

Cancer precursor project - characteristics of premalignant precursors, part 1 (carcinomas)

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The goal of our [cancer precursor project](#) is to better understand how cancer arises by compiling a regularly updated [spreadsheet](#) of all distinct human cancers (1231 as of 3Apr24) and their premalignant precursors (192 identified to date).

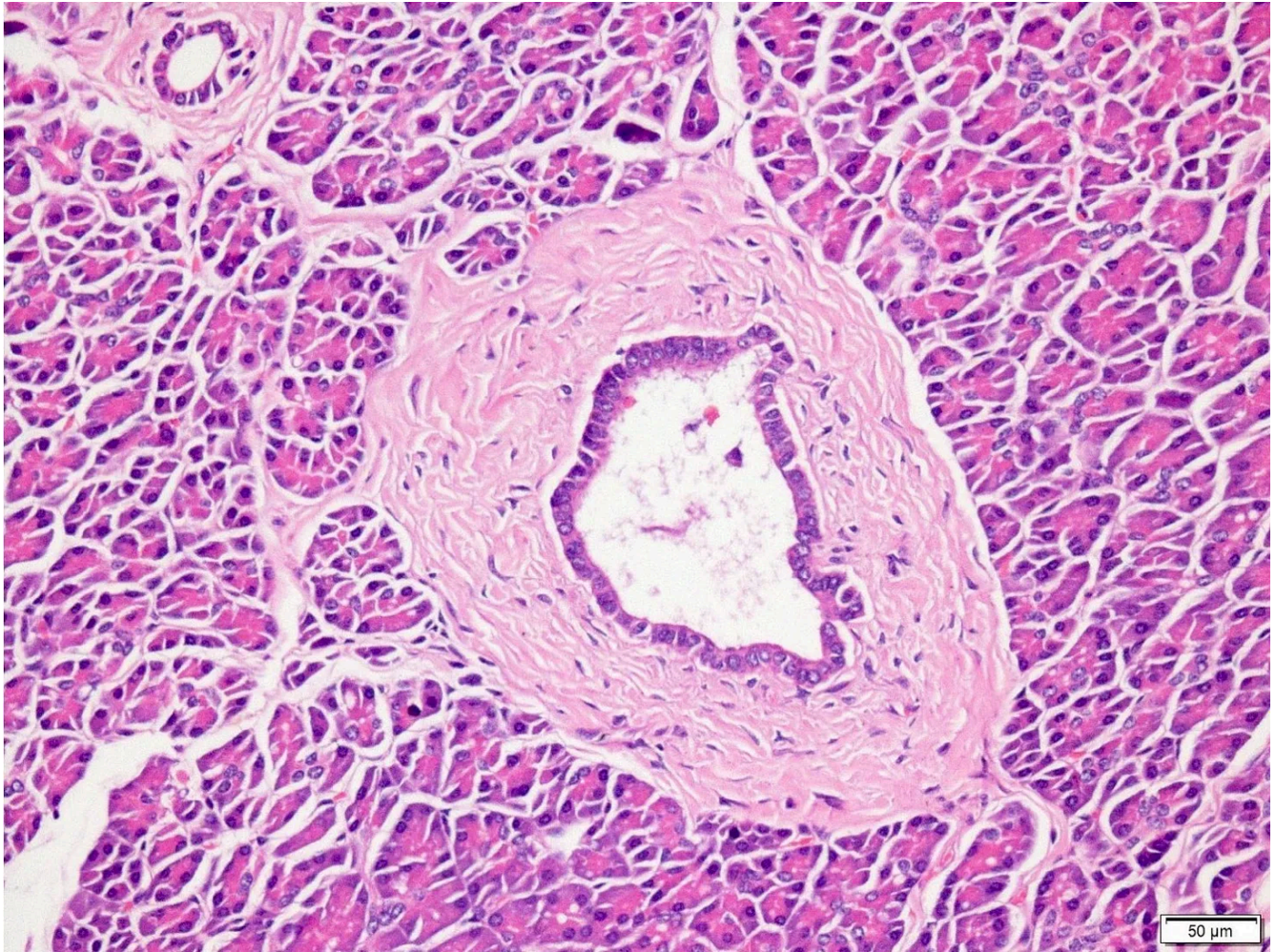
Although premalignant precursors have been identified for 15.6% of distinct malignancies, the percentage varies widely by pathology subspecialty:

	Cancers	Precursors	%
Neuropathology	114	2	1.8%
Dermatopathology	79	5	6.3%
Bone, joints and soft tissue	143	11	7.7%
Hematopathology	207	20	9.7%
Breast	58	8	13.8%
Head & neck	128	19	14.8%
Gyn	96	20	20.8%
GI / liver	203	47	23.2%
GU / adrenal	140	34	24.3%
Thoracic	63	26	41.3%
Grand total	1231	192	15.6%

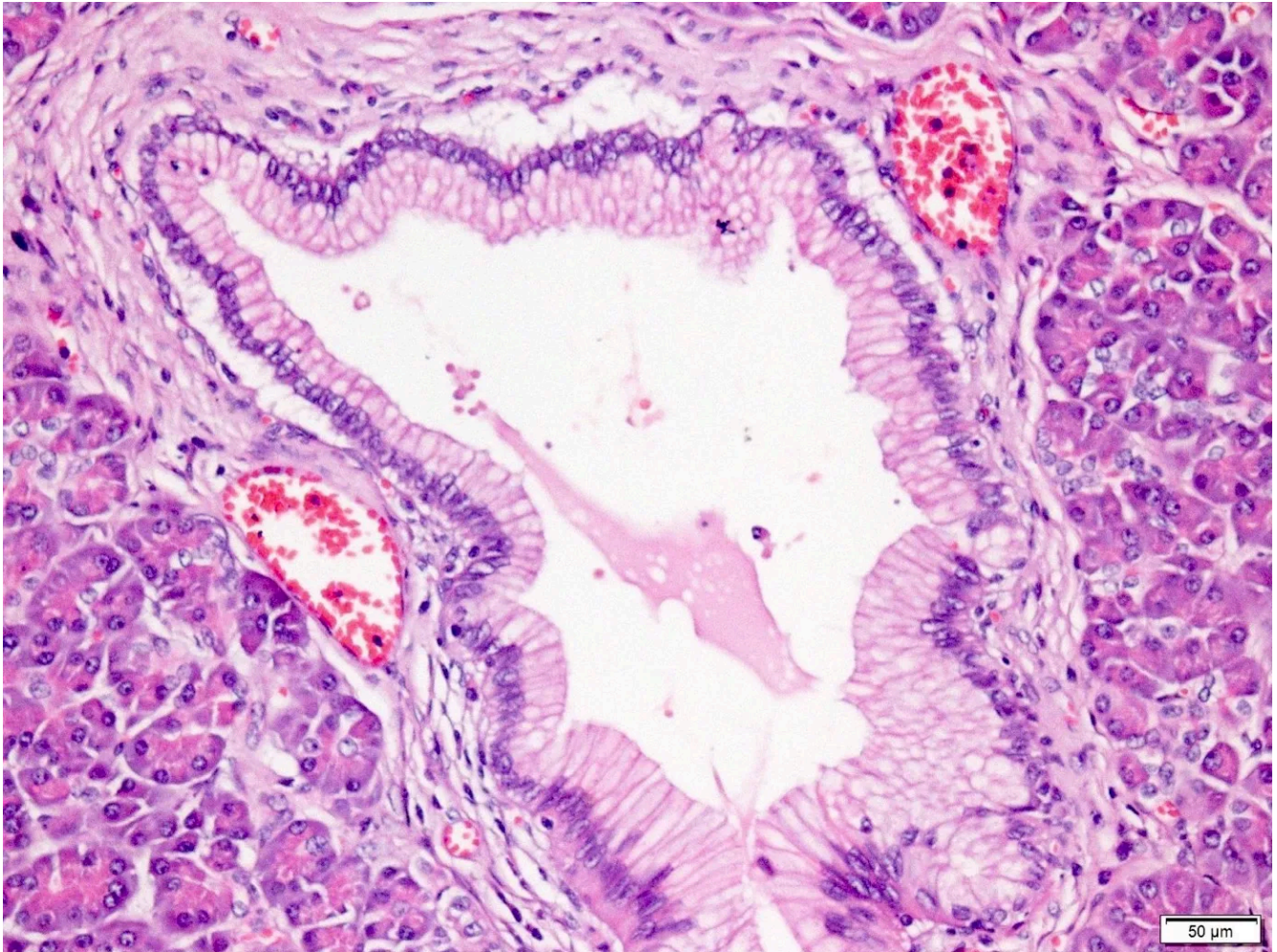
Premalignant precursors of distinct malignancies by subspecialty

The premalignant precursors of carcinomas (invasive epithelial cancers) have been characterized based on the intraepithelial neoplasia model, which describes epithelial lesions that are premalignant, microscopic and noninvasive (particularly high grade lesions) that can progress to carcinomas. Classification is based on the highest degree of cytologic atypia identified. Some of these premalignant lesions are termed dysplasia (low grade or high grade) or carcinoma in situ. Carcinomas may also arise from metaplastic lesions (metaplasia: the reversible substitution of one type of fully differentiated cell for another within a given tissue, such as [Barrett esophagus](#)). Examples of the intraepithelial neoplasia or dysplastic pathways follow for pancreatic adenocarcinoma and lung squamous cell carcinoma:

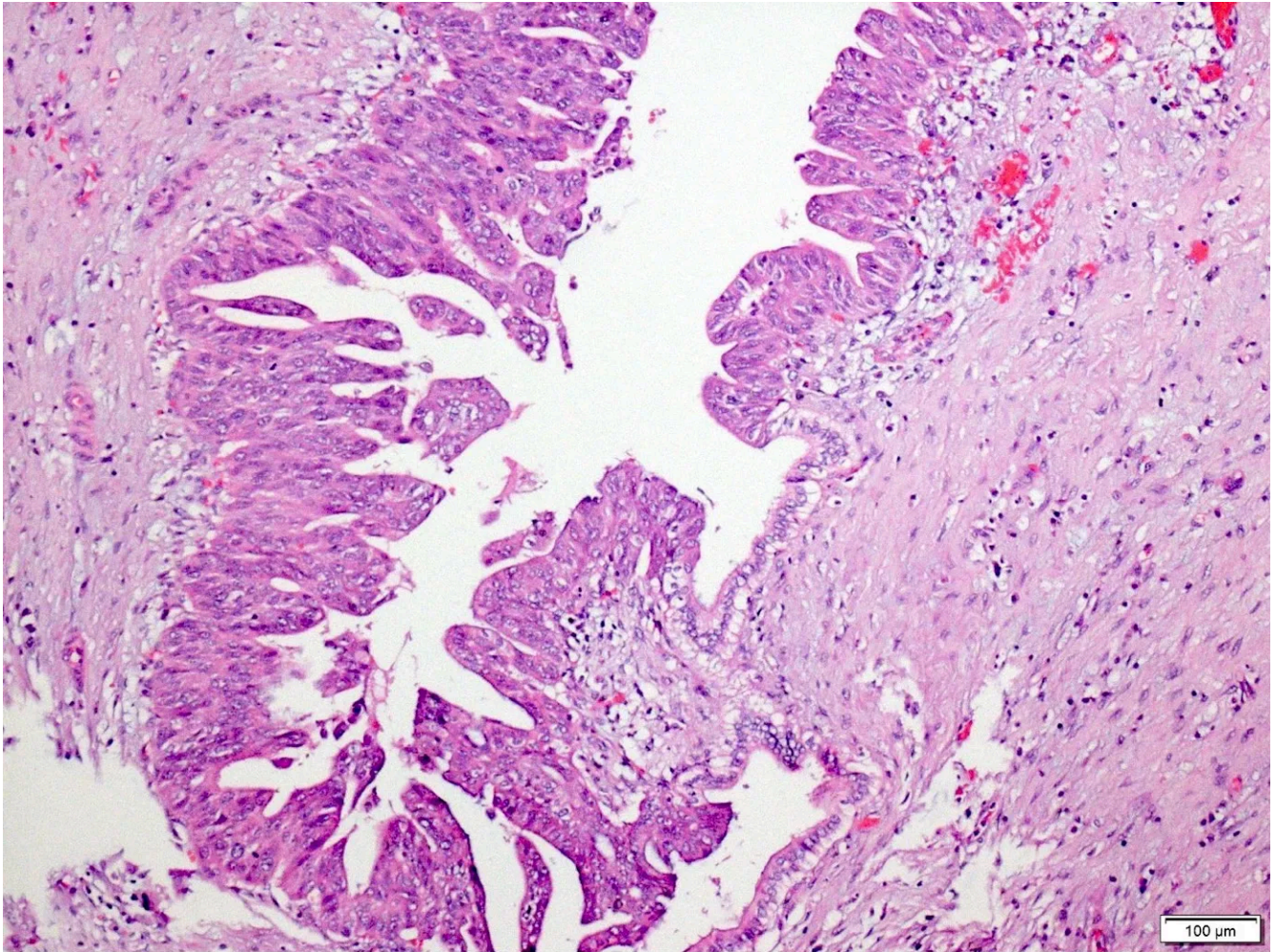
Malignant pathway of pancreatic adenocarcinoma



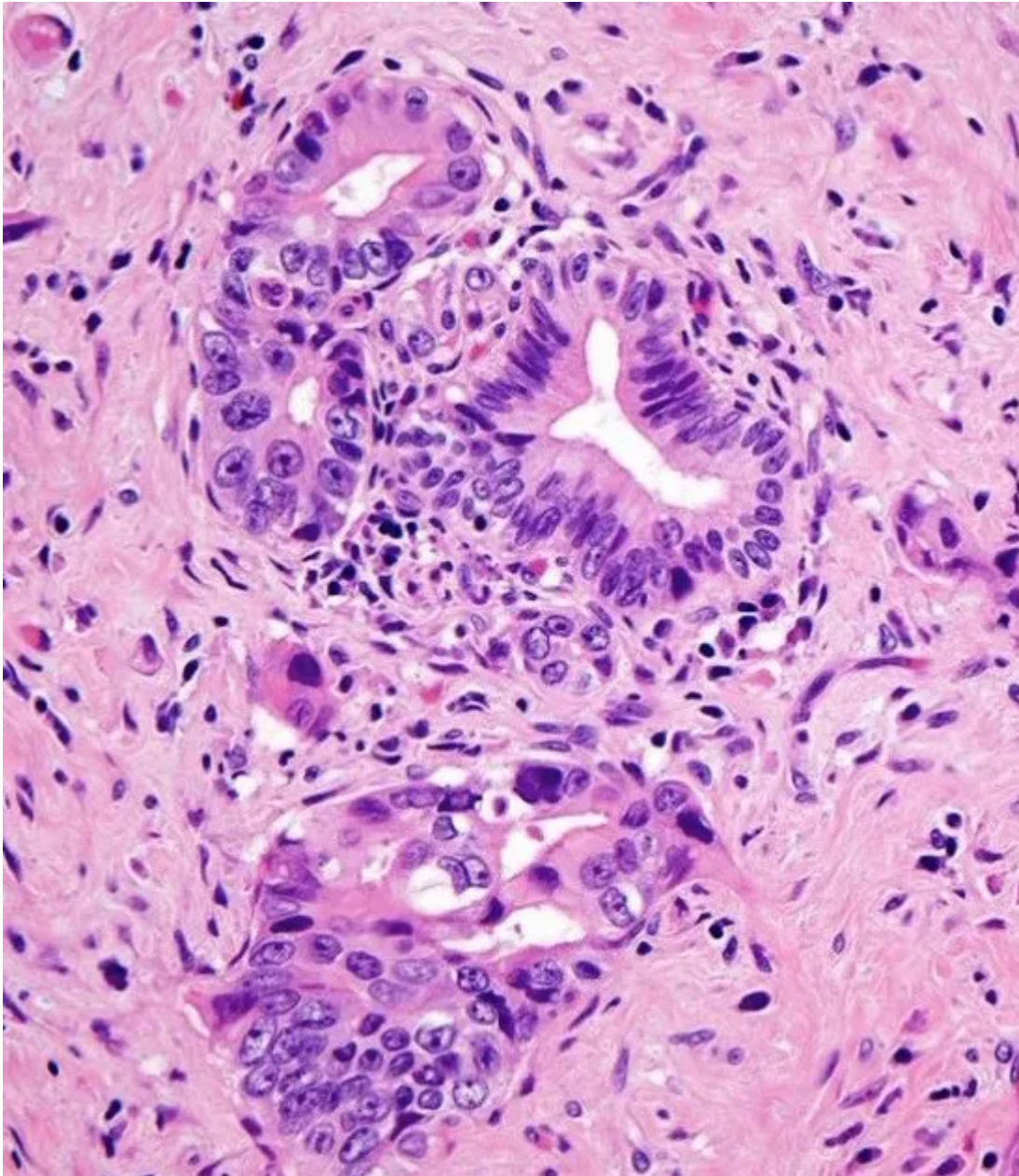
Normal: interlobular pancreatic duct lined by flat cuboidal epithelium.
Contributed by Ayşe Armutlu, M.D.



Low grade PanIN: duct lined by flat epithelium composed of tall columnar mucin producing cells with basally located nuclei and no cytologic atypia, no papillary architecture. Contributed by Ayşe Armutlu, M.D.

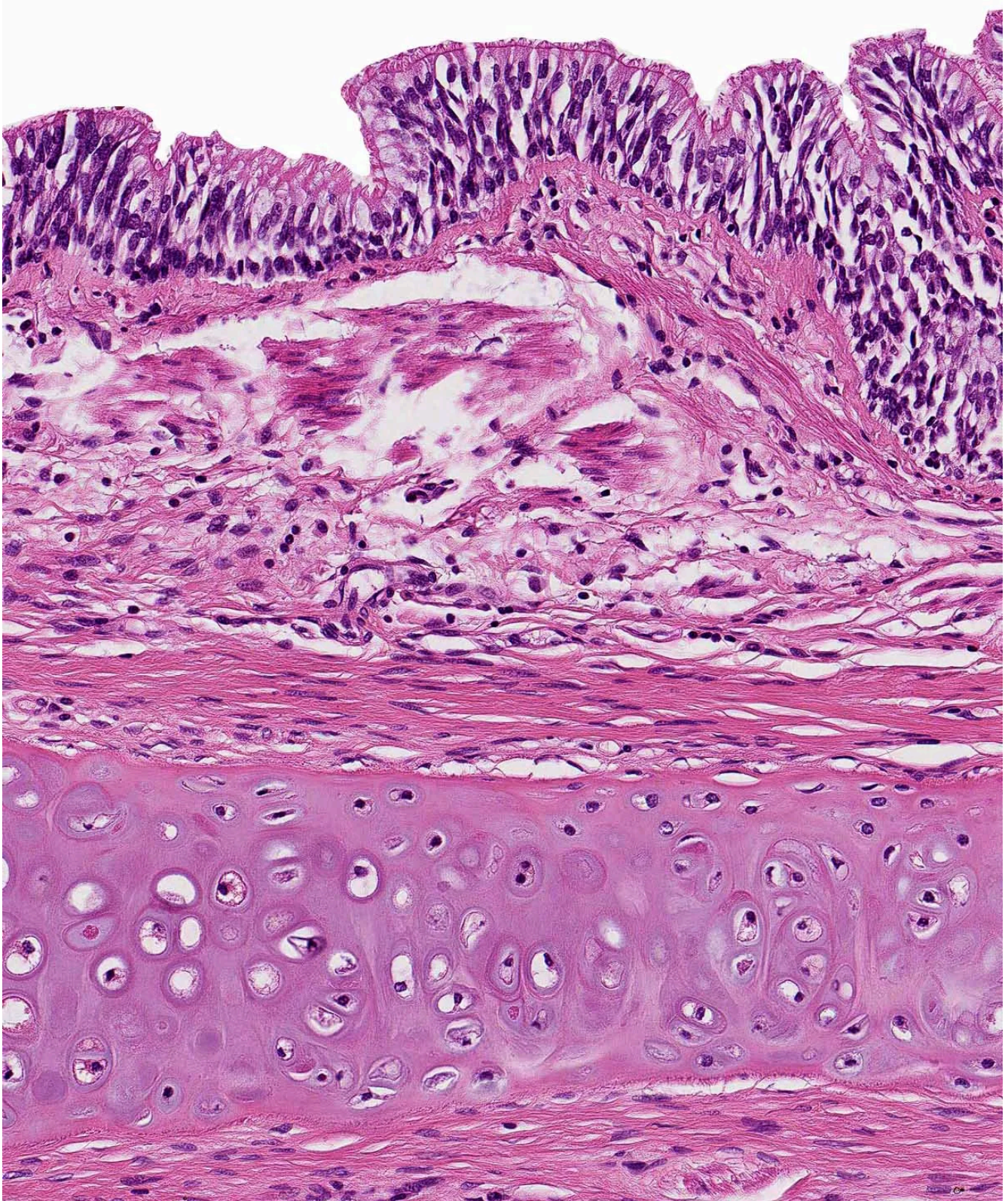


High grade PanIN: tufts and papillary elements lined by cells with remarkable cytologic atypia, including nuclear enlargement and prominent nucleoli. Contributed by Ayşe Armutlu, M.D.

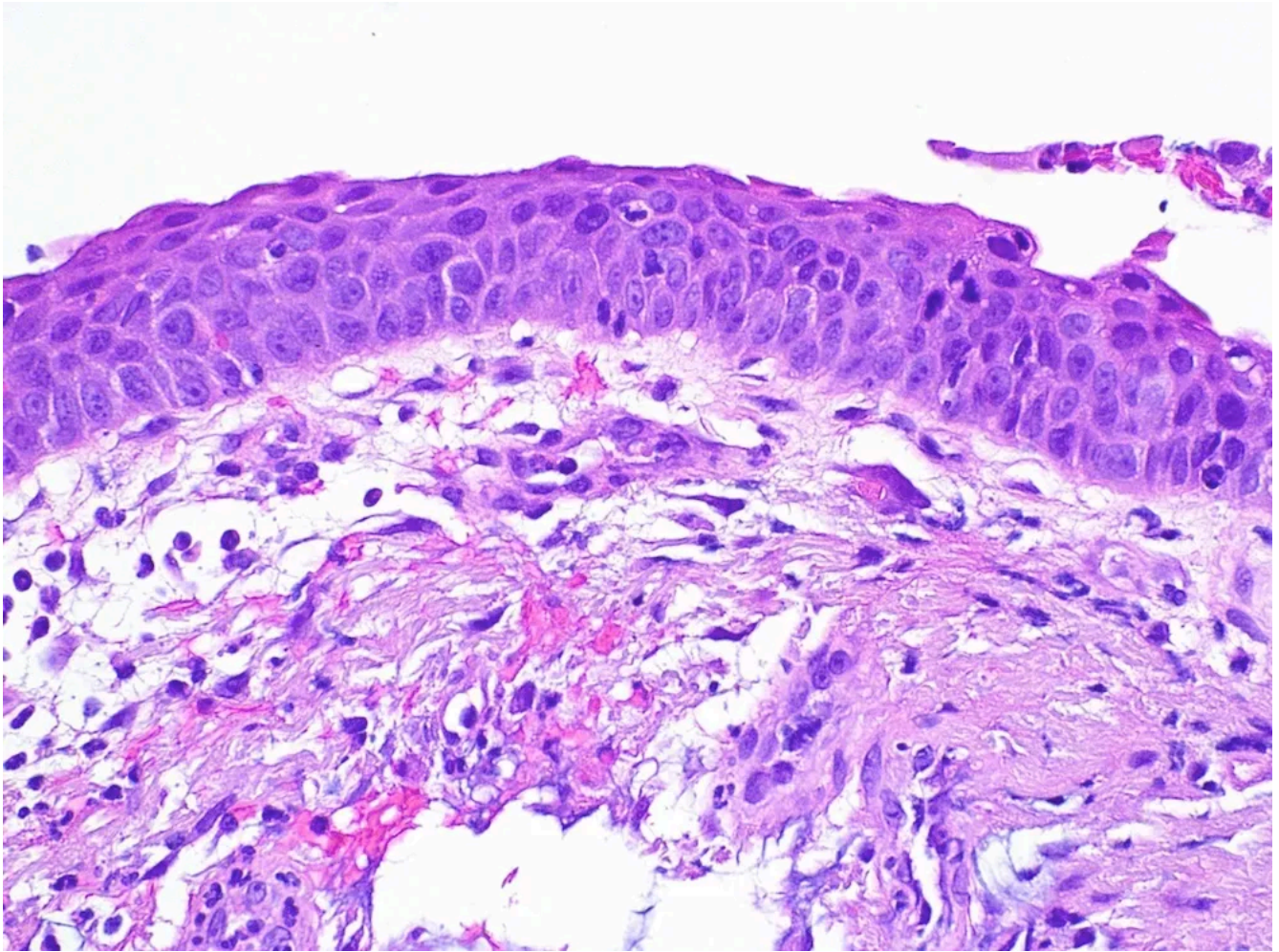


Pancreatic adenocarcinoma (invasive): marked nuclear pleomorphism with 4x anisonucleosis within one tumor gland. Contributed by Wei Chen, M.D., Ph.D.

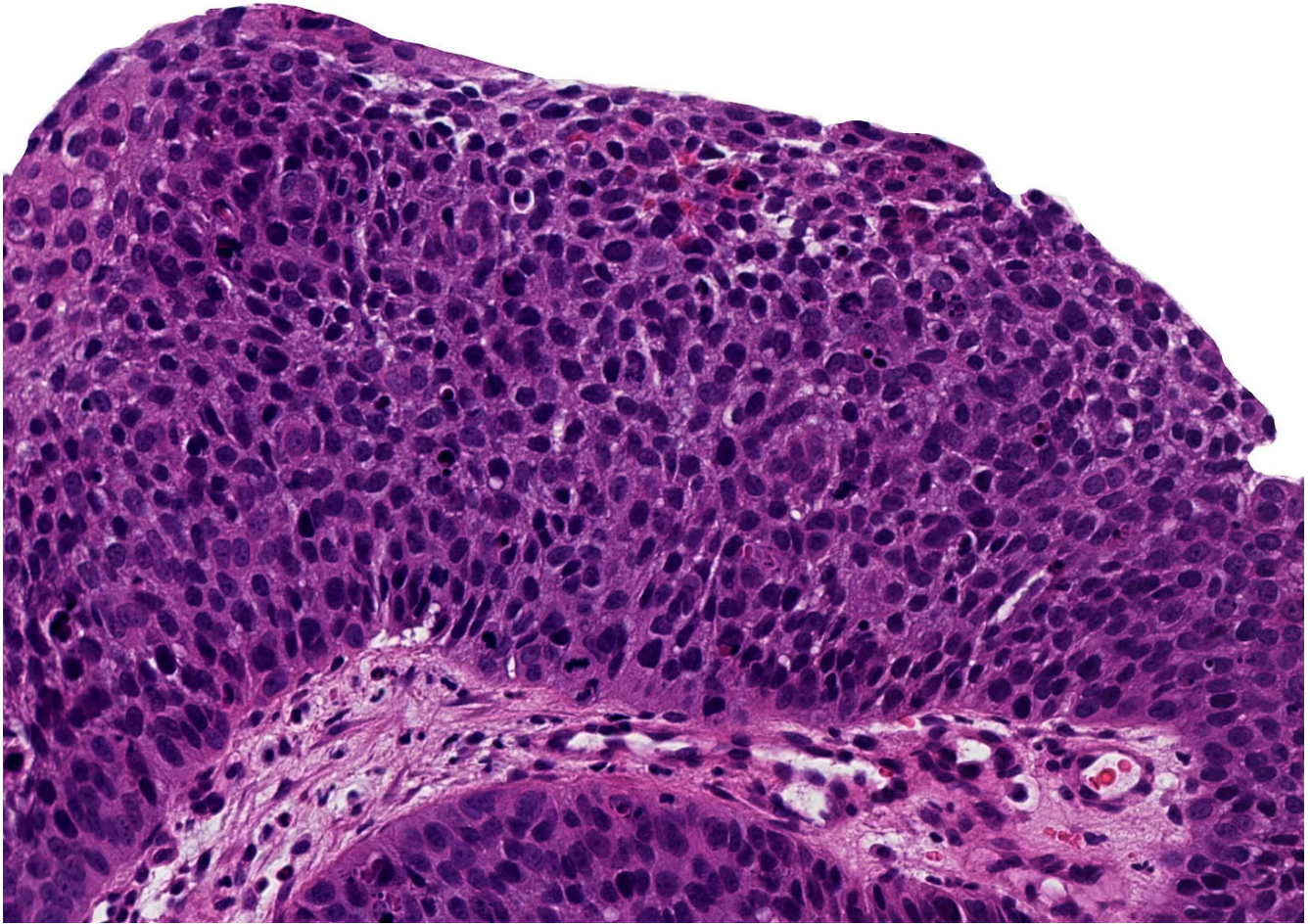
Malignant pathway of pulmonary squamous cell carcinoma



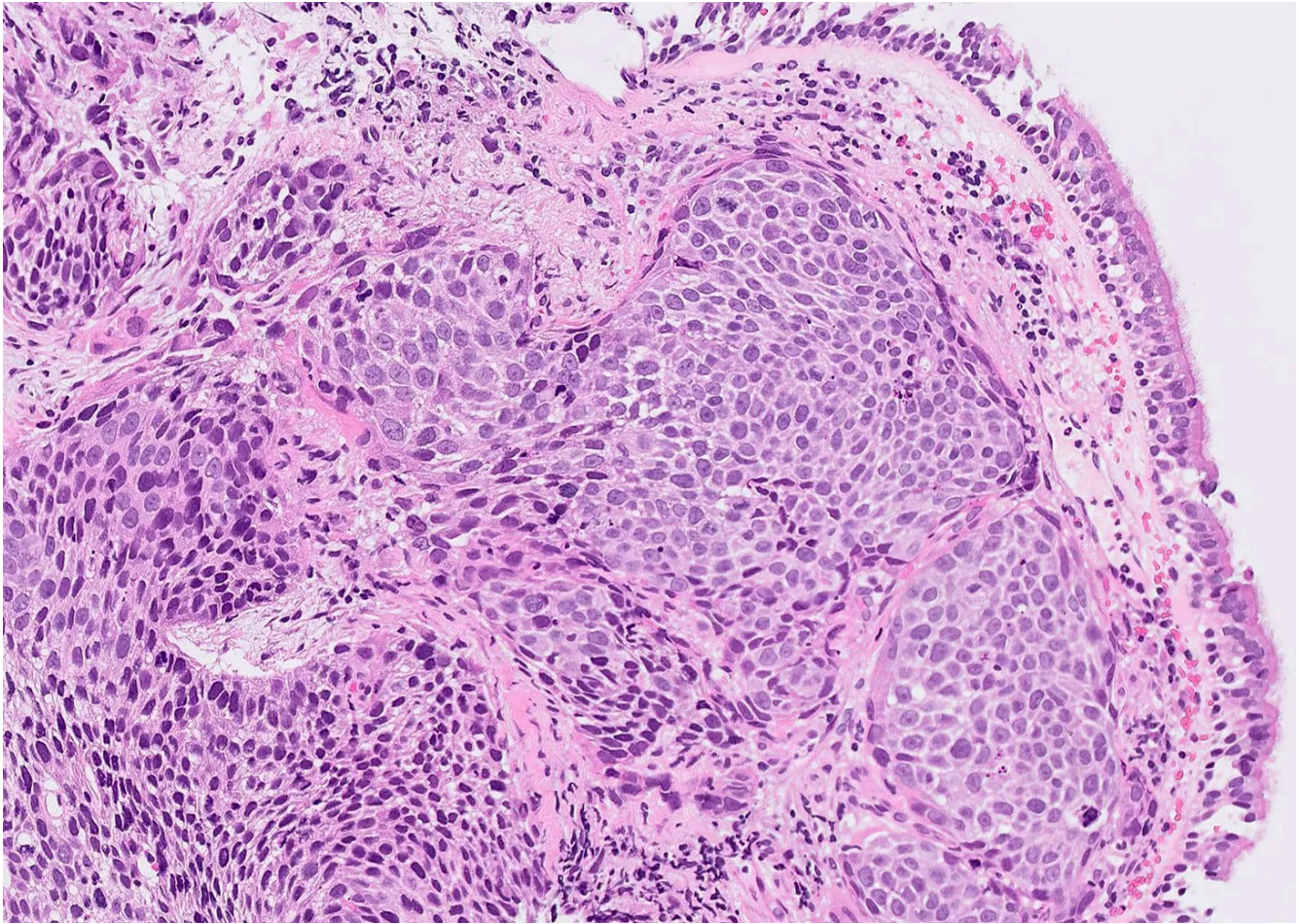
Normal bronchus containing respiratory epithelium composed of ciliated columnar epithelial cells. Contributed by Gheorghe-Emilian Olteanu, M.D., Ph.D.



Moderate to severe squamous dysplasia. Contributed by Roseann Wu, M.D.,
M.P.H.



Squamous cell carcinoma in situ with a polypoid-like growth pattern with areas of hemorrhage. Contributed by Luka Brčić, M.D., Ph.D.



Squamous cell lung carcinoma, bronchial biopsy: sheets of large polygonal cells with intercellular bridges. Contributed by Andrey Bychkov, M.D., Ph.D.

Premalignant precursors, although uncommon for some pathology subspecialties (neuropathology, dermatopathology, bone & soft tissue pathology and hematopathology), are common at epithelial sites - representative premalignant precursors are listed below:

Breast:

[Ductal carcinoma in situ, atypical ductal hyperplasia](#)

GI / liver:

Anus: [anal intraepithelial neoplasia \(anal IEN / AIN\)](#), [Buschke-Löwenstein tumor](#)

Appendix: [low grade and high grade appendiceal mucinous neoplasm \(LAMN / HAMN\)](#), [tubular adenoma](#)

Colon: [conventional adenoma](#), [serrated lesions](#), [dysplasia associated with inflammatory bowel disease](#)

Esophagus: [Barrett related dysplasia](#), [esophageal squamous intraepithelial neoplasia / squamous dysplasia](#)

Gallbladder & extrahepatic bile ducts: [intracholecystic papillary neoplasm](#), [biliary intraepithelial neoplasia / adenoma \(BiIN\)](#)

Liver & intrahepatic bile ducts: [hepatic intraductal papillary neoplasm of the bile ducts](#)

Pancreas: [pancreatic intraepithelial neoplasia \(PanIN\)](#), [intraductal papillary mucinous neoplasm \(IPMN\)](#)

Small intestine & ampulla: [intra-ampullary papillary tubular neoplasm](#)

Stomach: [dysplasia](#)

GU / adrenal gland:

Bladder & urothelial tract: [dysplasia](#), [carcinoma in situ](#)

Penis & scrotum: [penile intraepithelial neoplasia \(PeIN\)](#)

Prostate gland & seminal vesicles: [prostatic intraepithelial neoplasia \(HGPIN\)](#)

No premalignant epithelial precursors were identified in the adrenal gland, kidney and testis.

Gynecologic:

Cervix: [squamous intraepithelial lesion \(high grade /HSIL\)](#), [low grade / LSIL](#), [adenocarcinoma in situ \(AIS\)](#)

Fallopian tubes & broad ligament: [serous tubal intraepithelial carcinoma \(STIC\)](#)

Ovary: [serous borderline tumor](#), [mucinous borderline tumor](#)

Uterus: [endometrial atypical hyperplasia / endometrioid intraepithelial neoplasia](#) (AH / EIN)

Vulva & vagina: [vaginal intraepithelial neoplasia](#) (VAIN), [vulvar intraepithelial neoplasia](#) (VIN)

No premalignant epithelial precursors were identified in the placenta and peritoneum.

Head & neck:

Ear: [external ear-squamous dysplasia](#)

Eye: [conjunctival intraepithelial neoplasia](#)

Larynx, hypopharynx & trachea: [dysplasia](#)

Mandible & maxilla: [ameloblastoma](#), [calcifying epithelial odontogenic tumor](#)

Nasal cavity & nasopharynx: [squamous dysplasia](#), [sinonasal papilloma with dysplasia](#), [intestinal metaplasia](#)

Oral cavity & oropharynx: [epithelial dysplasia](#)

Salivary glands: [adenocarcinoma in situ](#), [pleomorphic adenoma](#)

No premalignant epithelial precursors were identified in the thyroid & parathyroid glands.

Thoracic:

Lung: [atypical adenomatous hyperplasia](#), [adenocarcinoma in situ](#), [squamous cell carcinoma in situ](#)

No premalignant epithelial precursors were identified in the heart, mediastinum and pleura.

We believe that studying these precursor lesions will help identify precursor lesions that we believe exist but are currently unknown, such as in the CNS (central nervous system or brain) and soft tissue.

Part 2 will discuss subspecialties with fewer identified precursors.

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- [Strategic plan to substantially reduce cancer deaths](#)
- [American Code Against Cancer](#) (how you can prevent cancer)
- [Cancer Precursor Project spreadsheet](#) and [General Overview](#)

Email me at Nat@PathologyOutlines.com - Unfortunately, I cannot provide medical advice.

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