# Inquadramento anatomo-patologico

Prof. Giovanni Lanza

Il percorso del paziente con neoplasia neuroendocrina nella provincia di Ferrara

Società Medico Chirurgica

Cona – Ferrara, 12 ottobre 2019

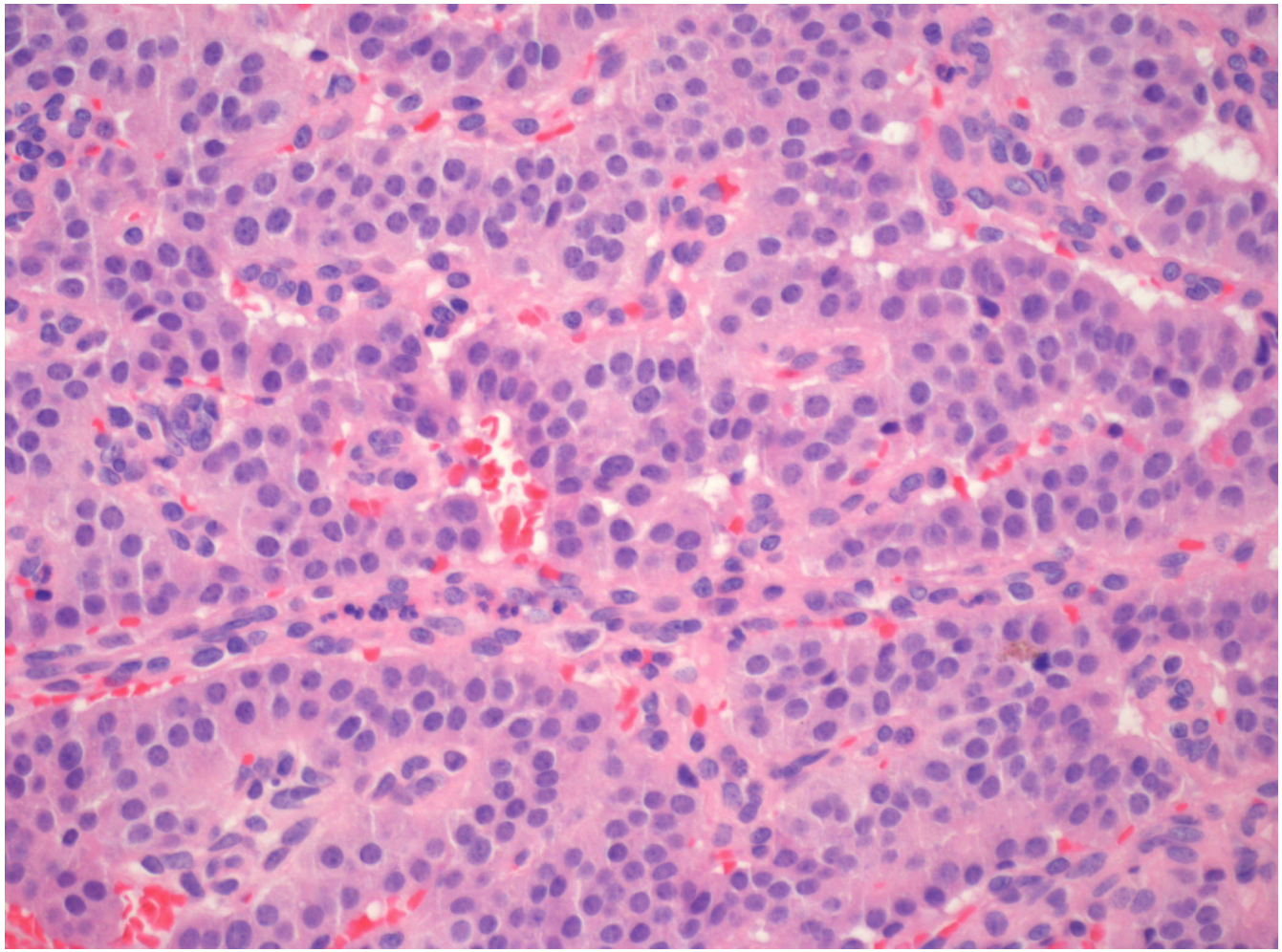
# Neoplasie neuroendocrine

Gruppo di tumori eterogeneo per numerose caratteristiche:

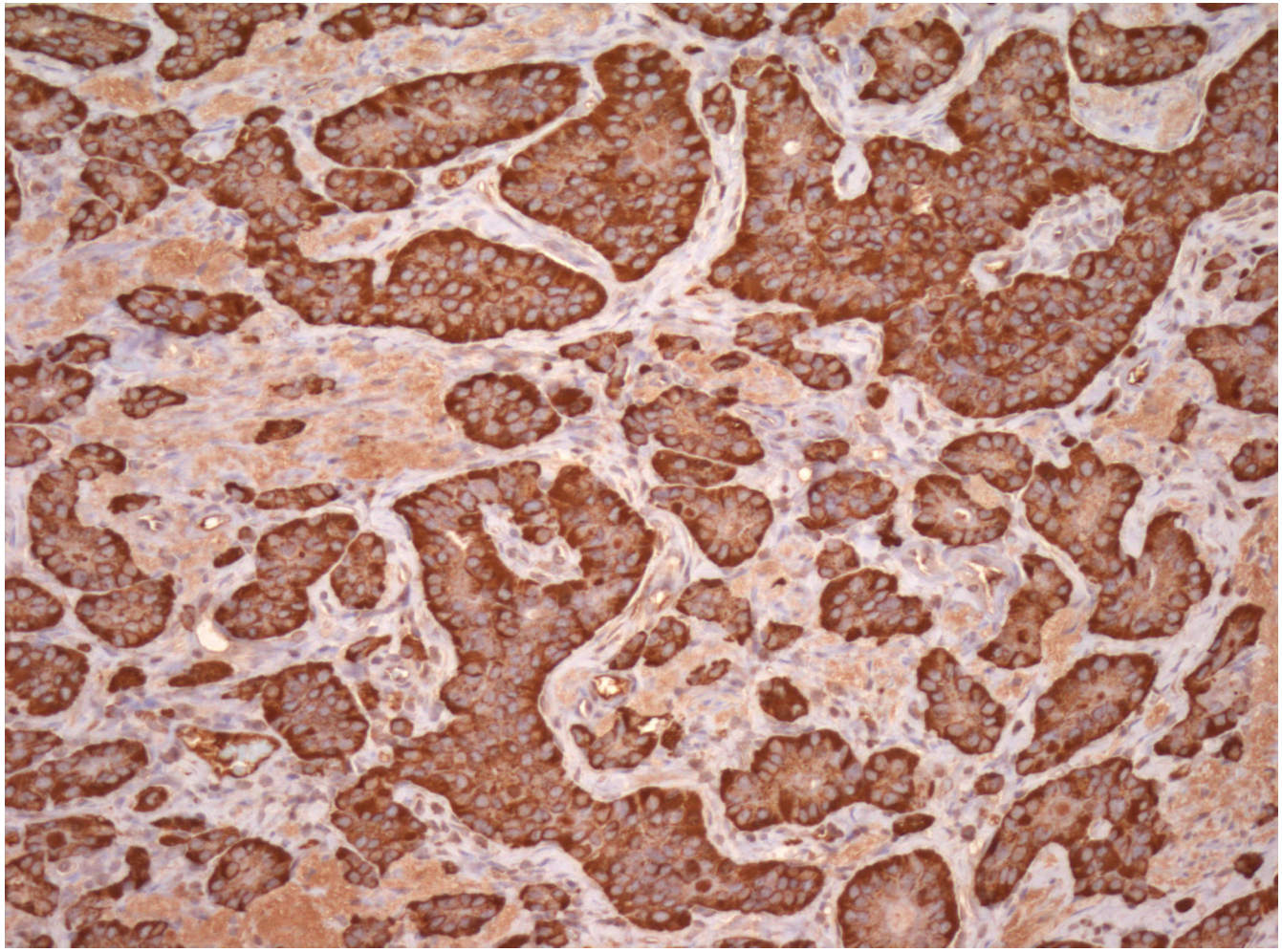
- Origine
- Modalità di sviluppo
- Stato funzionale
- Aspetto istologico
- Comportamento biologico e clinico

# Neoplasie neuroendocrine
# Ruolo del patologo

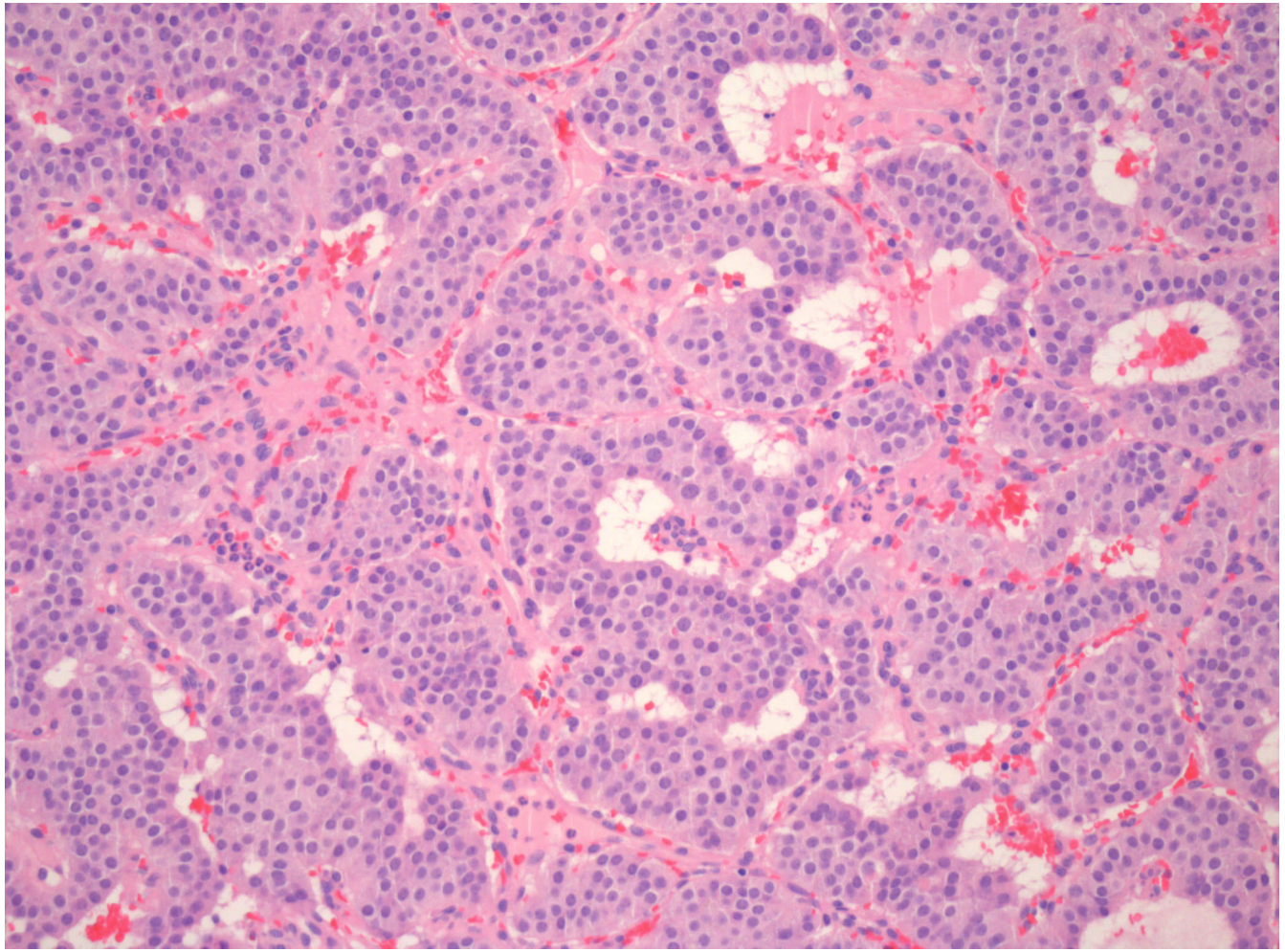
- Diagnosi
  - Tumore primitivo e metastasi
- Grading
- Staging (TNM)
- Valutare la presenza di altre alterazioni patologiche rilevanti
- Marcatori biomolecolari prognostici e predittivi



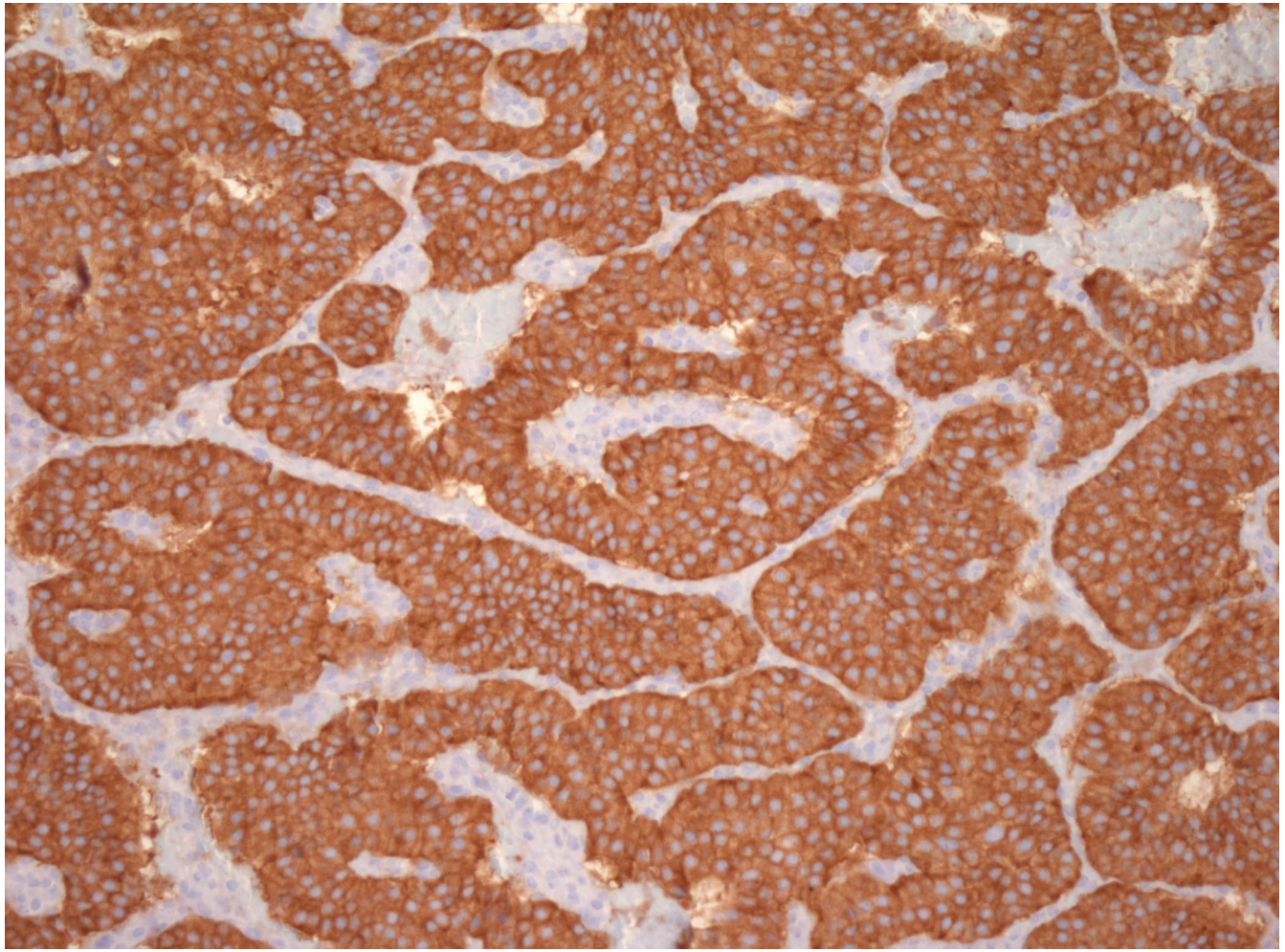
**Tumore neuroendocrino (NET)**



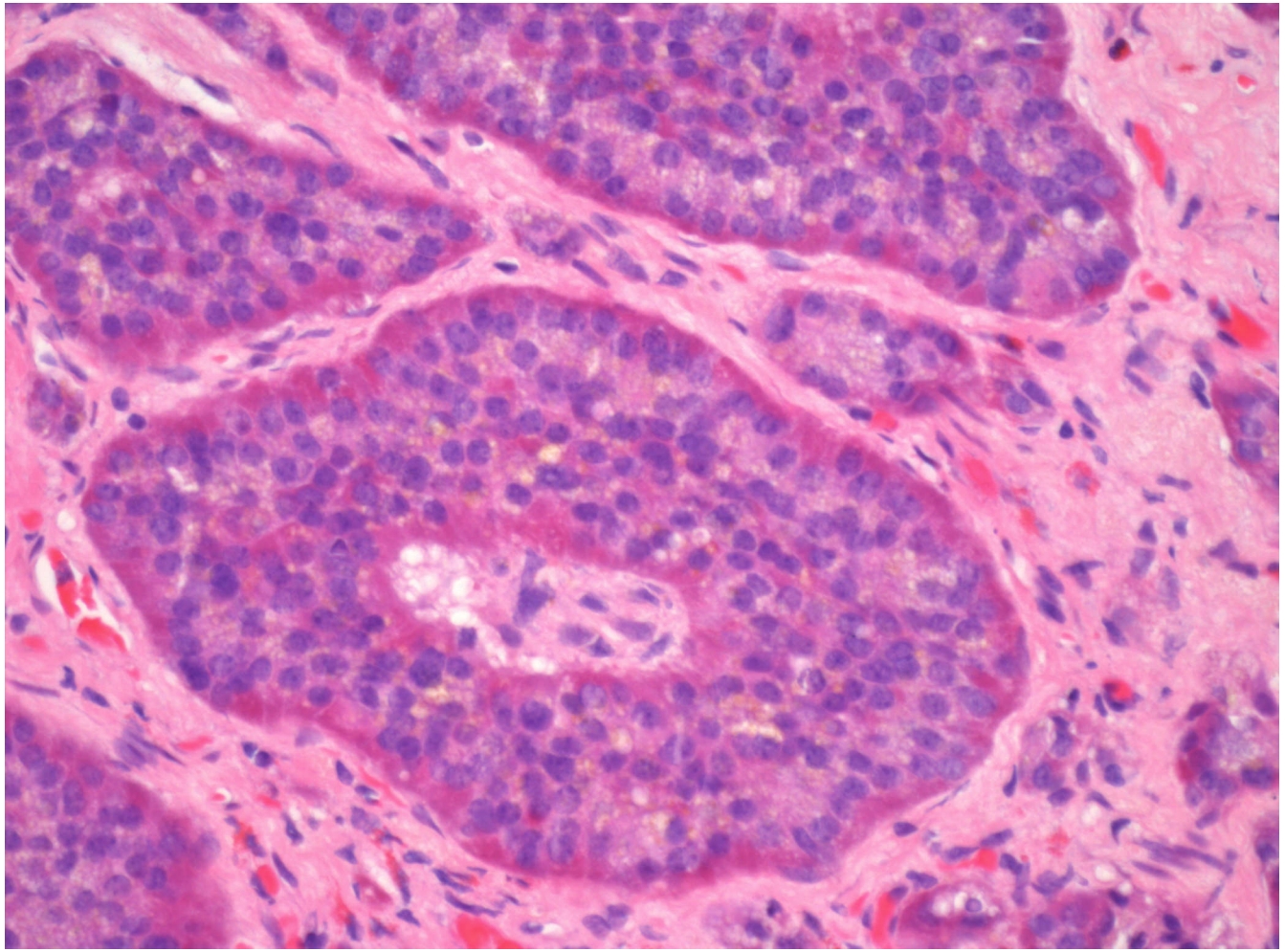
**Tumore neuroendocrino (NET) - cromogranina**



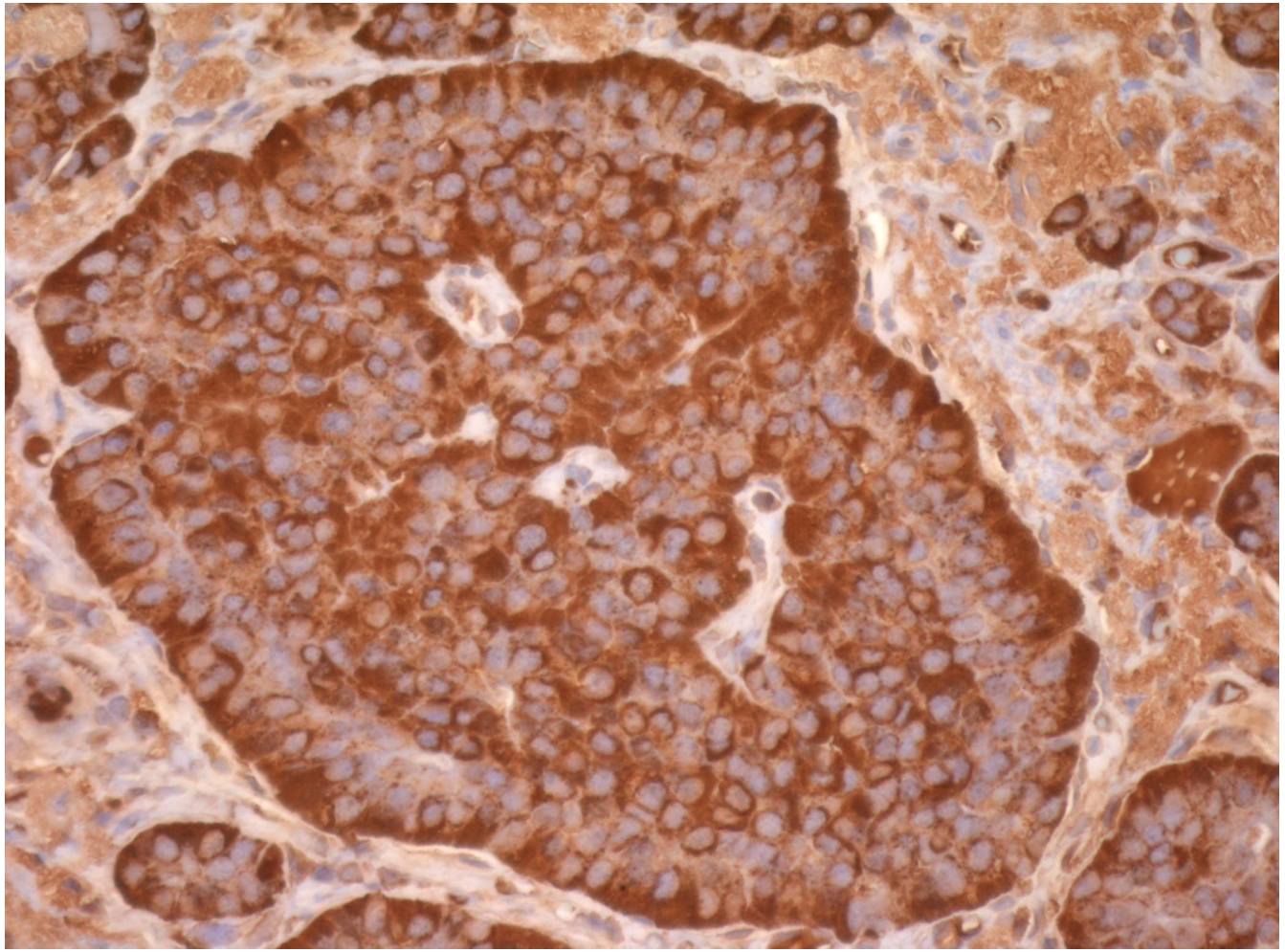
**Tumore neuroendocrino (NET)**



**Tumore neuroendocrino (NET) - sinaptofisina**



**Tumore neuroendocrino (NET) dell’ileo**



**Tumore neuroendocrino (NET) dell’ileo - cromogranina**

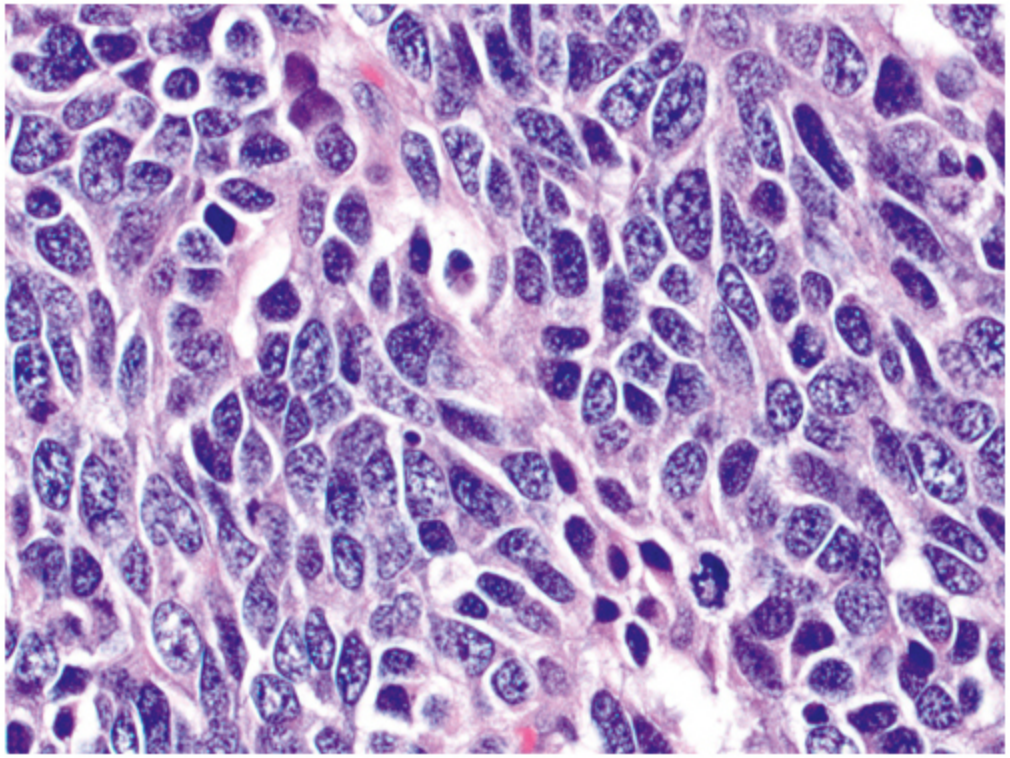


**FIGURE 29.21** A poorly differentiated, small cell–type neuroendocrine carcinoma in the gallbladder.

# Ulteriori informazioni patologiche - sede

- La determinazione della sede del tumore primitivo può essere di rilevanza clinica
- Esistono diversi marcatori anche se non completamente specifici
  - **TTF1**: neoplasie neuroendocrine polmonari
  - **CDX2**: neoplasie neuroendocrine intestinali

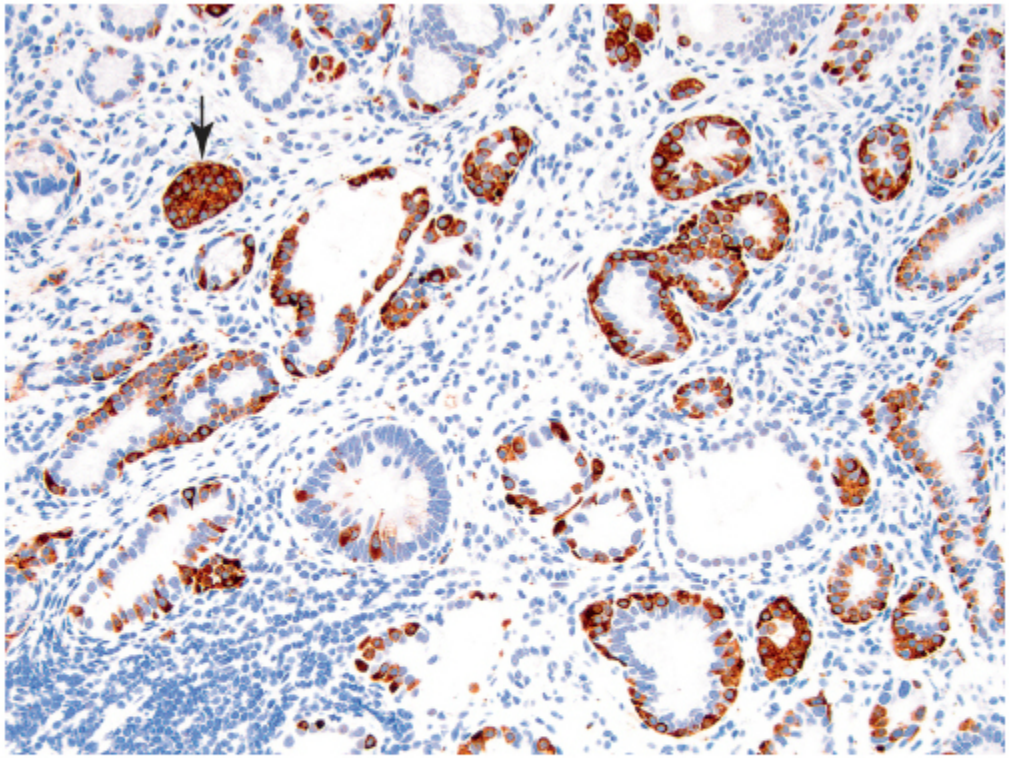


**FIGURE 29.1** Incipient neuroendocrine tumor in the setting of autoimmune gastritis. Linear and micronodular (*arrow*) enterochromaffin-like (ECL) cell hyperplasia, highlighted by chromogranin immunohistochemical stain, is common in the setting of secondary hypergastrinemia caused by autoimmune gastritis. These lesions are regarded as precursors of type A gastric neuroendocrine tumors.

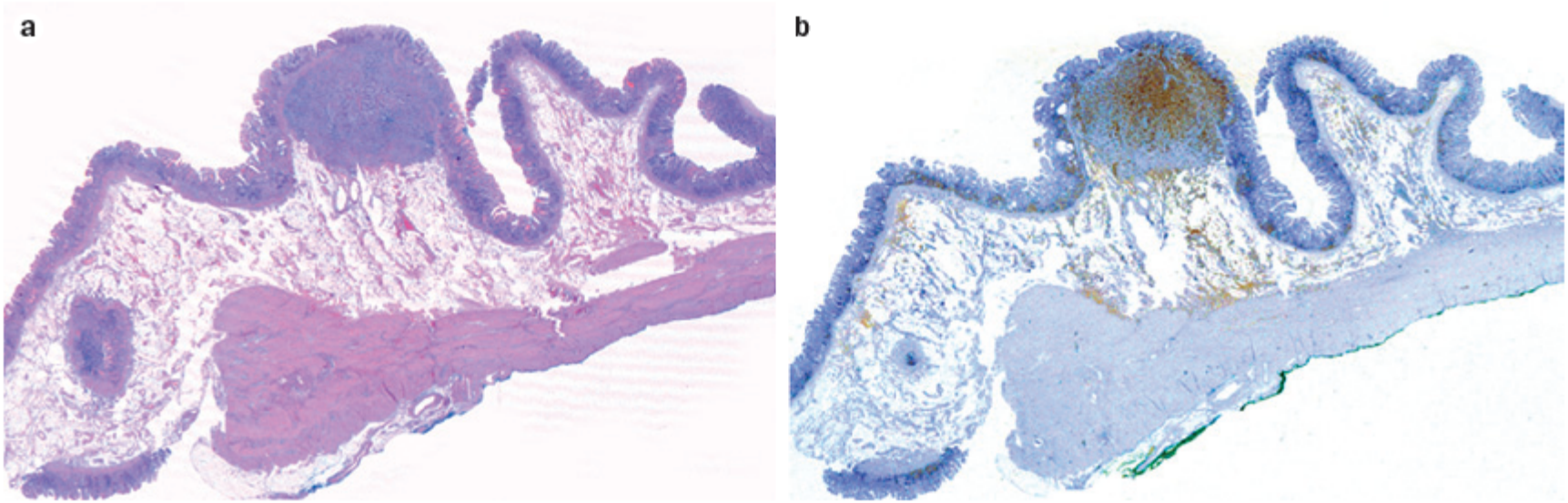



**Figure 6** | A small neuroendocrine tumour (carcinoid) in the stomach of a patient with autoimmune atrophic gastritis. The tumour is circumscribed, and although it expands into the submucosa, the growth pattern is not infiltrative. **a** | Staining with hematoxylin and eosin. **b** | Staining with anti-chromogranin antibodies.

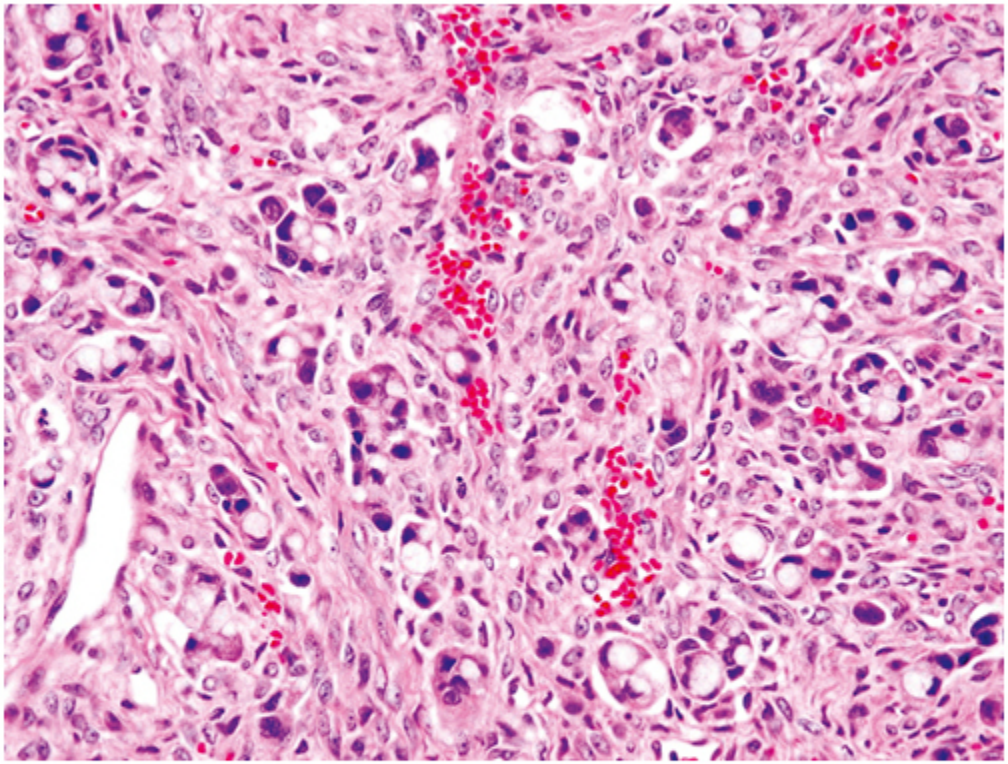


**FIGURE 29.26** All high-grade (dedifferentiated) goblet cell carcinoids (i.e., adenocarcinoma ex–goblet cell carcinoid) reveal at least some foci of the conventional goblet cell carcinoid pattern, but they also may display high-grade features and mixed patterns, as shown in this example by marked cytologic atypia, irregularity of the glandlike structures, and few cordlike and individual cells.

# *Classificazione WHO 2010*

## *Neoplasie neuroendocrine apparato digerente*

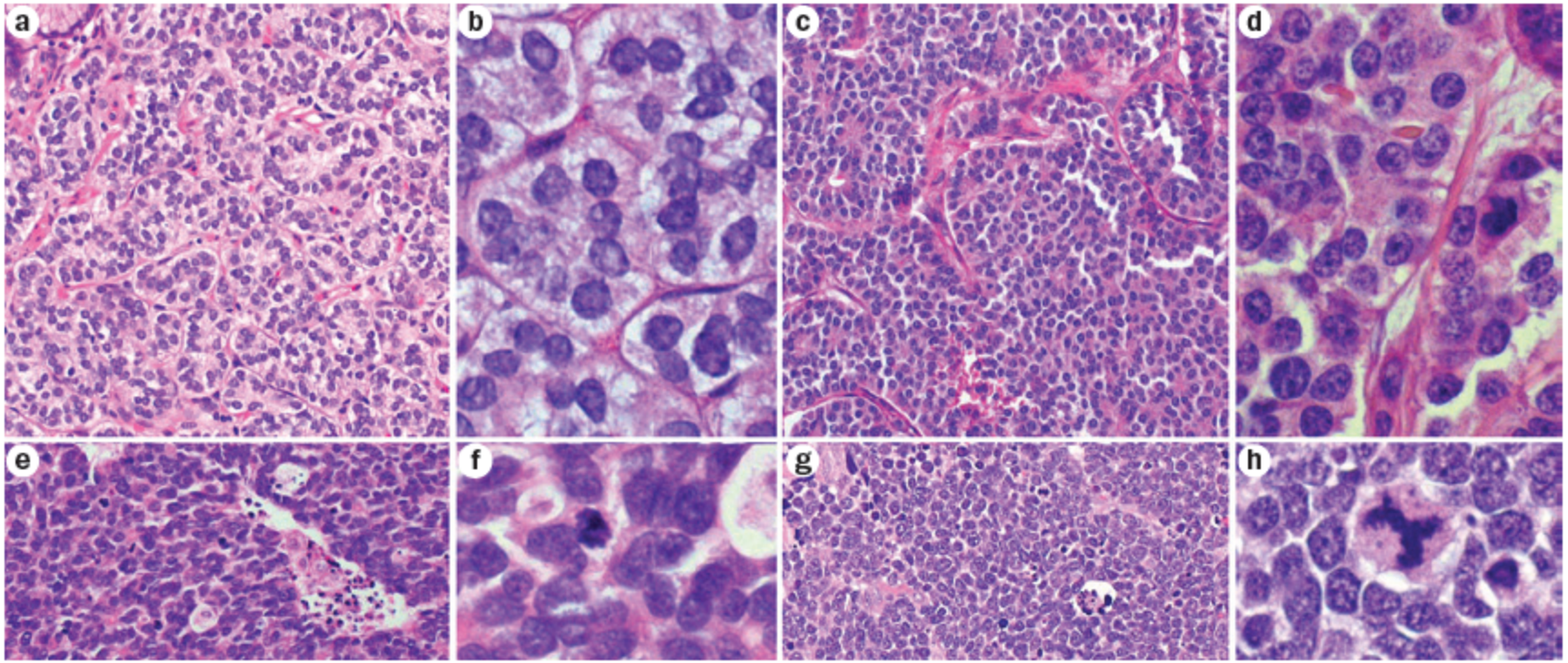
| | Grado | Mitosi (X 10 HPF) | Ki-67 index (%) |
|---|---|---|---|
| NET<br>Tumore neuroendocrino | G1 | < 2 | <= 2 |
| NET<br>Tumore neuroendocrino | G2 | 2 - 20 | 3 - 20 |
| NEC<br>Carcinoma neuroendocrino a piccole o a grandi cellule | G3 | > 20 | > 20 |

*Classificazione WHO 2010*

# *NET*

## Grado 1

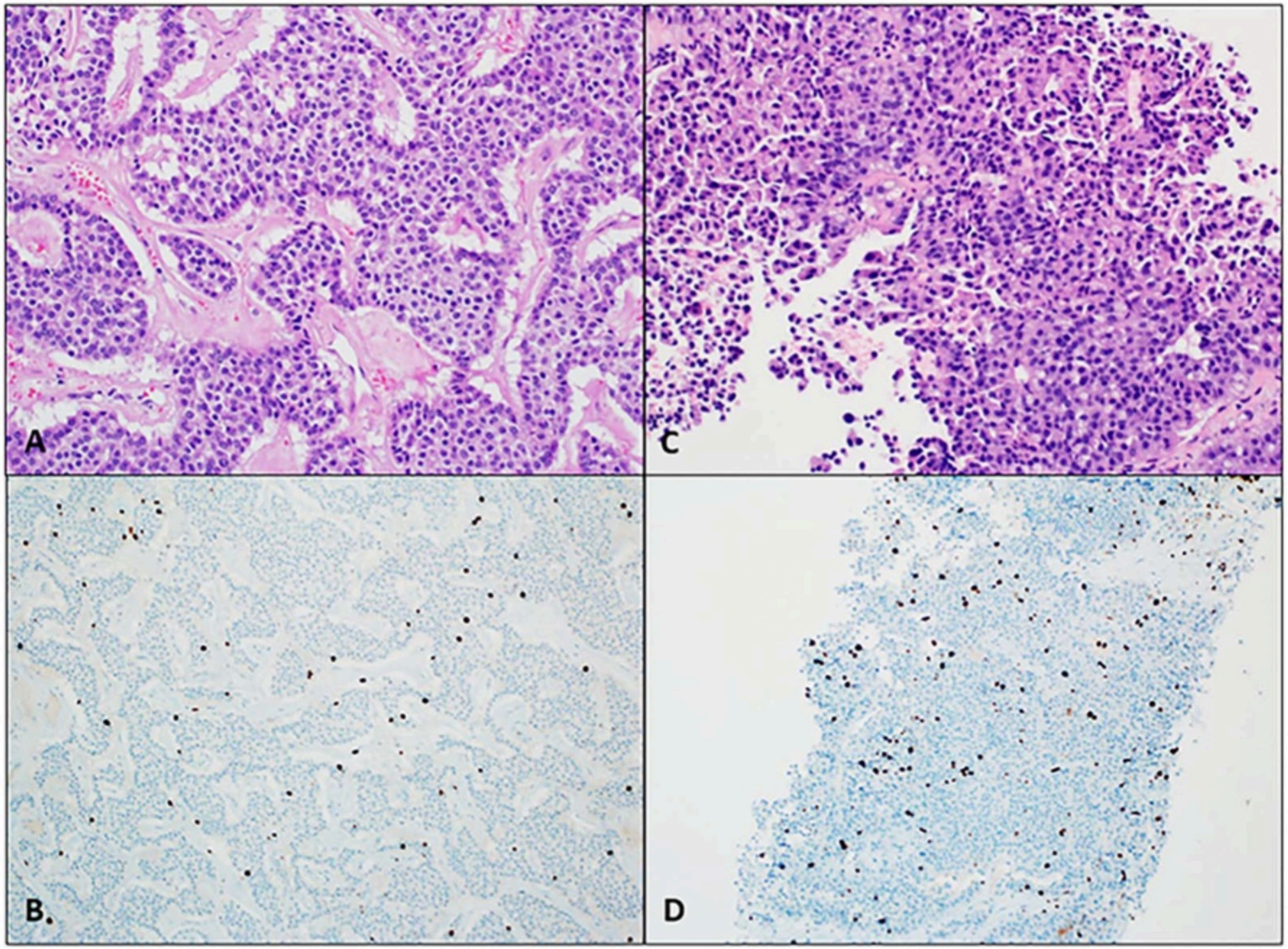
## Grado 2




**Grandi cellule**

**Piccole cellule**

## Grado 3 - NEC




PanNET G1

PanNET G2

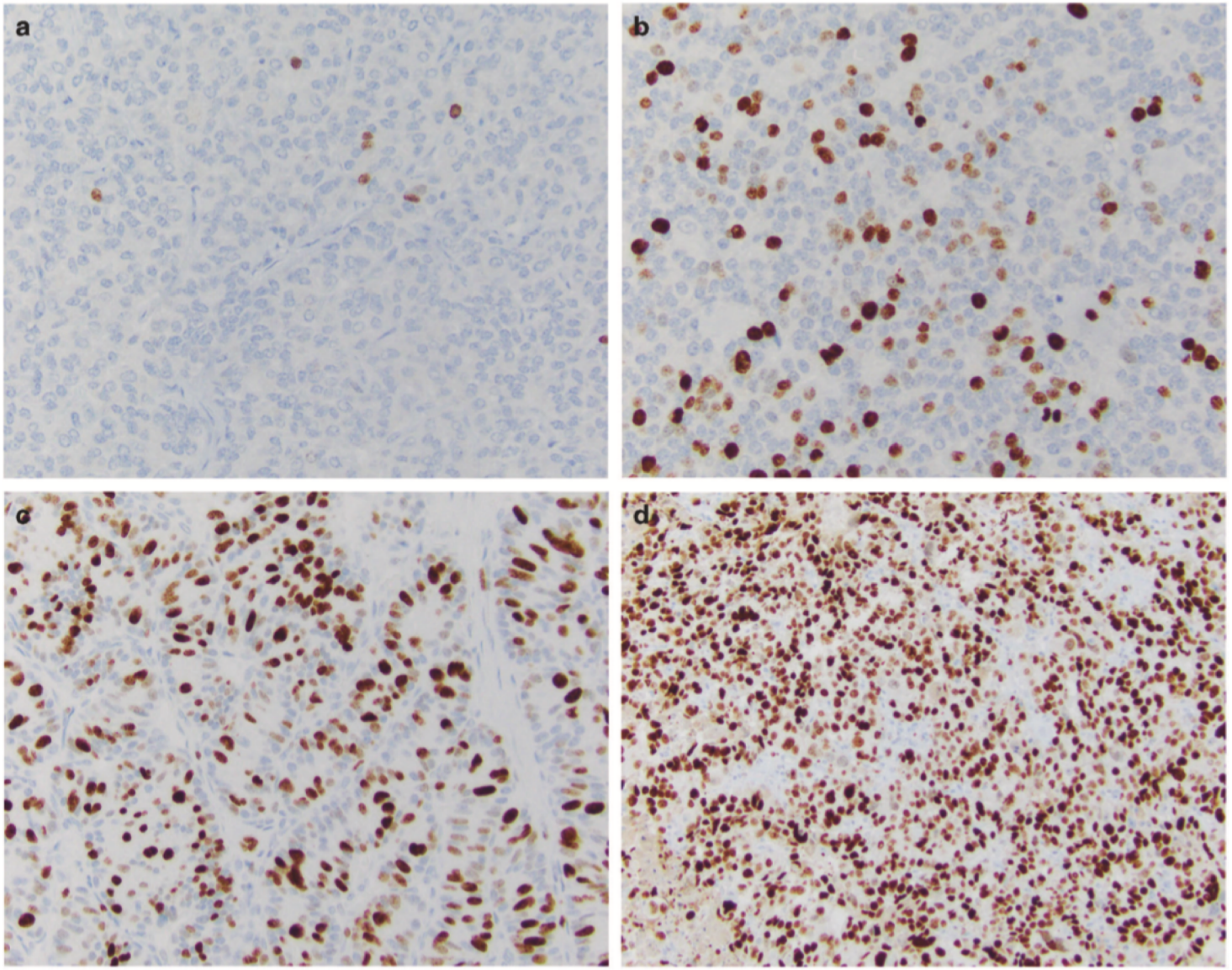



**Fig. 2** Ki-67 staining of NEN from different sites: **a** a grade 1 NET from the ileum, **b** a grade 2 NET from the lung (atypical carcinoid), **c** a grade 3 NET from the pancreas, and **d** a NEC (SCLC) from the lung

# Classificazione WHO 2015
# Tumori neuroendocrini del polmone

- Carcinoide tipico
  - < 2 mitosi per mm quadrato, assenza di necrosi, diametro >= 0,5 cm* (sopravvivenza a 5 anni 90%)
- Carcinoide atipico
  - 2-10 mitosi per mm quadrato e/o necrosi (sopravvivenza a 5 anni 60%)
- Carcinoma a piccole cellule
- Carcinoma neuroendocrino a grandi cellule
- * Proliferazioni nodulari neuroendocrine < 0,5 cm sono classificate come tumourlet

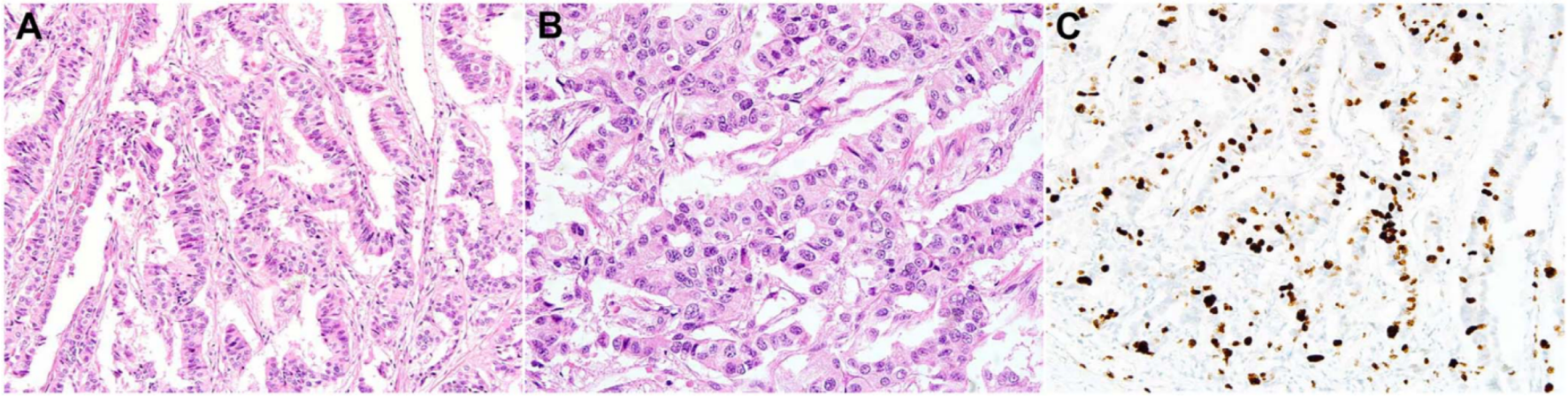



**Fig. 3.** Well differentiated G3 neuroendocrine tumor maintains organoid and trabecular pattern (A) with a mitotic count 2-20/10 high power fields (B) and a Ki-67 labeling index > 20% (C).

# 2017 WHO classification and grading of pancreatic neuroendocrine neoplasms (PanNENs)

| Classification/grade | Ki-67 index | Mitotic index |
|---|---|---|
| **Well-differentiated PanNENs (PanNETs)** | | |
| PanNET G1 | < 3% | < 2 |
| PanNET G2 | 3-20% | 2-20 |
| PanNET G3 | > 20% | > 20 |
| **Poorly differentiated PanNENs (PanNECs)** | | |
| PanNEC (G3)<br>Small cell type<br>Large cell type | > 20% | > 20 |
| **Mixed neuroendocrine-non-neuroendocrine neoplasms** | | |

# 2019 WHO Classification and grading criteria for neuroendocrine neoplasms of the digestive system

| Terminology/Differentiation/Grade | Ki-67 index | Mitotic rate (mitoses/2 mmq) |
|---|---|---|
| **Neuroendocrine tumour (NET)**<br>**Well differentiated** | | |
| NET G1 Low | < 3% | < 2 |
| NET G2 Intermediate | 3-20% | 2-20 |
| NET G3 High | > 20% | > 20 |
| **Neuroendocrine carcinoma (NEC)**<br>**Poorly differentiated** | | |
| NEC, small cell type (SCNEC) High<br>NEC, large cell type (LCNEC) High | > 20% | > 20 |
| **Mixed neuroendocrine-non-neuroendocrine neoplasm**<br>Well or poorly differentiated | Variable | Variable |

Histopathology

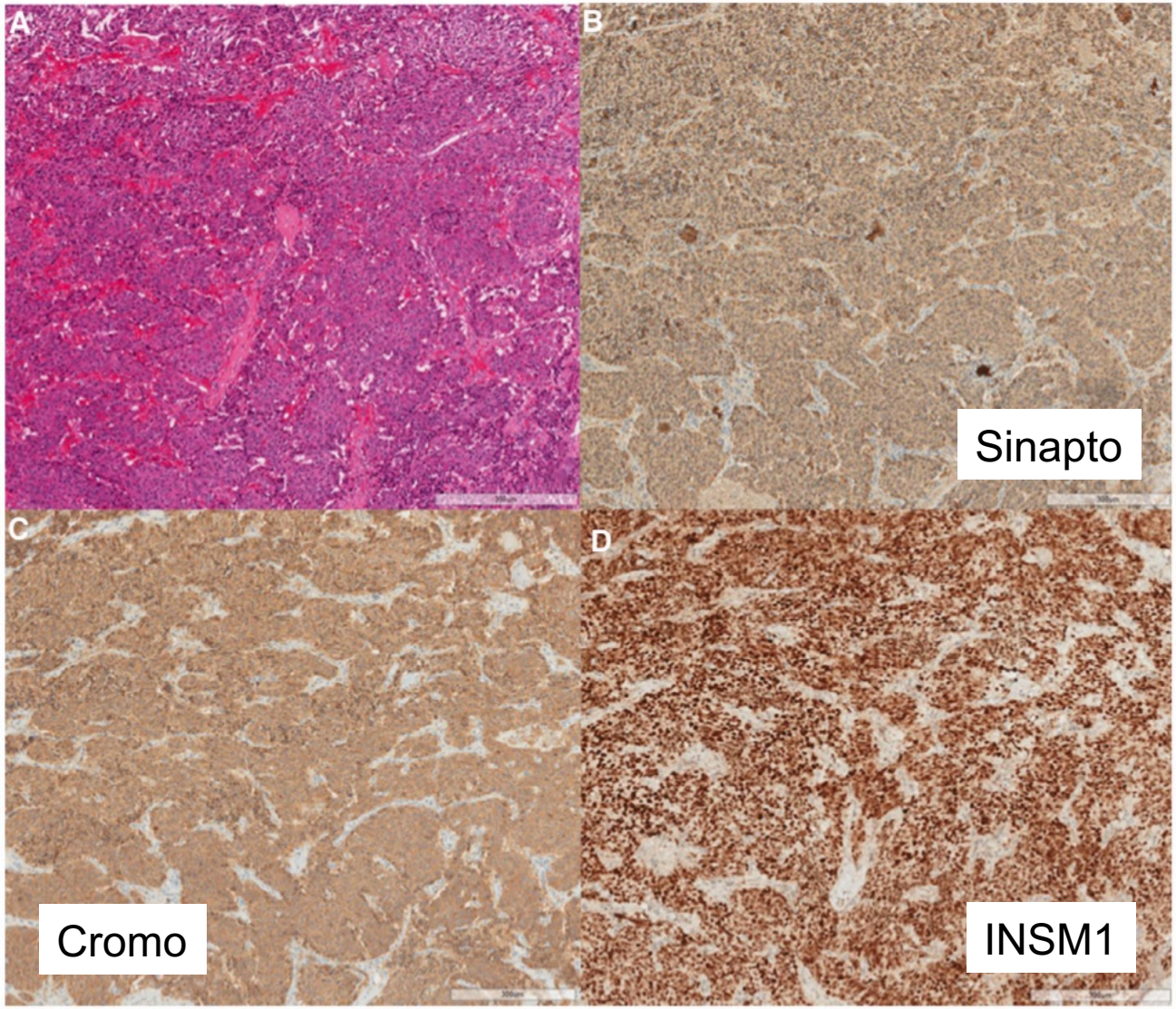
*Histopathology* 2019, **75**, 568–577. DOI: 10.1111/his.13899

# Insulinoma-associated protein 1 expression in primary and metastatic neuroendocrine neoplasms of the gastrointestinal and pancreaticobiliary tracts

Iván González,[1] Hsiang-Chih Lu,[1] Jared Sninsky,[2] Chen Yang,[1,†] Kumar Bishnupuri,[3] Brian Dieckgraefe,[3] Dengfeng Cao[1] & Deyali Chatterjee[1]

[1]*Department of Pathology and Immunology,* [2]*Department of Medicine, and* [3]*Division of Gastroenterology, Washington University School of Medicine, Saint Louis, MO, USA*

*Conclusions*: The nuclear reactivity and the high sensitivity and specificity of INSM1 make it a preferred neuroendocrine marker. In conclusion, INSM1 can be used as a single first-line marker for primary and metastatic GEP-NEN.


A
B
Sinapto
C
Cromo
D
INSM1

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ORIGINAL ARTICLE

# Whole-genome sequencing reveals distinct genetic bases for insulinomas and non-functional pancreatic neuroendocrine tumours: leading to a new classification system

Xiafei Hong,[1] Sitan Qiao,[2,3] Fuqiang Li,[2,3] Wenze Wang,[4] Rui Jiang,[1] Huanwen Wu,[4] Hao Chen,[1] Lulu Liu,[5] Junya Peng,[5] Jing Wang,[4] Congwei Jia,[4] Xiaolong Liang,[4] Hongmei Dai,[1] Jialin Jiang,[1] Taiping Zhang,[1] Quan Liao,[1] Menghua Dai,[1] Lin Cong,[1] Xianlin Han,[1] Dan Guo,[5,6] Zhiyong Liang,[4] Dongjing Li,[7] Zetian Zheng,[2,3] Chen Ye,[2,3] Siliang Li,[2,3] Yupei Zhao,[1,8] Kui Wu,[2,3] Wenming Wu[1]