprisingly uncommon

Observation	Teaching implication
Head/neck pancreatic location	Does not guarantee duct obstruction
No clinical jaundice	Cannot exclude a pancreatic tumor
Biliary obstruction	Evaluate anatomy on cross-sectional imaging

AFP: Useful but not universal

- Approximately 70–80% of pediatric pancreatoblastomas have elevated or secreted AFP
- AFP helps support a suspicion when morphology and imaging fit
- Normal AFP does not rule out pancreatoblastoma

~70–80%

Reported proportion with elevated/secreted AFP; Not diagnostic sensitivity in an unselected population.

AFP supports response assessment

- Document the pretreatment AFP value when elevated
- Falling AFP may corroborate treatment response
- A subsequent rise can trigger evaluation for recurrence
- Interpret serial values alongside imaging and clinical status

Baseline AFP



Therapy



Serial AFP + imaging



Recurrence assessment

AFP is not a tumor-specific stain

- AFP can be elevated in other pediatric tumors and conditions
- Biochemical evidence must be integrated with pancreatic origin
- A positive AFP result cannot replace tissue diagnosis

Serum marker

Anatomic imaging

Pathology

Unusual secretory manifestations

Ectopic hormone	Possible manifestation
ACTH	Cushing syndrome
Antidiuretic hormone	SIADH

Metastatic disease matters at diagnosis

- Metastases may be present when pancreatoblastoma is first recognized
- Liver, lymph nodes, and lungs are reported sites
- Tumor extent modifies surgical planning and overall prognosis

Pancreatic primary



Regional assessment



Liver and nodes



Thoracic evaluation

Imaging establishes origin and extent

- Ultrasound may identify a heterogeneous abdominal mass
- Contrast-enhanced CT or MRI clarifies pancreatic origin and local relations
- Chest imaging is relevant when metastatic evaluation is indicated

US detection



CT / MRI mapping



Metastatic survey



Team planning

Imaging appearance is heterogeneous

- Large masses may show mixed solid and cystic components
- Fibrous septa, hemorrhage, or necrosis contribute to heterogeneity
- Radiologic appearance alone cannot establish histologic subtype

Solid tumor

Fibrous septa

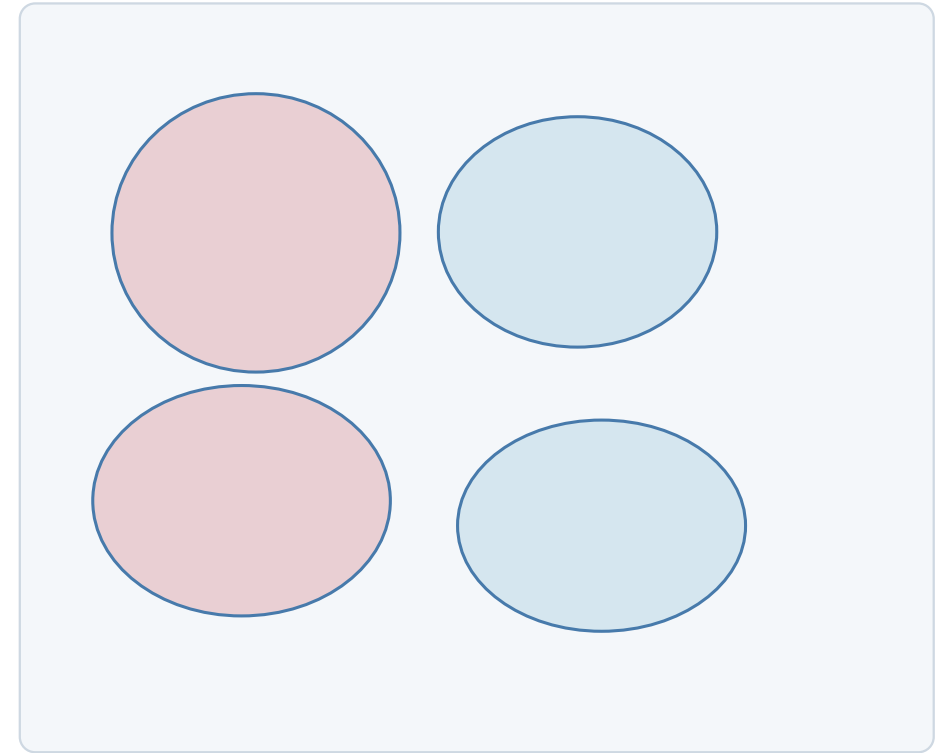
Cystic/necrotic change

Imaging cannot show a squamoid corpuscle

Imaging can assess	Histology must assess
Pancreatic origin and local invasion	Acinar differentiation
Vascular and organ relationships	Squamoid islands
Possible metastases	Neoplastic cell phenotype

Macroscopy: A lobulated mass

- Pancreatoblastomas may form large, soft, circumscribed lesions
- Fibrous partitions can divide the mass into lobules
- Hemorrhage, necrosis, and variable cystic change may occur



Lobules separated by broad fibrous partitions

Schematic — not a photomicrograph

Gross appearance is not a diagnosis

- Circumscription does not prove benign behavior
- Cystic degeneration can resemble other pediatric pancreatic lesions
- Sample solid areas, interface, and heterogeneous regions appropriately

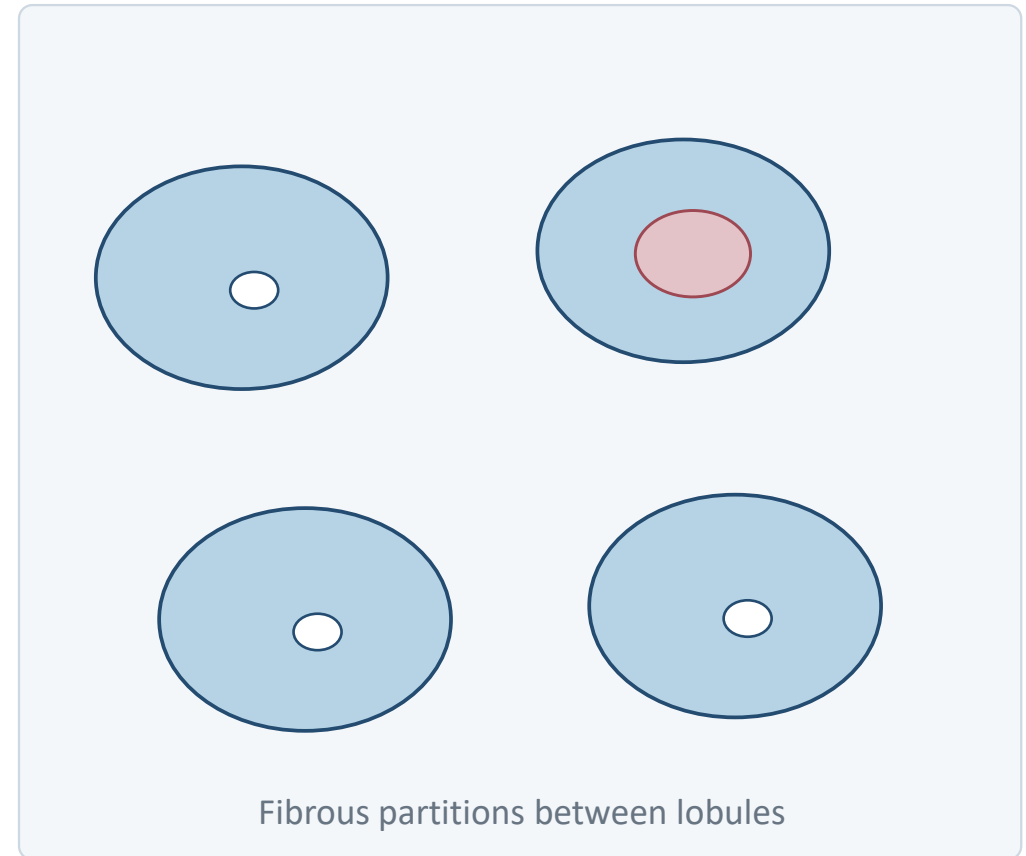
Gross sampling

Microarchitecture

Final classification

Microscopic architecture: Lobules and bands

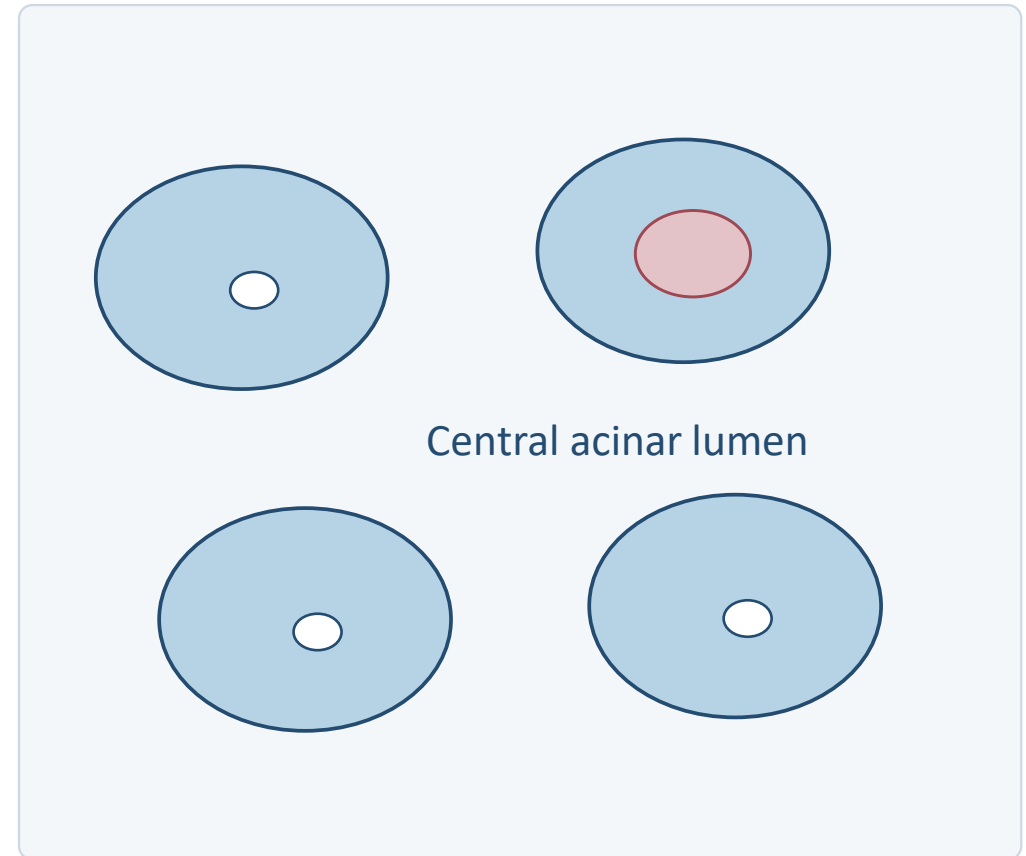
- Cell-rich lobules can be separated by broad fibrous septa
- Acinar, trabecular, and solid patterns can coexist
- This heterogeneity makes low-power architectural review useful



Schematic — not a photomicrograph

Acinar differentiation is the epithelial backbone

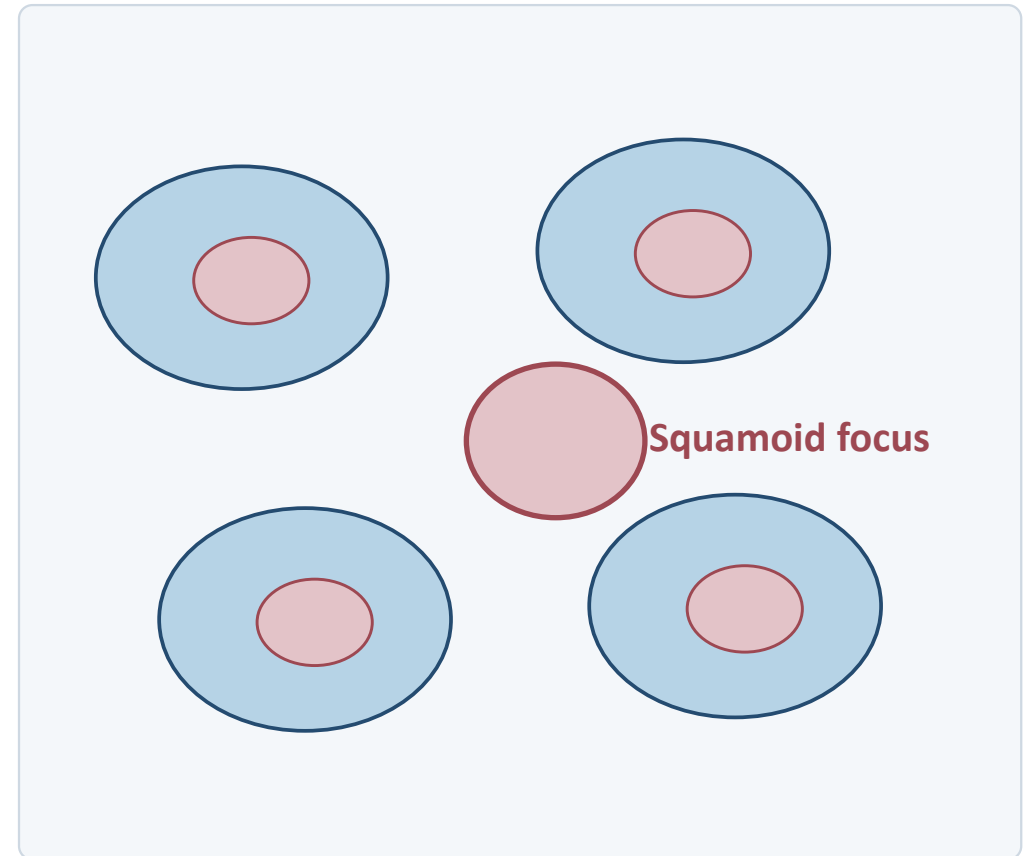
- Neoplastic cells may organize around small luminal spaces
- Cytoplasm can have granular eosinophilic character
- Acinar architecture alone is not specific for pancreatoblastoma



Schematic — not a photomicrograph

Squamoid corpuscles are the diagnostic pivot

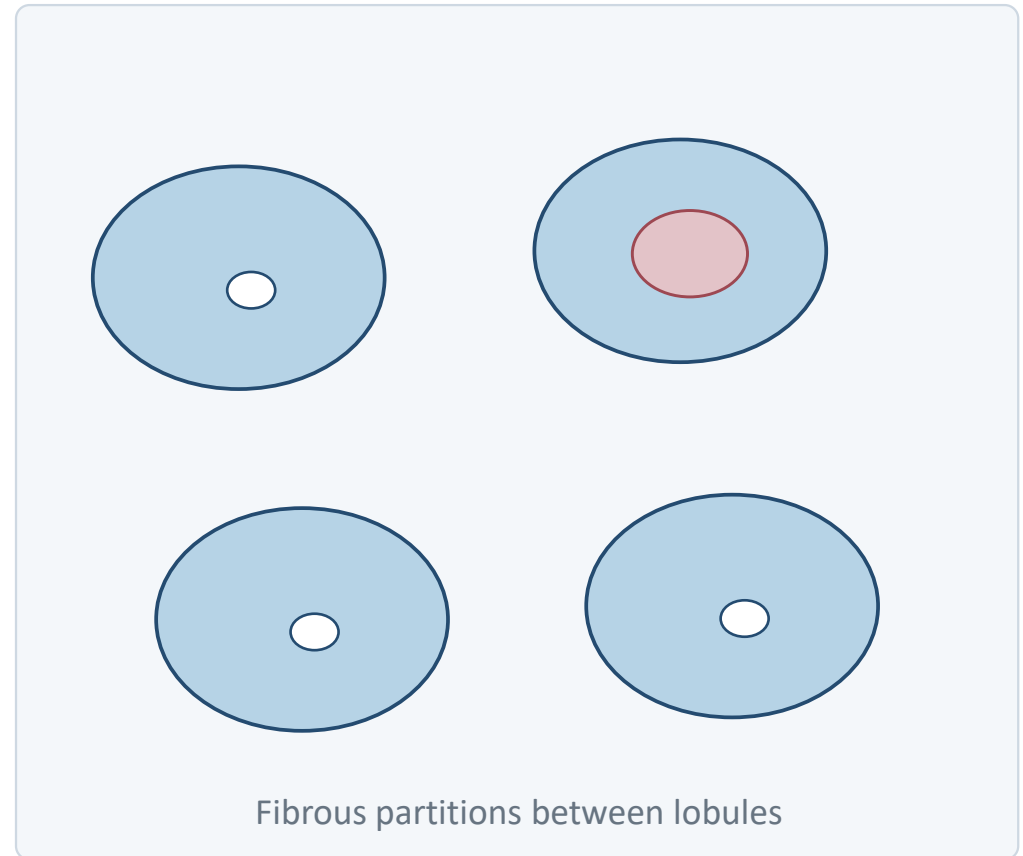
- Pale squamoid islands occur among the acinar-pattern tumor cells
- They may form compact nests or whorled groups
- Their recognition is particularly helpful against acinar cell carcinoma



Schematic — not a photomicrograph

What “squamoid” means here

- The corpuscles represent an unusual epithelial differentiation focus
- They need not resemble an overt invasive squamous carcinoma
- Interpret them within the surrounding acinar neoplastic architecture



Schematic — not a photomicrograph

Sampling: The danger of a small biopsy

- Squamoid nests may be sparse or absent from a limited core
- An acinar-rich core can resemble acinar cell carcinoma
- Correlate multiple levels and broader sampling with the clinical setting

Small core



Acinar-only appearance



Expand sampling



Seek squamoid foci

Acinar markers confirm differentiation

Marker	Role
Trypsin	Acinar differentiation
Chymotrypsin	Acinar differentiation
BCL10	Acinar differentiation

β-catenin staining requires localization

- Aberrant nuclear labeling can occur in squamoid corpuscles
- Cytoplasmic staining alone should not be equated with pathway activation
- The distribution of labeling across components can be informative

Tumor component

Subcellular location

Integrated interpretation

Neuroendocrine markers can mislead

Finding	Correct response
Focal synaptophysin	Assess full architecture
Focal chromogranin	Check extent and other lineage markers
Acinar + squamoid pattern	Maintain pancreatoblastoma in differential

A disciplined immunohistochemistry strategy

- First, establish epithelial and acinar differentiation
- Then inspect squamoid foci and β -catenin localization
- Use neuroendocrine markers to test mixed differentiation
- Avoid interpreting any single marker in isolation

Morphology



Acinar stains



Squamoid / β -catenin



Integrated report

Primary differential: Acinar cell carcinoma

Pancreatoblastoma	Acinar cell carcinoma
Childhood predominance	Usually adult presentation
Squamoid corpuscles characteristic	Squamoid corpuscles usually absent
Acinar markers positive	Acinar markers positive
Wnt activation frequent	Wnt alterations also described

Solid pseudopapillary neoplasm: Major mimic

Pancreatoblastoma	Solid pseudopapillary neoplasm
Acinar + squamoid	Pseudopapillary structures
AFP often elevated	AFP generally normal
Malignant pediatric embryonal tumor	Usually indolent / low-grade behavior

Neuroendocrine tumor: Lineage over focal stains

Question	Discriminating clue
Dominant lineage?	Acinar vs neuroendocrine
Squamoid nests?	Support pancreatoblastoma
Marker distribution?	Focal versus extensive endocrine pattern

Ductal adenocarcinoma: A different architecture

Pancreatoblastoma	Ductal adenocarcinoma
Acinar + squamoid	Infiltrative malignant ducts
Usually pediatric	Predominantly older adults
Distinct molecular context	KRAS, TP53, CDKN2A, SMAD4 in Robbins

An AFP-positive hepatic mass requires care

- Pancreatoblastoma can metastasize to the liver
- AFP elevation may suggest an embryonal tumor elsewhere
- Correlate liver findings with pancreatic imaging and tissue phenotype
- Do not infer primary organ solely from a serum marker

Liver lesion + AFP



Find primary site



Compare morphology



Integrated diagnosis

Discordant findings should trigger review

- Young child + large pancreatic mass may favor pancreatoblastoma
- Limited tissue without squamoid nests may remain ambiguous
- Shared molecular findings do not settle acinar versus pseudopapillary lineage
- Escalate to additional sections or expert consultation when needed

Clinicoradiology



Tissue review



Targeted stains



Expert integration

A practical diagnostic algorithm

- Confirm pancreatic origin and tumor extent
- Examine low-power architecture and targeted squamoid nests
- Use acinar and other lineage markers judiciously
- Reconcile age, AFP, morphology, and molecular findings

Pancreatic mass



Acinar / squamoid review



Lineage stains



Integrated classification

Tumor classification precedes management

- Pancreatoblastoma is malignant despite occasional circumscription
- Resectability and metastases are distinct from tumor identity
- Extent and histologic subtype must both be communicated

Histologic identity

Extent of disease

Treatment plan

Resectability is a multidisciplinary decision

- Surgical planning considers vascular and adjacent-organ involvement
- Cross-sectional imaging informs feasibility and expected morbidity
- Rare pediatric pancreatic tumors warrant specialist team review

Imaging extent



Surgeon assessment



Pathology input



Pediatric tumor board

Pathology reporting after resection

- Record anatomic location, size, and adjacent-tissue involvement
- Document resection margins and sampled regional lymph nodes
- Report differentiation, squamoid foci, and relevant ancillary results
- Use the actual institutional protocol; Do not invent entity-specific staging cutoffs

Localized disease: Complete resection matters

- NCI PDQ identifies surgery as the main treatment modality
- Complete resection is central to cure when technically feasible
- Pancreaticoduodenectomy may be required for head-region lesions

Localized lesion



Complete excision if feasible



Pathologic margin review



Follow-up

Unresectable disease: Chemotherapy may help

- Larger or initially unresectable tumors may receive neoadjuvant chemotherapy
- Pediatric literature commonly uses cisplatin-containing regimens
- Response may permit reassessment for definitive surgery

Initially unresectable



Systemic therapy



Reimage / reassess



Potential resection

Metastatic disease requires individual planning

- Management commonly combines systemic therapy and surgery when appropriate
- Stage and organ involvement guide multidisciplinary decisions
- Published estimates come from small heterogeneous pediatric cohorts

Systemic disease

Local control

Long-term assessment

Treatment evidence has important limits

Better established	More uncertain
Value of complete resection	Optimal radiation strategy
Activity of cisplatin regimens	Best salvage drug sequence
Need for specialist center	Reliable comparisons among small series

How prognosis differs from ductal carcinoma

Favorable context	Higher-risk context
Completely resected localized tumor	Residual / unresectable tumor
No metastases	Metastatic presentation
Coordinated multimodal care	Limited response or recurrence

Post-treatment surveillance is multimodal

- Track clinical symptoms and physical findings
- Measure serial AFP only when informative at baseline
- Use cross-sectional imaging appropriate to disease and treatment course
- Interpret discordant AFP and imaging results cautiously

Clinical review



AFP if informative



Imaging



Re-evaluation

Hypothetical case: Child with abdominal mass

- A 5-year-old has progressive abdominal enlargement
- Imaging identifies a pancreatic-origin solid mass
- Serum AFP is elevated
- Biopsy shows acinar differentiation and squamoid islands

Clinical question

Which two microscopic findings are most decisive for classification?

Case interpretation: Phenotype over a marker

- Acinar differentiation establishes an exocrine pancreatic component
- Squamoid islands strongly support pancreatoblastoma
- Elevated AFP supports the clinical picture but is not definitive
- Disease extent still needs assessment

Acinar phenotype

Squamoid islands

Pancreatoblastoma

Hypothetical case: An adolescent pancreatic mass

- An adolescent has a mixed solid-cystic pancreatic lesion
- Biopsy shows pseudopapillary structures
- There are no convincing acinar structures or squamoid corpuscles
- Nuclear β -catenin is present

Clinical question

Which diagnosis should be high in the differential?

Case interpretation: Shared β -catenin biology

Finding	Weight
Pseudopapillary architecture	Strongly favors SPN
No squamoid corpuscles	Weakens pancreatoblastoma
Nuclear β -catenin	Seen in both; not decisive

Hypothetical case: Tiny acinar-positive core

- A young child has a large pancreatic mass
- The core biopsy is trypsin-positive but lacks squamoid foci
- Clinical and imaging findings still raise pancreatoblastoma
- The initial differential includes acinar cell carcinoma

Clinical question

What is the appropriate next pathology step?

Case interpretation: Recognize sampling error

- Request deeper sections or more representative tissue where feasible
- Review architecture for focal squamoid islands
- Correlate AFP, age, imaging, and directed stains
- Do not force a definitive subtype from inadequate material

Limited tissue



Broader sampling



Integrated review



Defensible diagnosis

What an expert must communicate

01

Pancreatoblastoma is a distinct malignant pediatric pancreatic tumor

02

The key histologic combination is squamoid + acinar differentiation

03

Wnt activation is common but not exclusive

04

Extent, resection status, and AFP trends influence care

References and evidence boundaries

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026), ch. 19, p. 812
- NCI PDQ: Childhood Pancreatic Cancer Treatment, Health Professional Version (consulted 2026)
- Patterson KN et al. Front Pediatr. 2022;10:966943 (CC BY)
- Primary Robbins passage is short; expanded content is independently sourced in speaker notes