

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

- Initially reported as “breast tumor resembling tall cell variant of papillary thyroid carcinoma” (Eusebi, 2003)
 - Solid papillary carcinoma resembling tall cell variant of papillary thyroid carcinoma (Foschini, 2017)
- Rare: ~50 reported cases to date
- No thyroglobulin or TTF-1 expression; no *BRAF* or *RET* alterations
 - unrelated to papillary thyroid carcinomas

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

- **Primarily older women (median age, 64 yrs)**
- **Small, mostly mammographically detected (median size, 1.5 cm)**

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

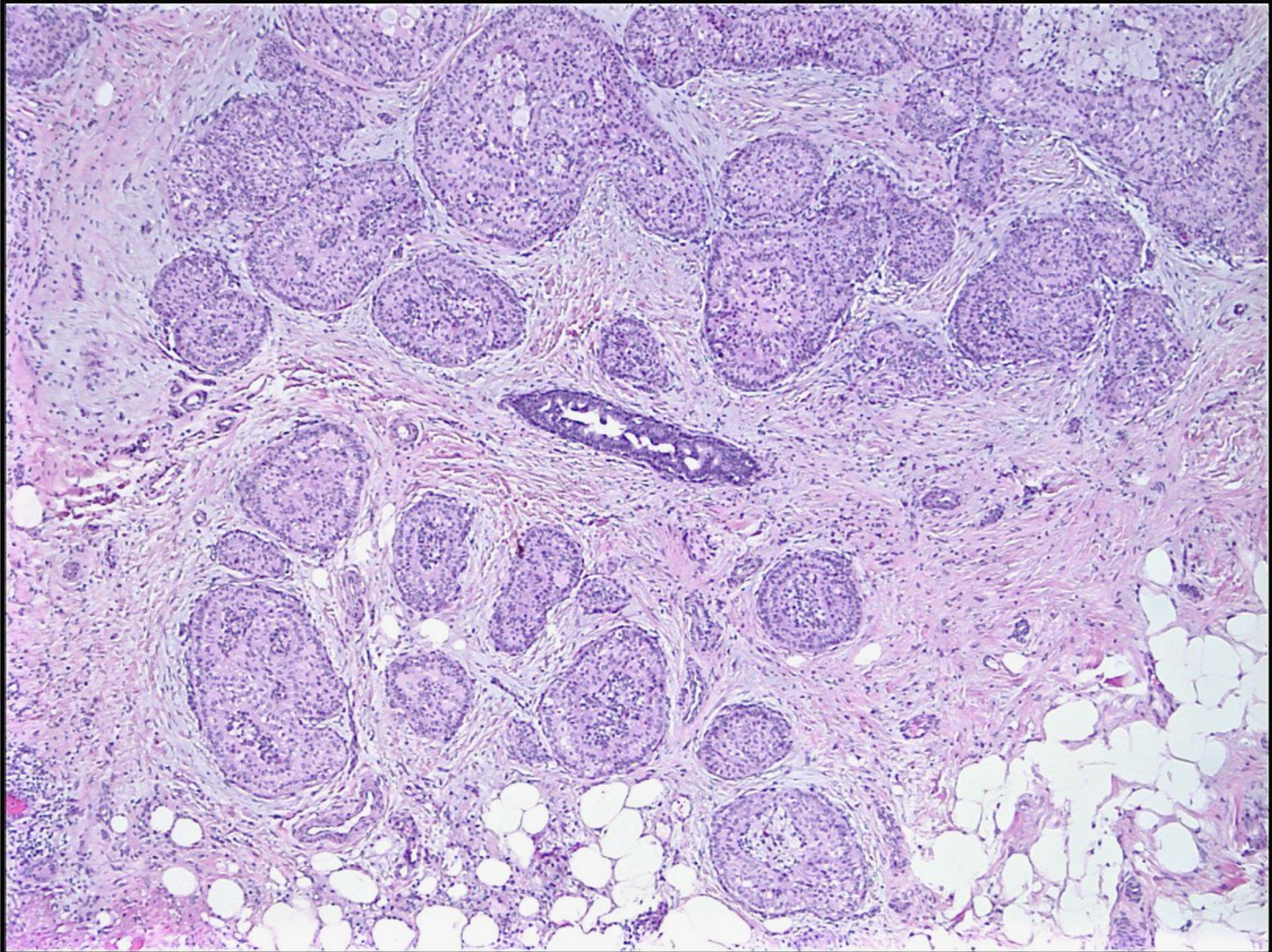
Key Histologic Features

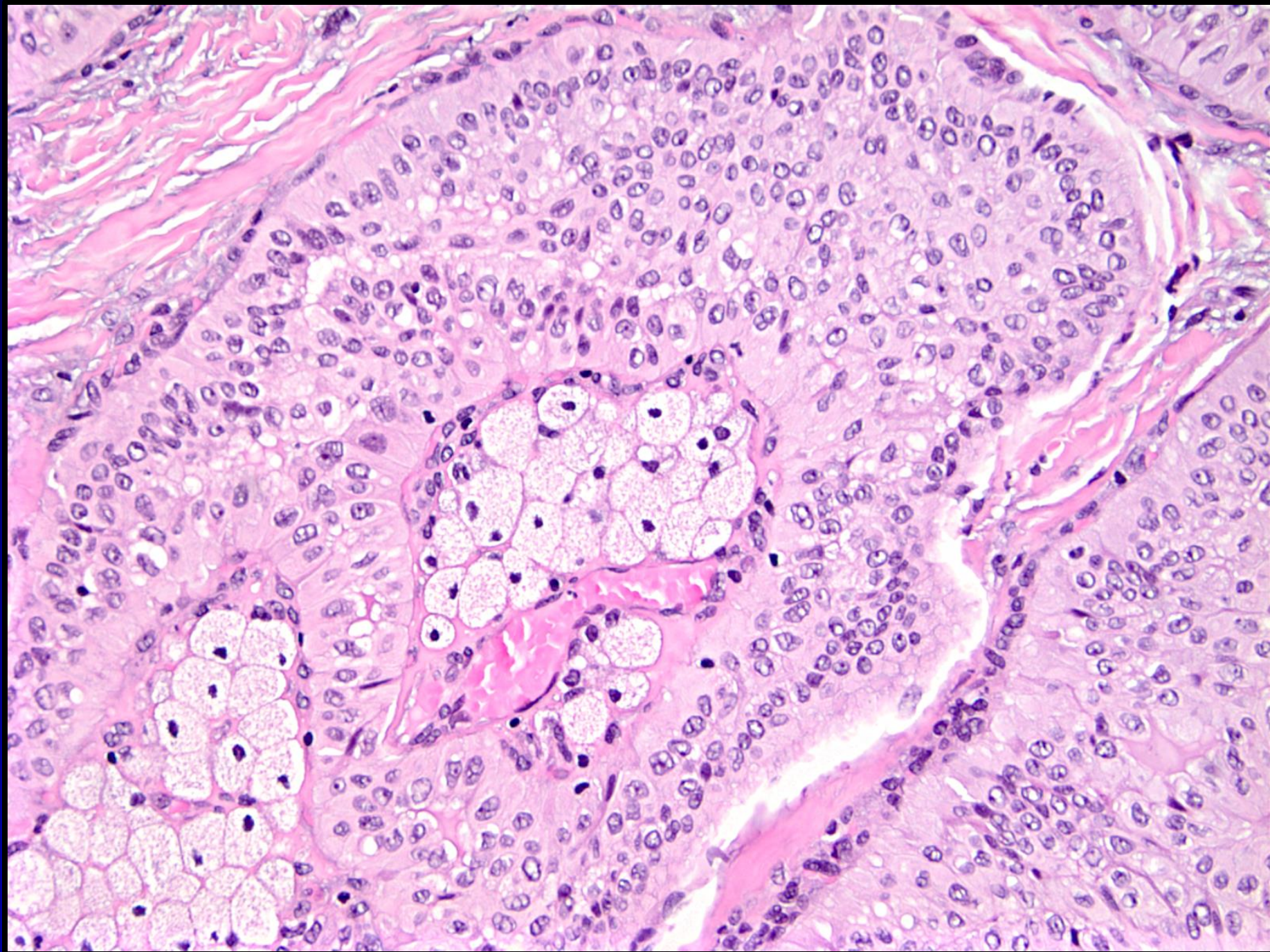
- **Solid, circumscribed nodules of columnar epithelial cells haphazardly distributed throughout breast stroma**
- **Many nodules contain fibrovascular cores, some with foamy histiocytes**
- **Collagenous stroma with little desmoplasia**

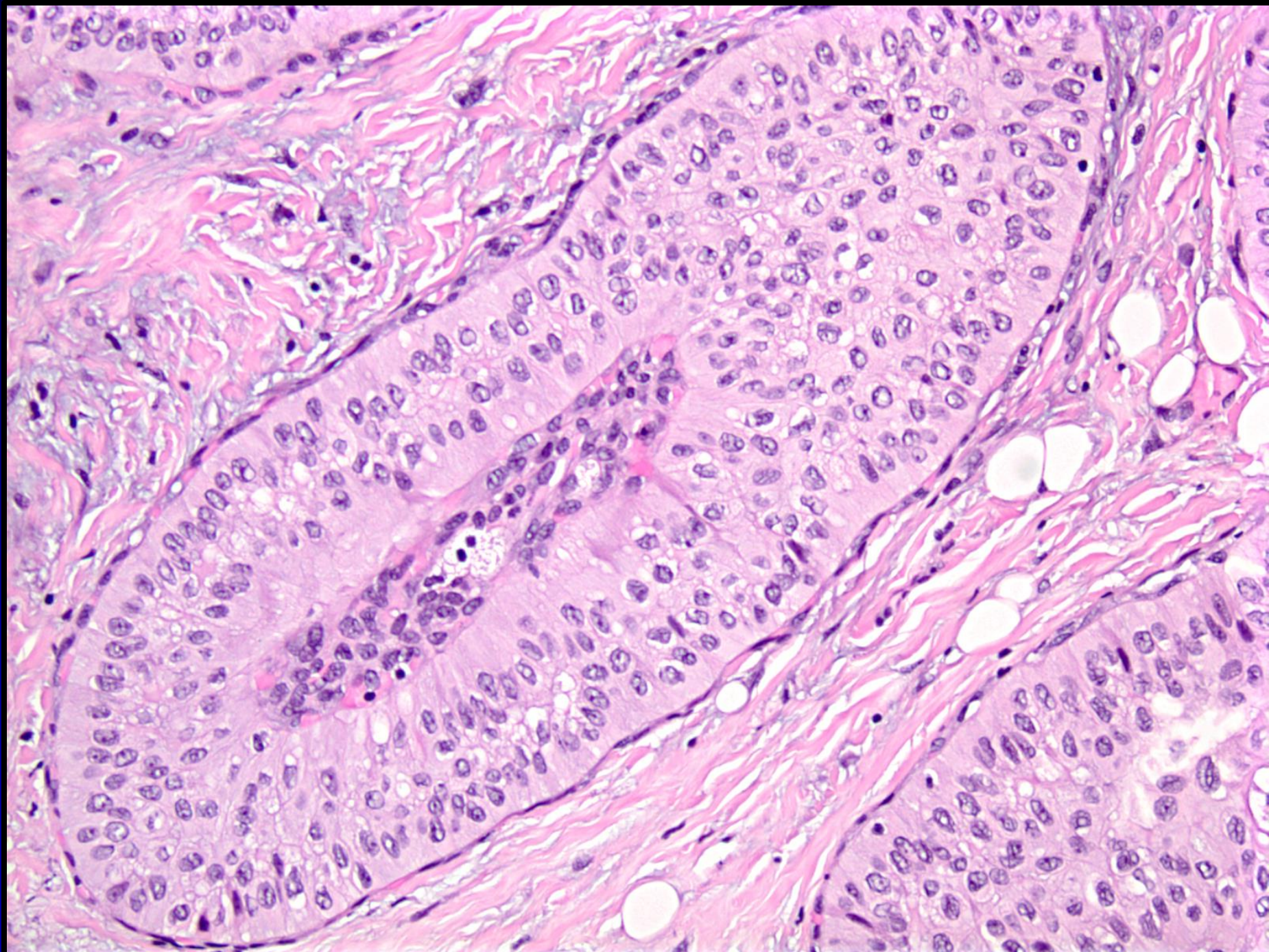
Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Key Histologic Features

- **Columnar epithelium often present in double layer with cells appearing back to back**
- **Low to intermediate grade nuclei**
- **Nuclear grooves/inclusions may be seen**
- **Nuclei at apical rather than basal pole (reverse polarity)**



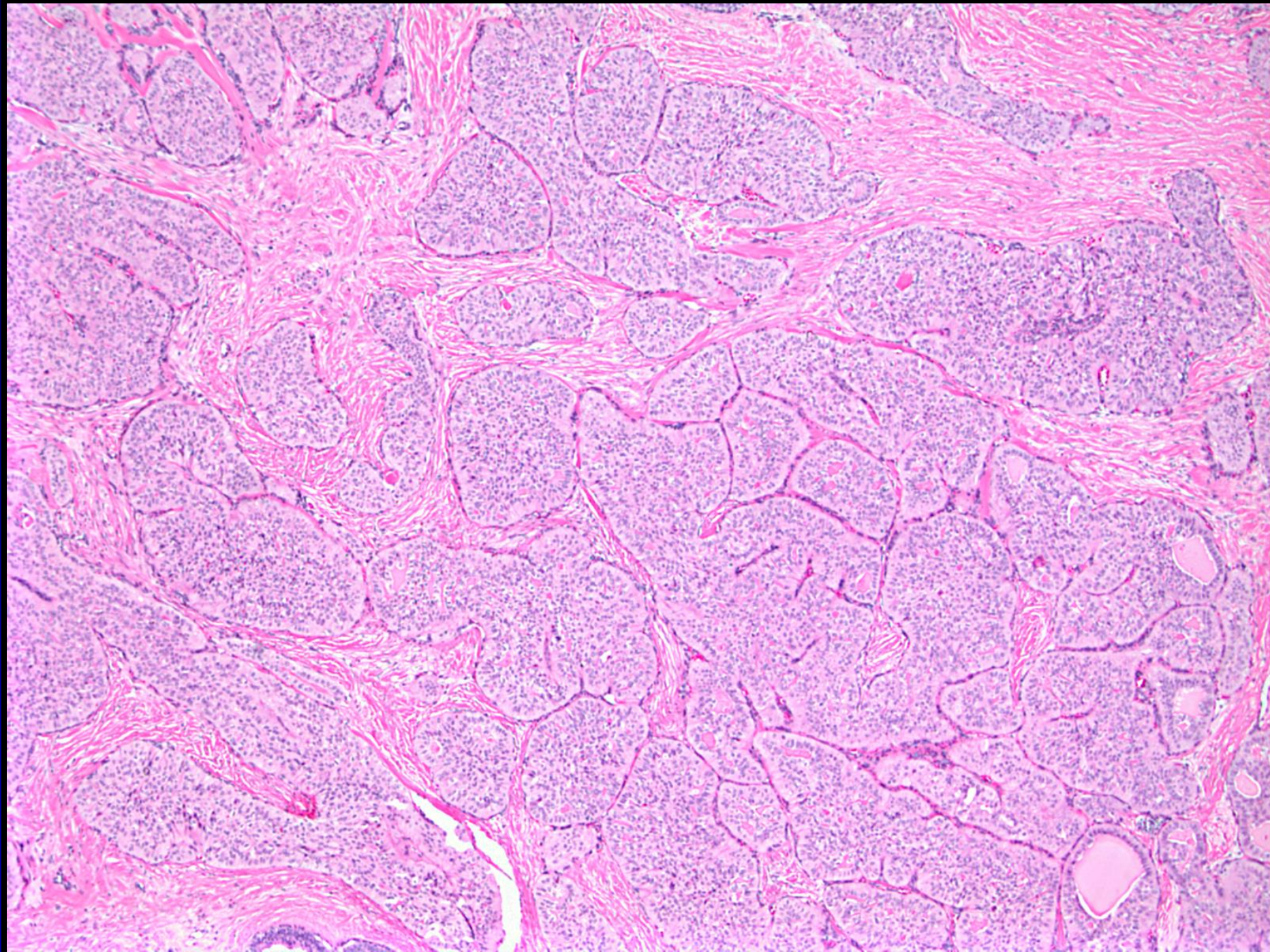




Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Less Frequent Histologic Features

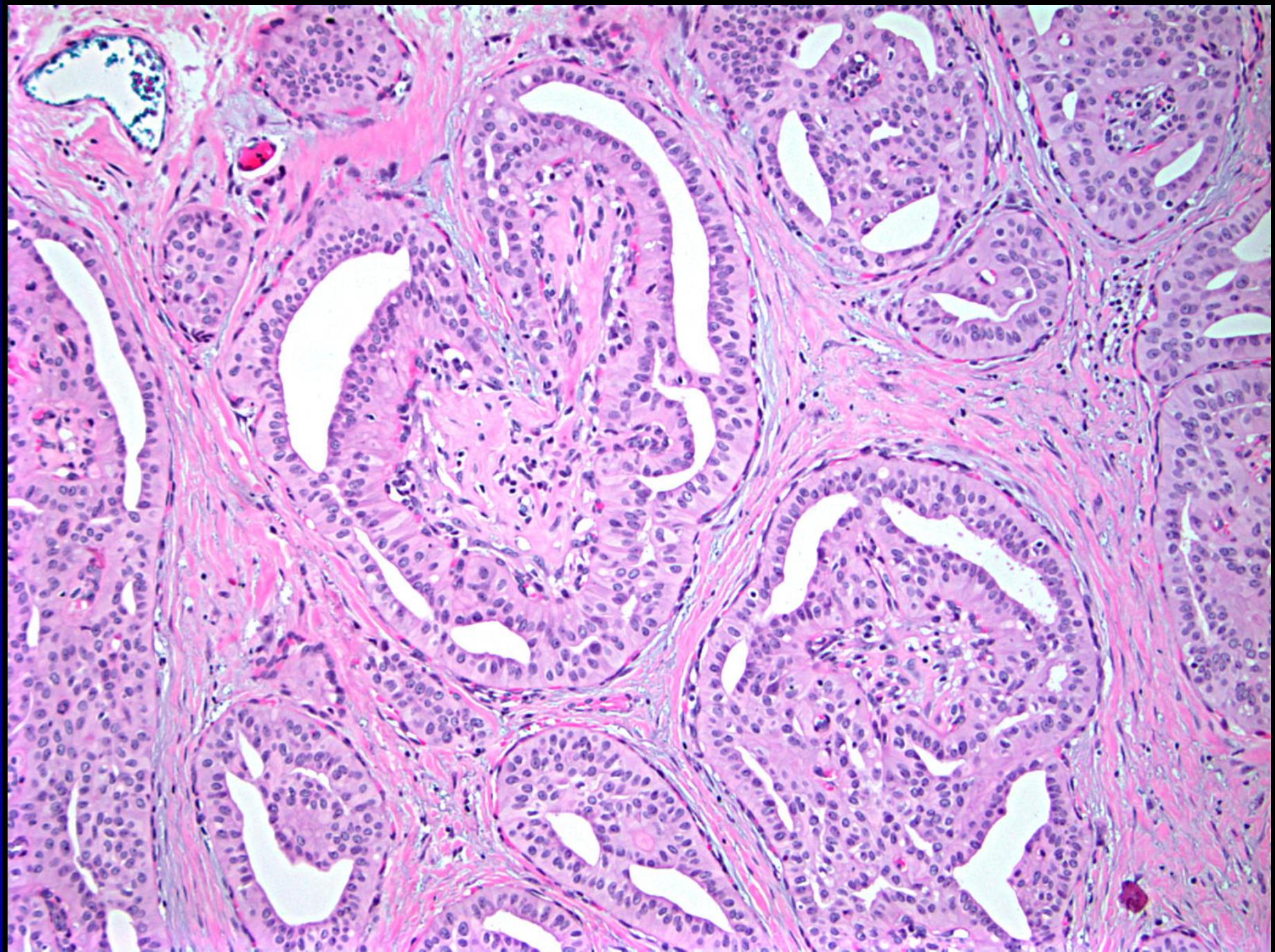
- **Jigsaw pattern of cell nests**

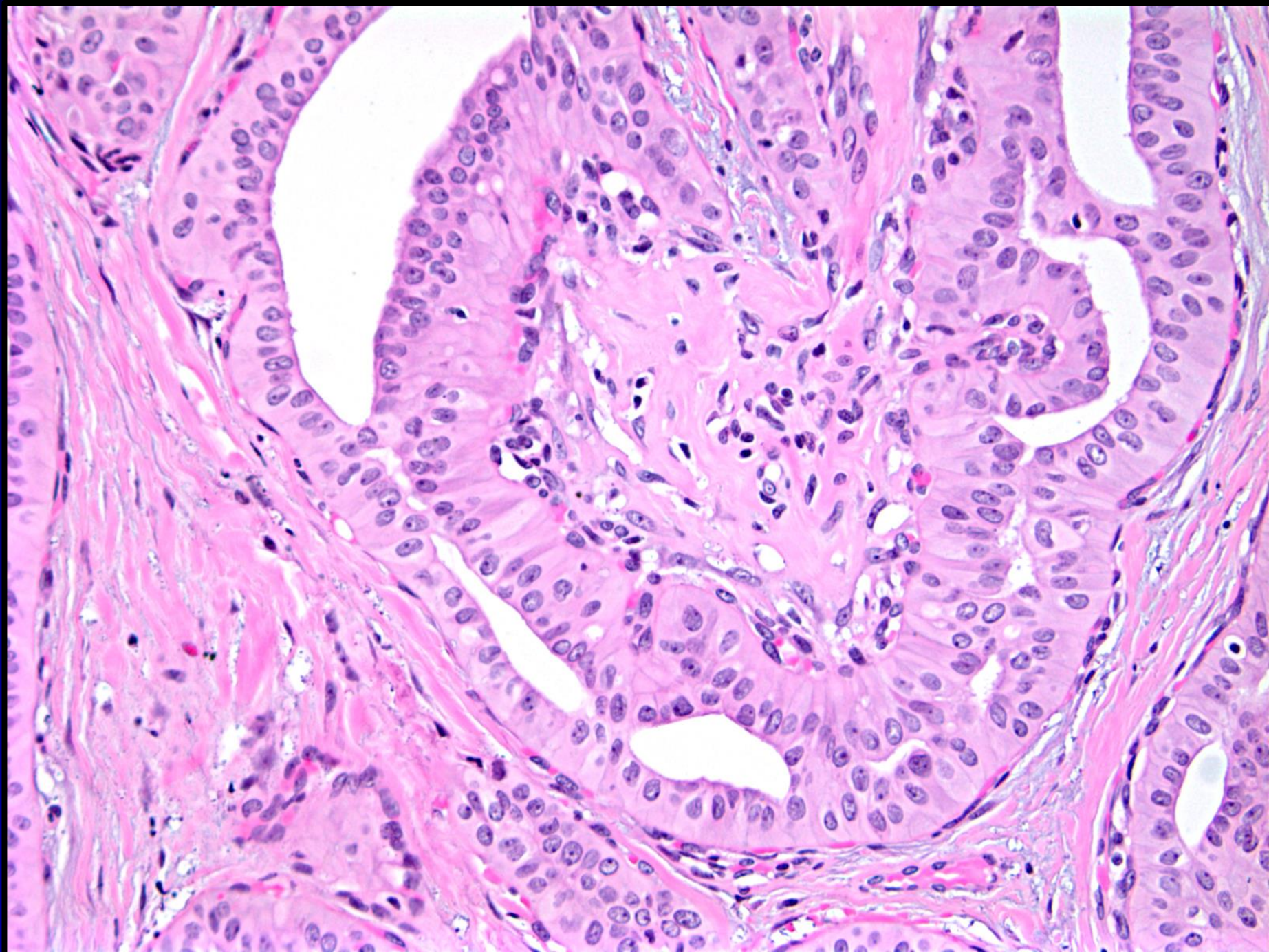


Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Less Frequent Histologic Features

- **Jigsaw pattern of cell nests**
- **Frankly papillary areas**





Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Immunophenotype

- **No myoepithelial cells around tumor nodules**
- **Positive for low AND high molecular weight cytokeratins**
- **GCDFP and mammaglobin each positive in ~60%**
- **All cases negative for TTF-1 and thyroglobulin**

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Immunophenotype

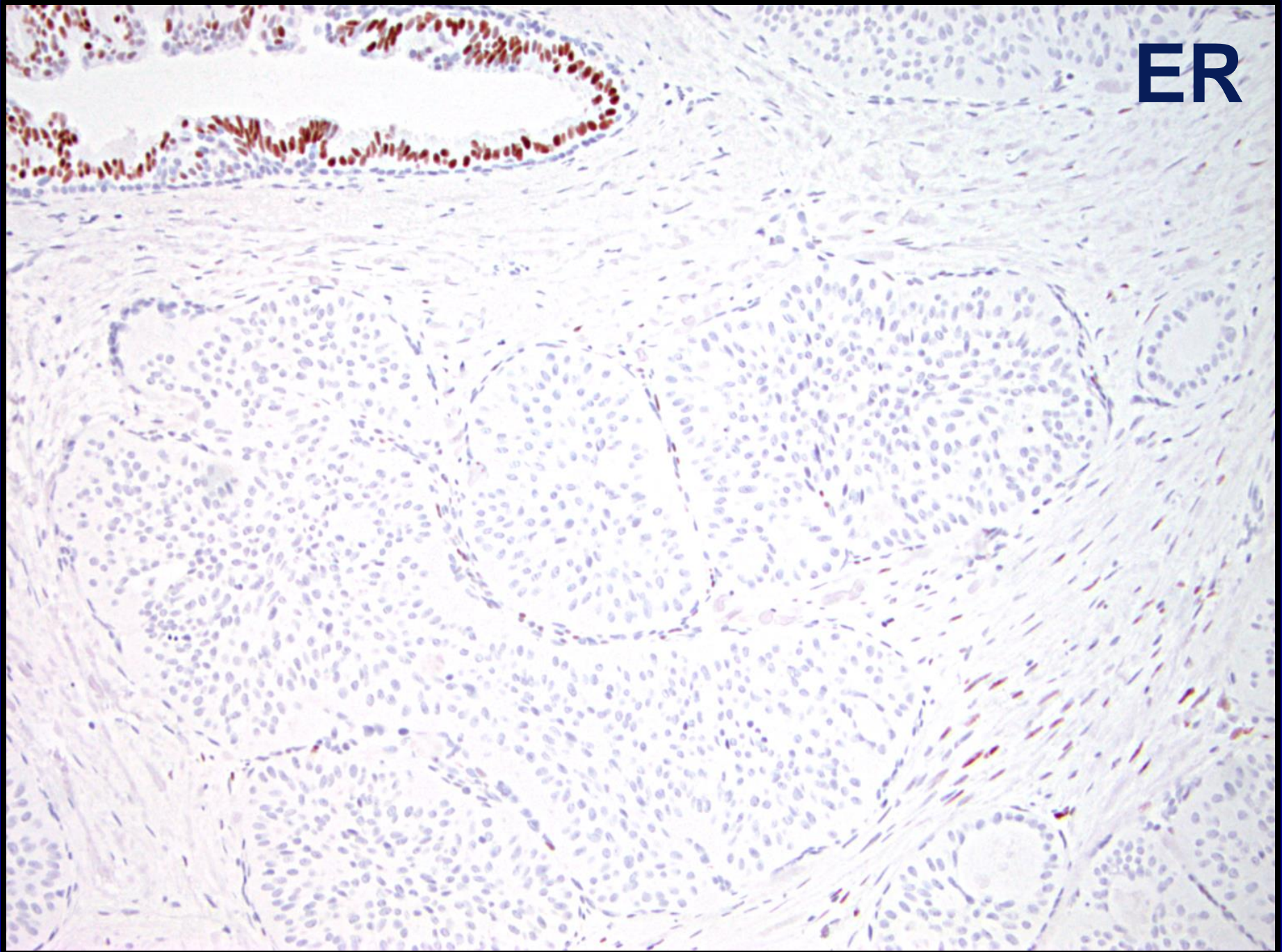
- **Either entirely ER negative or low ER positive (1-10%); PR negative in 85% of cases**
- **HER2 negative**
- **Most triple negative**
- **Low proliferation rate by Ki67 (<5%)**
- **Rich vascular network around nests on CD31 and CD34 stains**
- **Calretinin positive (Alsadoun, 2018)**

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

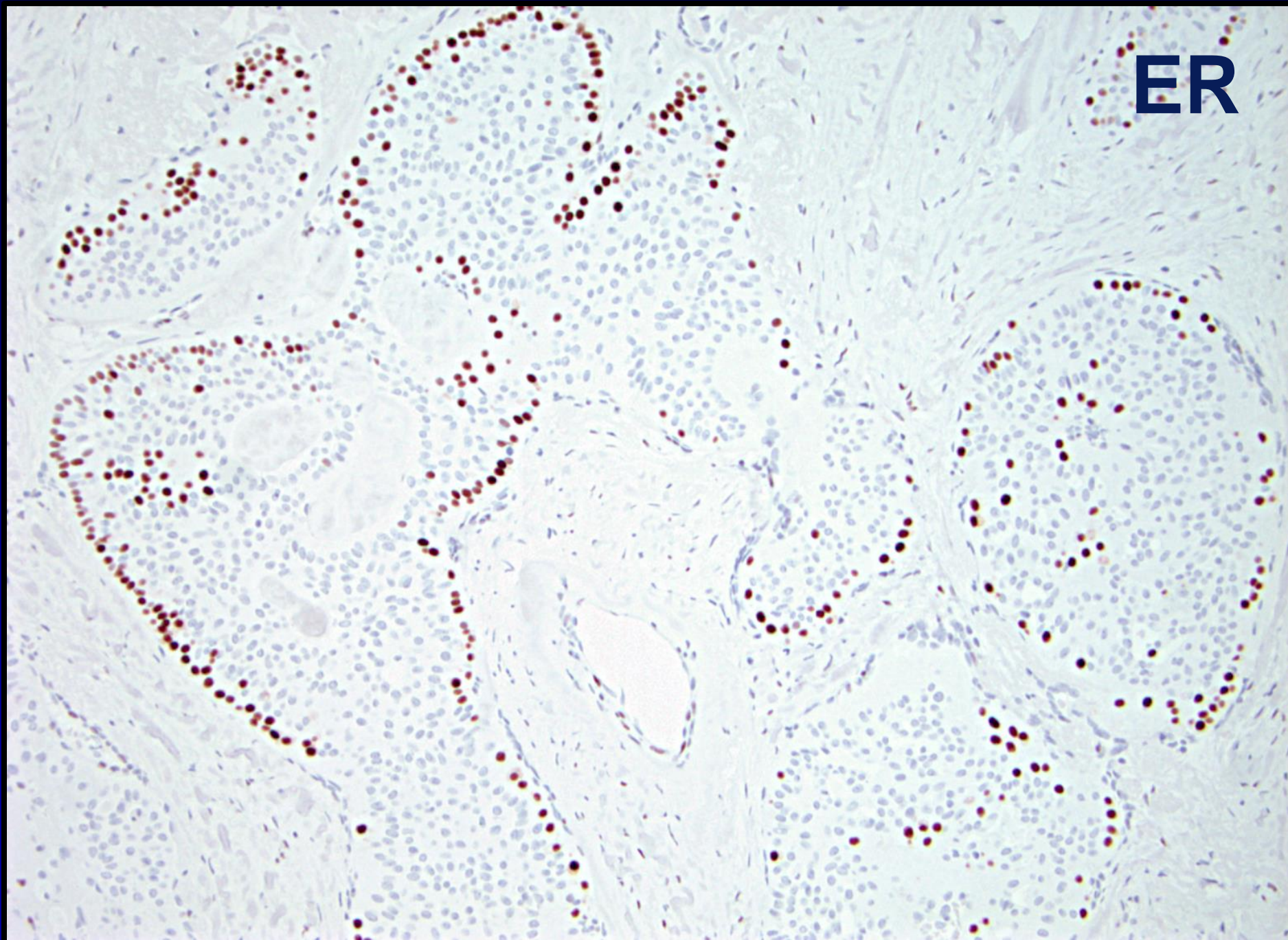
Immunophenotype

- **E-cadherin: Strong lateral membrane staining**
- **MUC1: Apical membrane staining seen on ends of cells closest to nucleus (reverse polarity)**

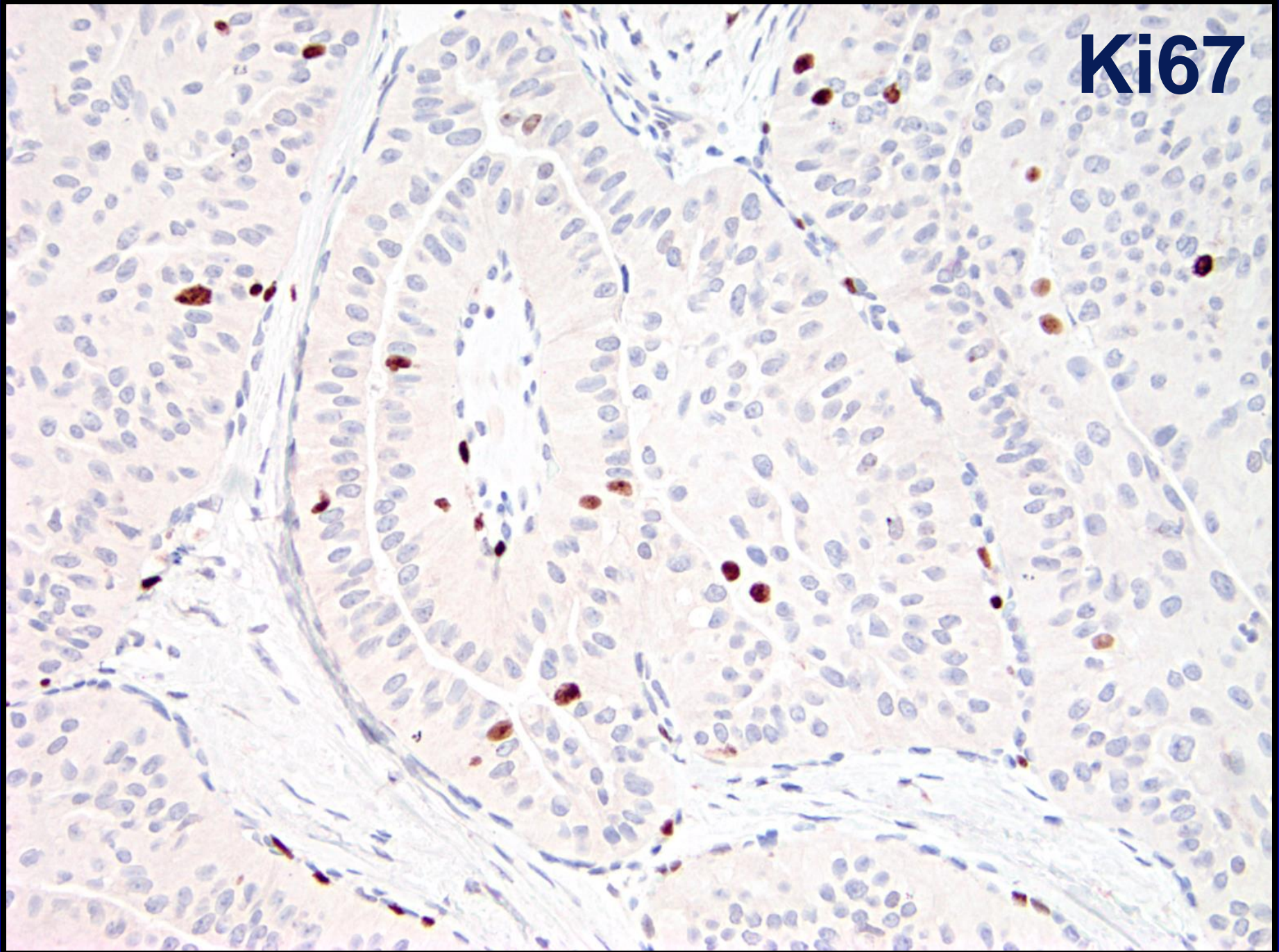
ER



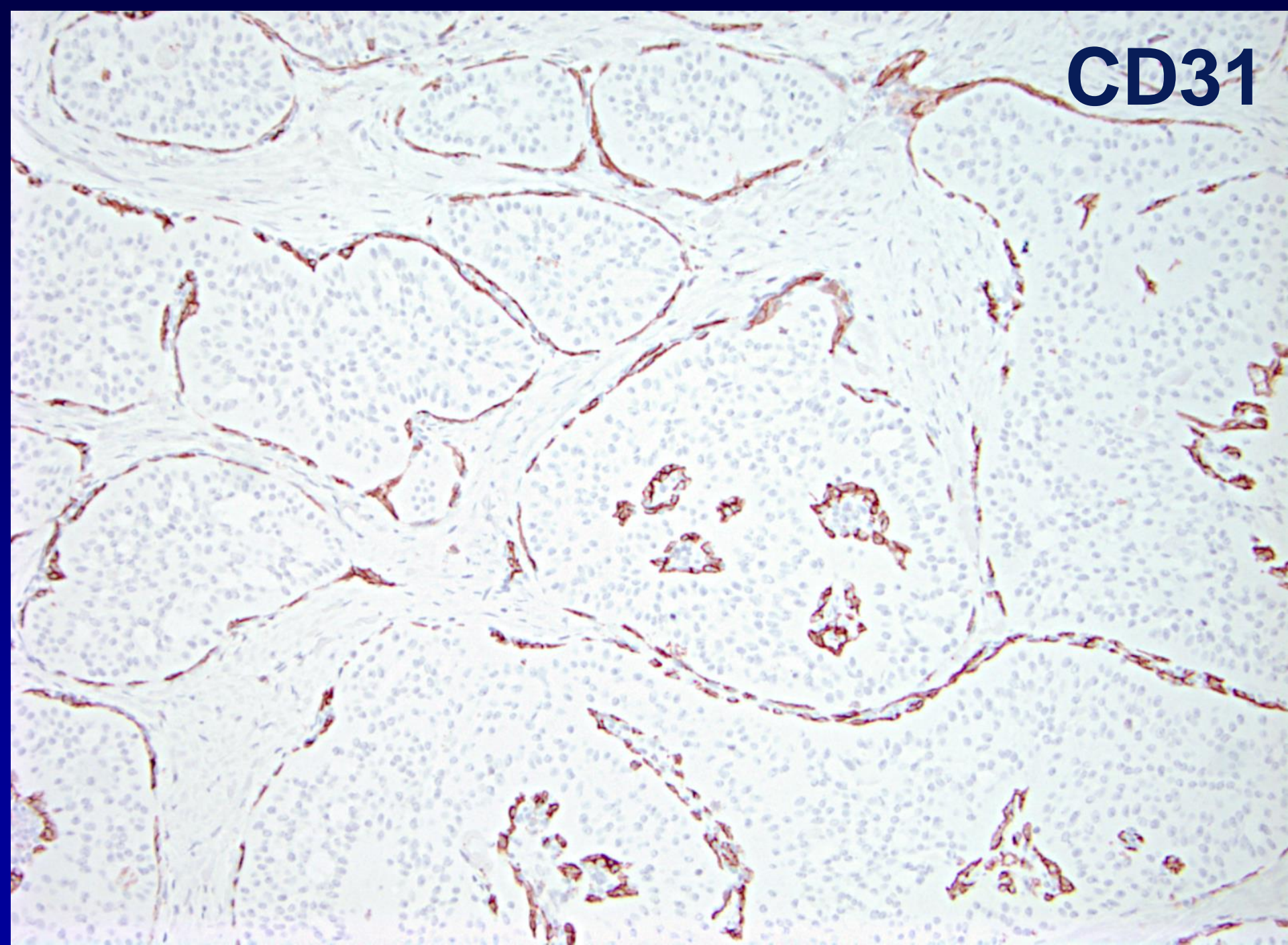
ER



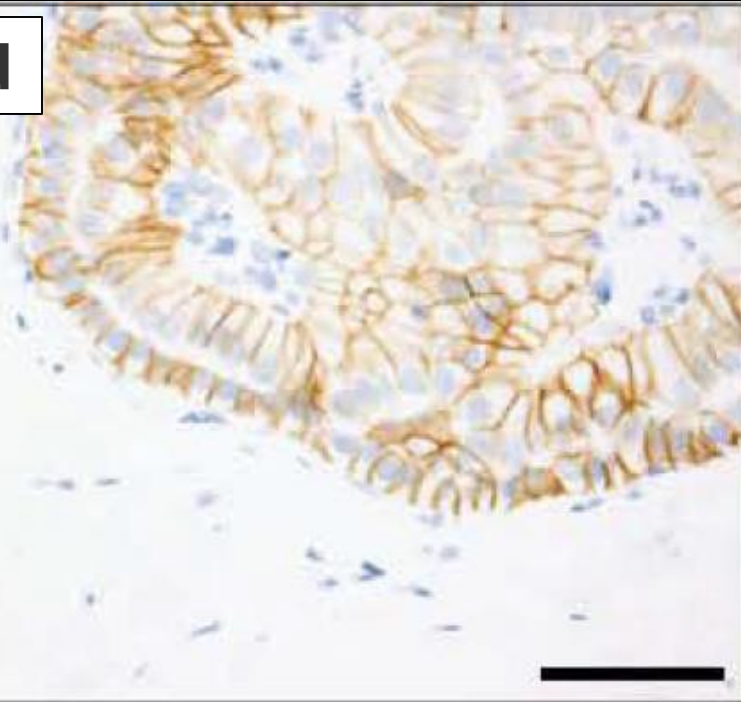
Ki67



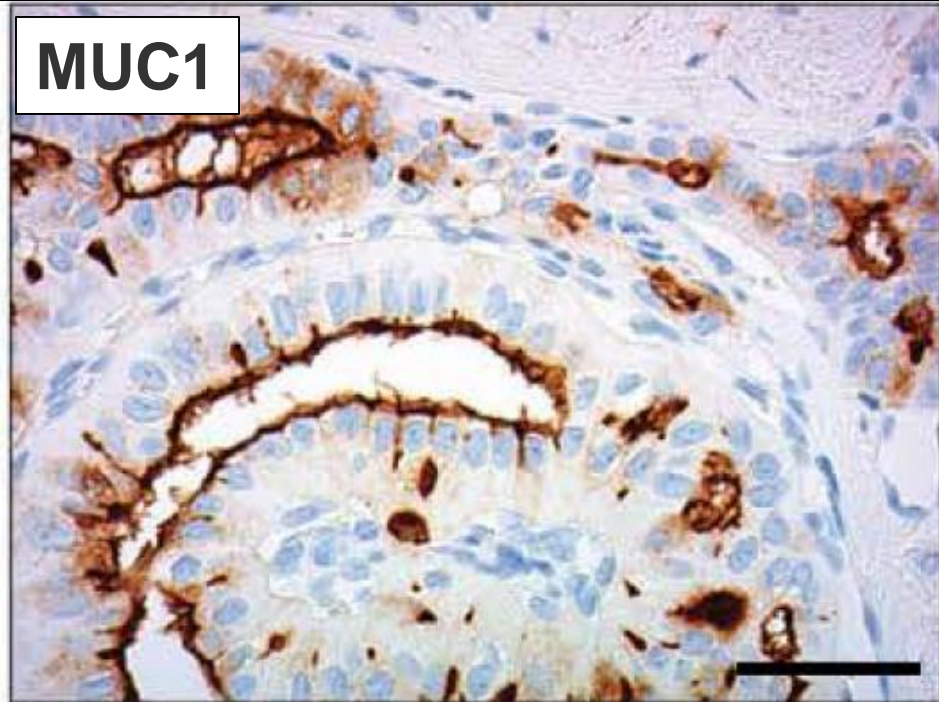
CD31



E-cad



MUC1



***IDH2* Mutations Define a Unique Subtype of Breast Cancer with Altered Nuclear Polarity**

Sarah Chiang¹, Britta Weigelt¹, Huei-Chi Wen¹, Fresia Pareja¹, Ashwini Raghavendra¹, Luciano G. Martelotto¹, Kathleen A. Burke¹, Thais Basili¹, Anqi Li¹, Felipe C. Geyer¹, Salvatore Piscuoglio¹, Charlotte K.Y. Ng¹, Achim A. Jungbluth¹, Jörg Balss², Stefan Pusch², Gabrielle M. Baker³, Kimberly S. Cole⁴, Andreas von Deimling^{2,5}, Julie M. Batten⁶, Jonathan D. Marotti⁷, Hwei-Choo Soh⁸, Benjamin L. McCalip⁹, Jonathan Serrano¹⁰, Raymond S. Lim¹, Kalliopi P. Siziopikou¹¹, Song Lu¹², Xiaolong Liu¹³, Tarek Hammour¹⁴, Edi Brogi¹, Matija Snuderl¹⁰, A. John Iafrate^{6,15}, Jorge S. Reis-Filho¹, and Stuart J. Schnitt^{15,16}

- ***IDH2* (R172) hotspot mutations in 10/13 cases (77%)**
 - Not previously reported in breast cancers
- **8 concurrently displayed mutations in PI3 kinase pathway (*PIK3CA* or *PIK3R1*)**
- **Functional studies**
 - ***IDH2* and *PIK3CA* mutations appear to be driver alterations resulting in reverse polarization phenotype**

***IDH2* (R172) Hotspot Mutations in Solid Papillary Carcinoma with Reverse Polarity**

- 30 cases studied to date (including our 13 original cases)
- *IDH2* (R172) hotspot mutations in 24 (80%)
- 7/9 cases studied expressed IDH1/2 mutant protein by IHC (Alsadoun, 2018)
 - ?alternative to sequencing to identify IDH2 mutation

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Clinical course

- **Indolent**
- **4 cases with axillary LN metastases**
- **1 case with distant metastases to bone**

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

Summary of unusual features

- **Histologically low grade, but**
 - ER negative (most triple negative)
 - Express high molecular weight cytokeratins
- **Reverse nuclear polarity**
- ***IDH2* (R172) hotspot mutations**
 - Not reported in any other breast cancers

Solid Papillary Carcinoma with Reverse Polarity (SPCRP)

- **Another special type breast cancer with a recurrent genetic alteration**
 - **Adenoid cystic carcinoma**
 - **Secretory carcinoma**