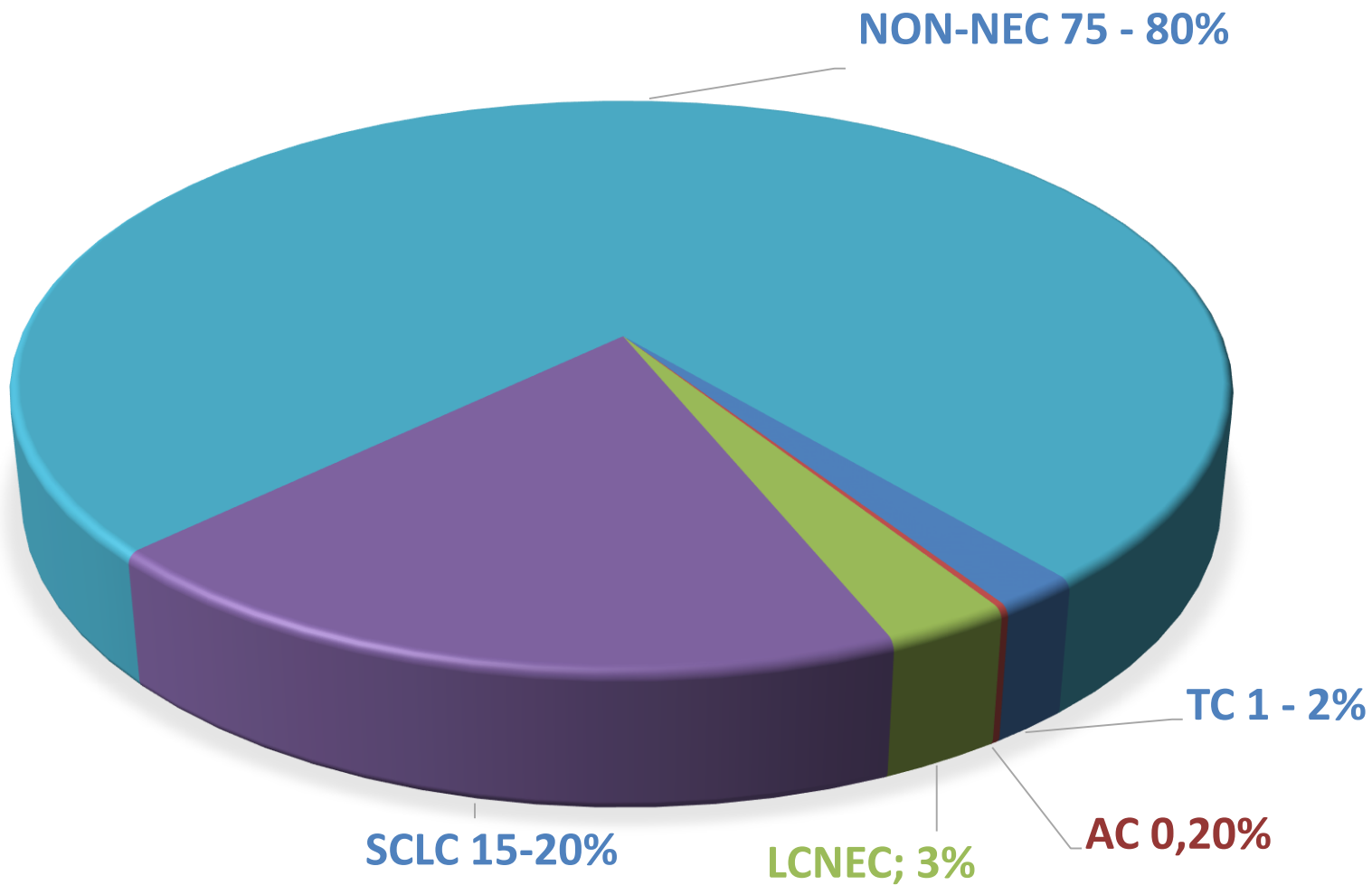




# **Современная классификация нейроэндокринных опухолей легкого.**

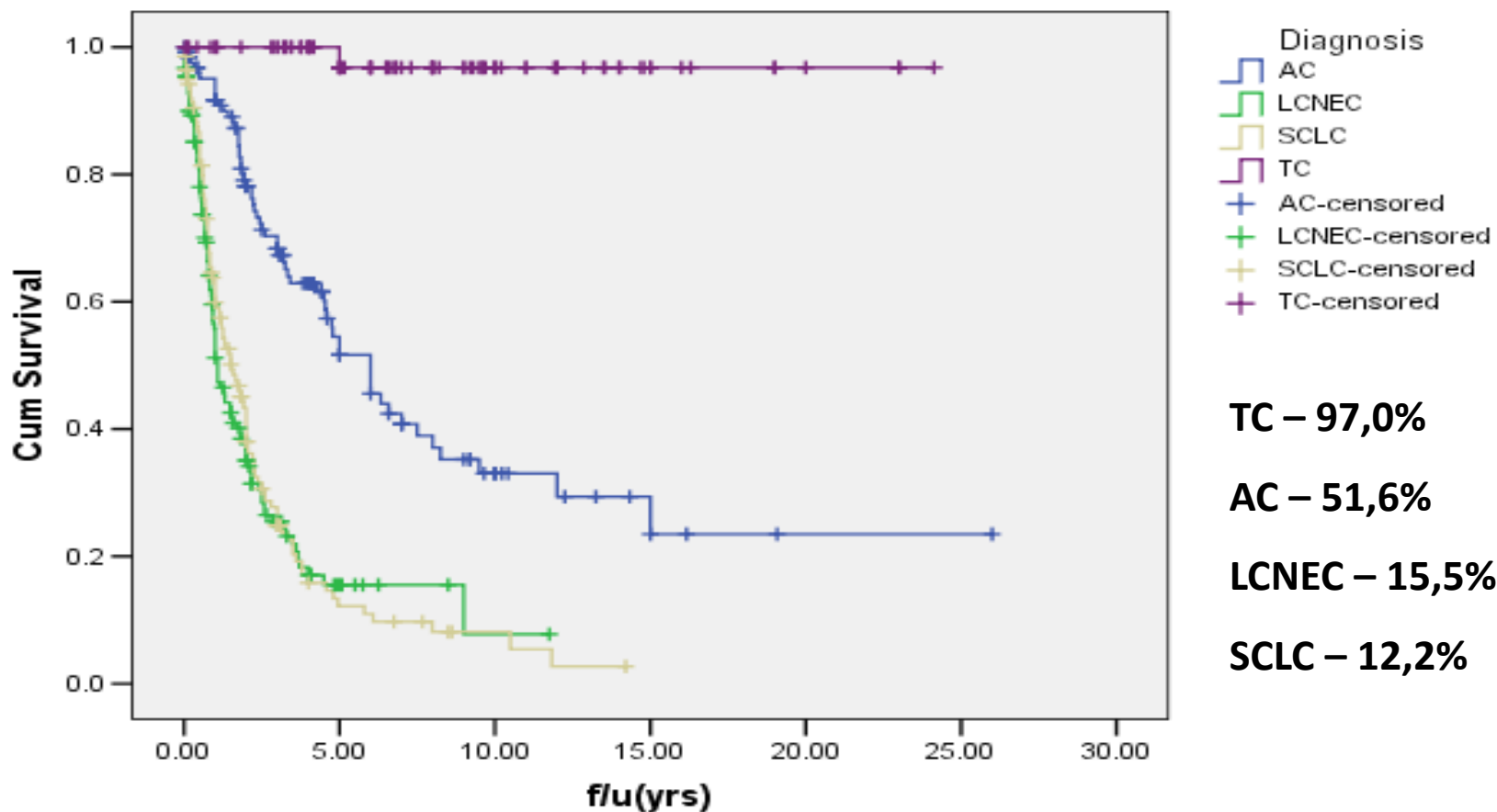


**Нейроэндокринные опухоли легкого** – это группа опухолей со схожей морфологией, ультраструктурными, иммуногистохимическими и молекулярными характеристиками.





## Survival Functions

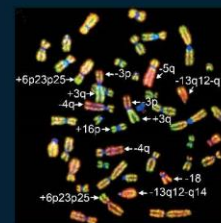
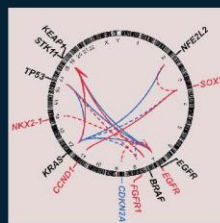
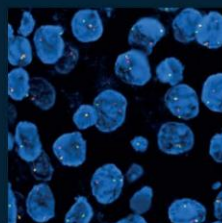
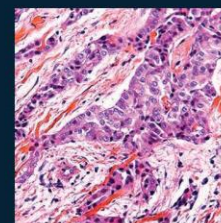
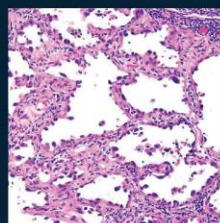
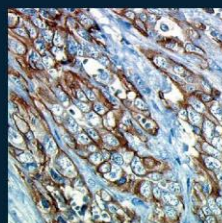
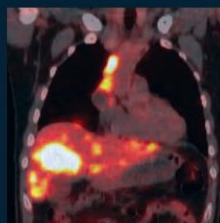




# WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart

Edited by

William D. Travis, Elisabeth Brambilla, Allen P. Burke, Alexander Marx, Andrew G. Nicholson





**TABLE 1. 2015 WHO Classification of Lung Tumors<sup>a,b,c</sup>**

| Histologic Type and Subtypes                                 | ICDO Code           |
|--|---------------------|
| <b>Epithelial tumors</b>                                     |                     |
| Adenocarcinoma   | 8140/3              |
| Lepidic adenocarcinoma <sup>a</sup>                          | 8250/3 <sup>d</sup> |
| Acinar adenocarcinoma  | 8551/3 <sup>d</sup> |
| Papillary adenocarcinoma                                     | 8260/3              |
| Micropapillary adenocarcinoma <sup>a</sup>                   | 8265/3              |
| Solid adenocarcinoma   | 8230/3              |
| Invasive mucinous adenocarcinoma <sup>a</sup>                | 8253/3 <sup>d</sup> |
| Mixed invasive mucinous and nonmucinous adenocarcinoma       | 8254/3 <sup>d</sup> |
| Colloid adenocarcinoma                                       | 8480/3              |
| Fetal adenocarcinoma   | 8333/3              |
| Enteric adenocarcinoma <sup>a</sup>                          | 8144/3              |
| Minimally invasive adenocarcinoma <sup>a</sup>               |                     |
| Nonmucinous  | 8256/3 <sup>d</sup> |
| Mucinous   | 8257/3 <sup>d</sup> |
| Preinvasive lesions  |                     |
| Atypical adenomatous hyperplasia                             | 8250/0 <sup>d</sup> |
| Adenocarcinoma in situ <sup>a</sup>                          |                     |
| Nonmucinous  | 8250/2 <sup>d</sup> |
| Mucinous   | 8253/2 <sup>d</sup> |
| Squamous cell carcinoma                                      | 8070/3              |
| Keratinizing squamous cell carcinoma <sup>a</sup>            | 8071/3              |
| Nonkeratinizing squamous cell carcinoma <sup>a</sup>         | 8072/3              |
| Basaloid squamous cell carcinoma <sup>a</sup>                | 8083/3              |
| Preinvasive lesion   |                     |
| Squamous cell carcinoma in situ                              | 8070/2              |
| <b>Neuroendocrine tumors</b>                                 |                     |
| Small cell carcinoma   | 8041/3              |
| Combined small cell carcinoma                                | 8045/3              |
| Large cell neuroendocrine carcinoma                          | 8013/3              |
| Combined large cell neuroendocrine carcinoma                 | 8013/3              |
| <b>Carcinoid tumors</b>                                      |                     |
| Typical carcinoid tumor                                      | 8240/3              |
| Atypical carcinoid tumor                                     | 8249/3              |
| Preinvasive lesion   |                     |
| Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia | 8040/0 <sup>d</sup> |
| Large cell carcinoma   | 8072/3              |
| Adenosquamous carcinoma                                      | 8560/3              |
| <b>Sarcomatoid carcinomas</b>                                |                     |
| Pleomorphic carcinoma  | 8022/3              |
| Spindle cell carcinoma                                       | 8032/3              |
| Giant cell carcinoma   | 8031/3              |
| Carcinosarcoma   | 8980/3              |
| Pulmonary blastoma   | 8972/3              |
| <b>Other and Unclassified carcinomas</b>                     |                     |
| Lymphoepithelioma-like carcinoma                             | 8082/3              |
| NUT carcinoma <sup>a</sup>                                   | 8023/3 <sup>d</sup> |
| <b>Salivary gland-type tumors</b>                            |                     |
| Mucoepidermoid carcinoma                                     | 8430/3              |
| Adenoid cystic carcinoma                                     | 8200/3              |
| Epithelial-myoepithelial carcinoma                           | 8562/3              |
| Pleomorphic adenoma  | 8940/0              |

(Continued)

**TABLE 1. (Continued)**

| Histologic Type and Subtypes  | ICDO Code           |
|---|---------------------|
| <b>Papillomas</b>   |                     |
| Squamous cell papilloma   | 8052/0              |
| Exophytic   | 8052/0              |
| Inverted  | 8053/0              |
| Glandular papilloma   | 8260/0              |
| Mixed squamous and glandular papilloma  | 8560/0              |
| <b>Adenomas</b>   |                     |
| Sclerosing pneumocytoma <sup>a</sup>  | 8832/0              |
| Alveolar adenoma  | 8251/0              |
| Papillary adenoma   | 8260/0              |
| Mucinous cystadenoma  | 8470/0              |
| Mucous gland adenoma  | 8480/0              |
| <b>Mesenchymal tumors</b>   |                     |
| Pulmonary hamartoma   | 8992/0 <sup>d</sup> |
| Chondroma   | 9220/0              |
| <b>PEComatous tumors<sup>a</sup></b>  |                     |
| Lymphangioliomyomatosis   | 9174/1              |
| PEComa, benign <sup>a</sup>   | 8714/0              |
| Clear cell tumor  | 8005/0              |
| PEComa, malignant <sup>a</sup>  | 8714/3              |
| Congenital peribronchial myofibroblastic tumor  | 8827/1              |
| Diffuse pulmonary lymphangiomatosis   |                     |
| Inflammatory myofibroblastic tumor  | 8825/1              |
| Epithelioid hemangioendothelioma  | 9133/3              |
| Pleuropulmonary blastoma  | 8973/3              |
| Synovial sarcoma  | 9040/3              |
| Pulmonary artery intimal sarcoma  | 9137/3              |
| Pulmonary myxoid sarcoma with <i>EWSRI-CREB1</i> translocation <sup>a</sup>             | 8842/3 <sup>d</sup> |
| <b>Myoepithelial tumors<sup>a</sup></b>   |                     |
| Myoepithelioma  | 8982/0              |
| Myoepithelial carcinoma   | 8982/3              |
| <b>Lymphohistiocytic tumors</b>   |                     |
| Extranodal marginal zone lymphomas of mucosa-associated lymphoid tissue (MALT lymphoma) | 9699/3              |
| Diffuse large cell lymphoma   | 9680/3              |
| Lymphomatoid granulomatosis   | 9766/1              |
| Intravascular large B cell lymphoma <sup>a</sup>  | 9712/3              |
| Pulmonary Langerhans cell histiocytosis   | 9751/1              |
| Erdheim-Chester disease   | 9750/1              |
| <b>Tumors of ectopic origin</b>   |                     |
| <b>Germ cell tumors</b>   |                     |
| Teratoma, mature  | 9080/0              |
| Teratoma, immature  | 9080/1              |
| Intrapulmonary thymoma  | 8580/3              |
| Melanoma  | 8270/3              |
| Meningioma, NOS   | 9530/0              |
| <b>Metastatic tumors</b>  |                     |

<sup>a</sup>The morphology codes are from the ICDO. Behavior is coded /0 for benign tumors, /1 for unspecified, borderline or uncertain behavior, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumors.

<sup>b</sup>The classification is modified from the previous WHO classification<sup>3</sup> taking into account changes in our understanding of these lesions.

<sup>c</sup>This table is reproduced from the 2015 WHO Classification by Travis et al.<sup>1</sup>

<sup>d</sup>These new codes were approved by the International Agency on Cancer Research/WHO Committee for ICDO.

<sup>e</sup>New terms changed or entities added since 2004 WHO Classification.<sup>3</sup>

LCNEC, large cell neuroendocrine carcinoma, WHO, World Health Organization; ICDO International Classification of Diseases for Oncology.



Basaloid squamous cell carcinoma<sup>a</sup> 8083/3

Preinvasive lesion

Squamous cell carcinoma in situ 8070/2

Neuroendocrine tumors

Small cell carcinoma 8041/3

Combined small cell carcinoma 8045/3

Large cell neuroendocrine carcinoma 8013/3

Combined large cell neuroendocrine carcinoma 8013/3

Carcinoid tumors

Typical carcinoid tumor 8240/3

Atypical carcinoid tumor 8249/3

Preinvasive lesion

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia 8040/0<sup>d</sup>

Large cell carcinoma 8012/3

Adenosquamous carcinoma 8560/3 1

Sarcomatoid carcinomas

Pleomorphic carcinoma 8022/3

Spindle cell carcinoma 8032/3

Giant cell carcinoma 8031/3



# WHO Classifications

**1967** - HE

**1981** - HE, Mucin

**1999** - HE, Mucin & IHC

**2004** - HE, Mucin, IHC & Genetics

**2015** - HE, Mucin, IHC, Genetics & Radiology





# 2004 WHO Classification

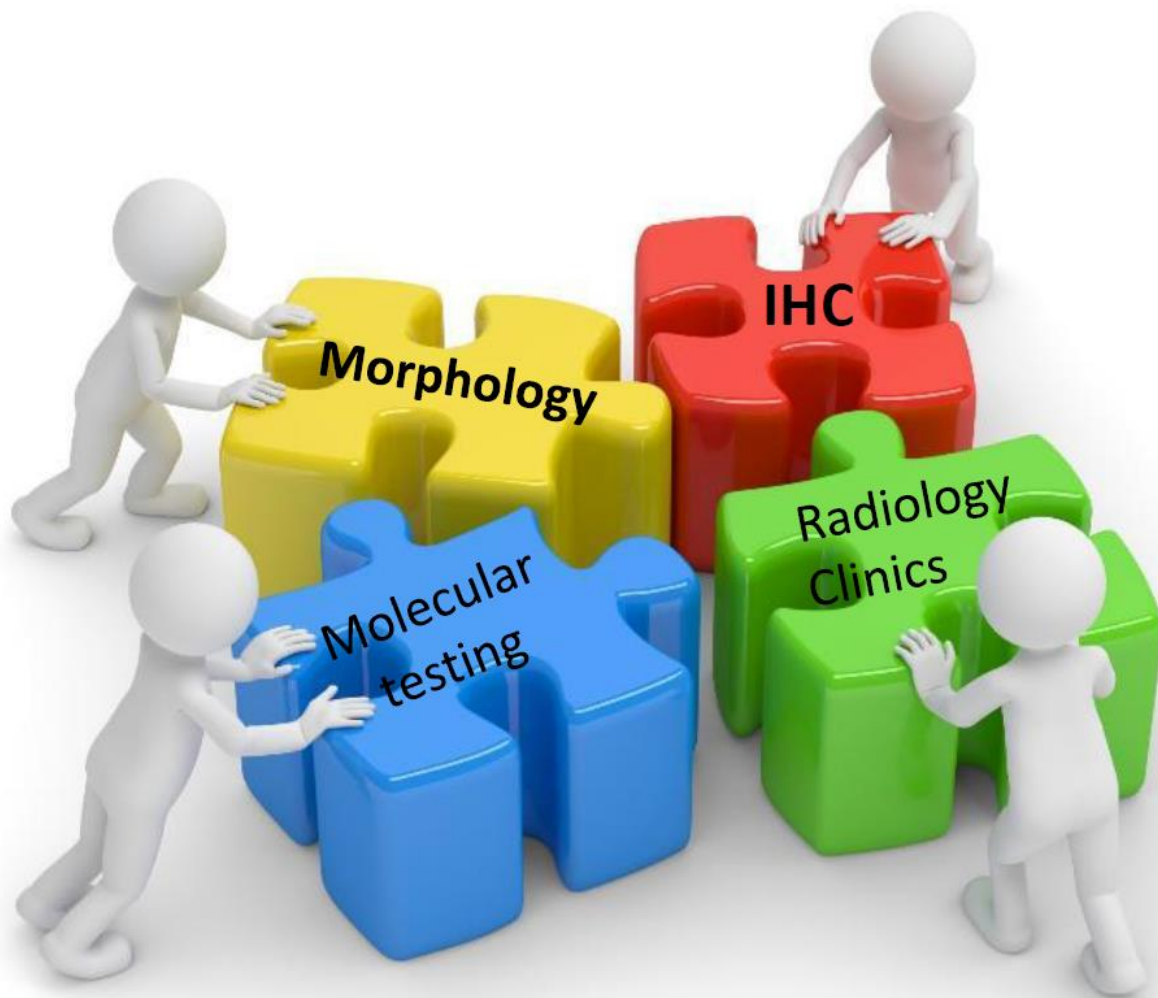
## Carcinoid tumors

- Atypical Carcinoid
- Typical Carcinoid

## Small cell carcinoma

## Large cell carcinoma

- Large cell neuroendocrine carcinoma





# 2015 WHO Classification

## Neuroendocrine tumors

### Carcinoid tumors

- Atypical Carcinoid
- Typical Carcinoid

### Small cell lung carcinoma

- Combined SCL

### Large cell neuroendocrine carcinoma

- Combined LCNEC

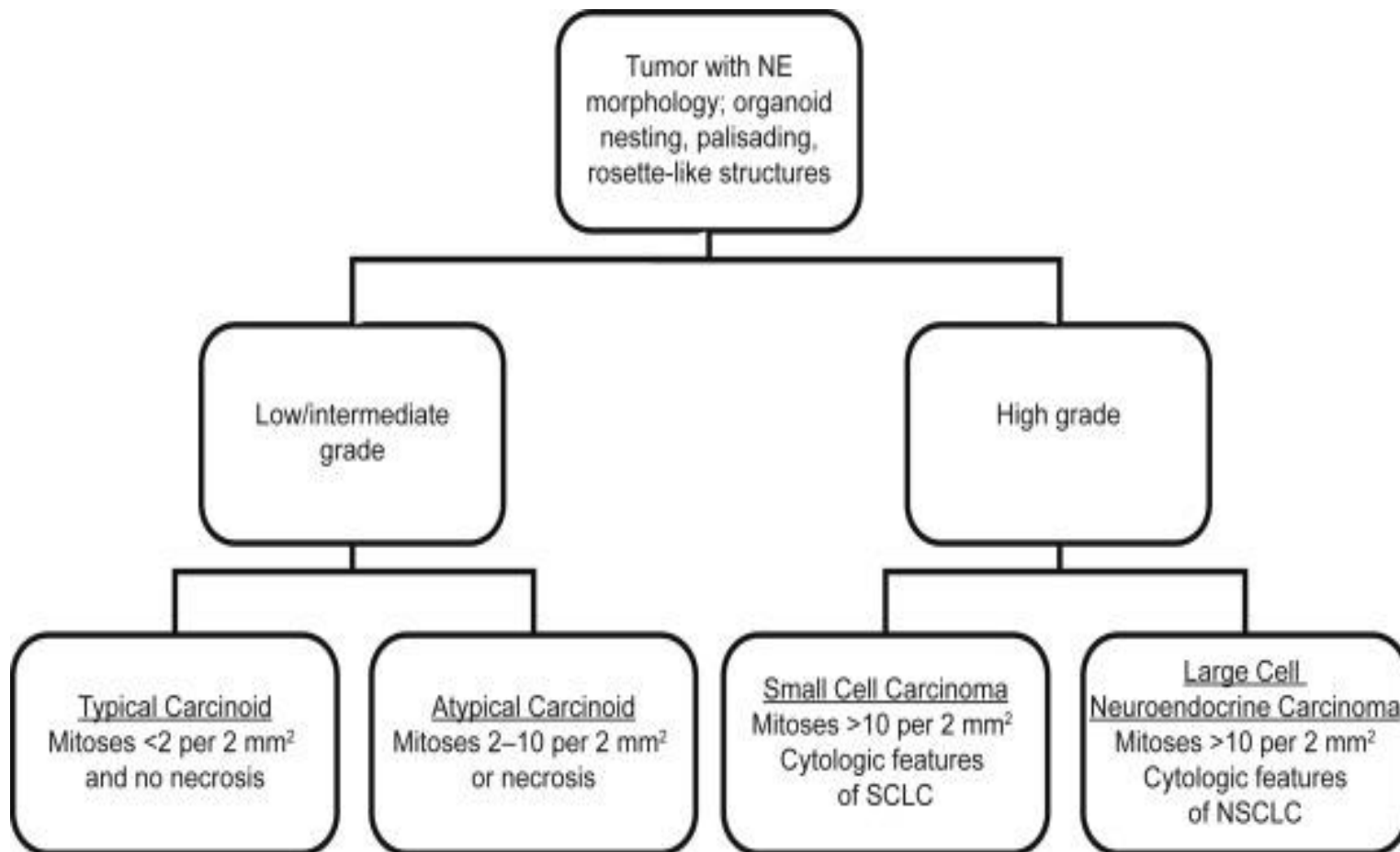
### Preinvasive lesion

- Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia



# Grading

Основывается на морфологии, количестве митозов и наличию некрозов.

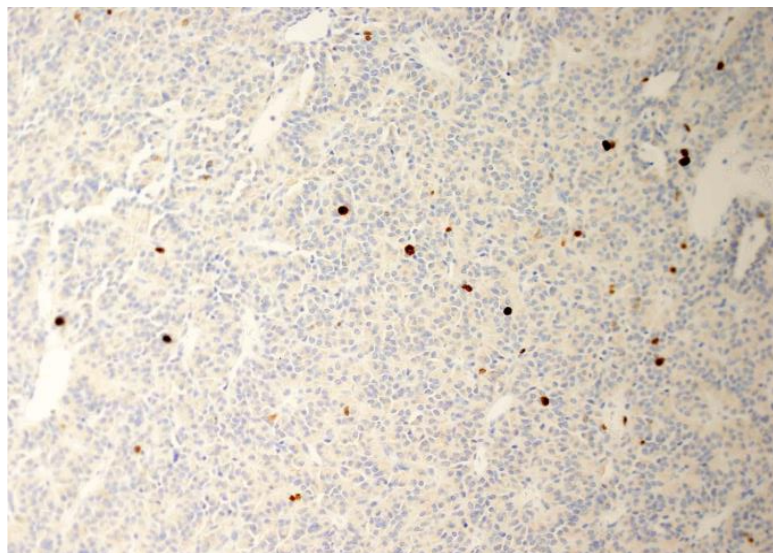




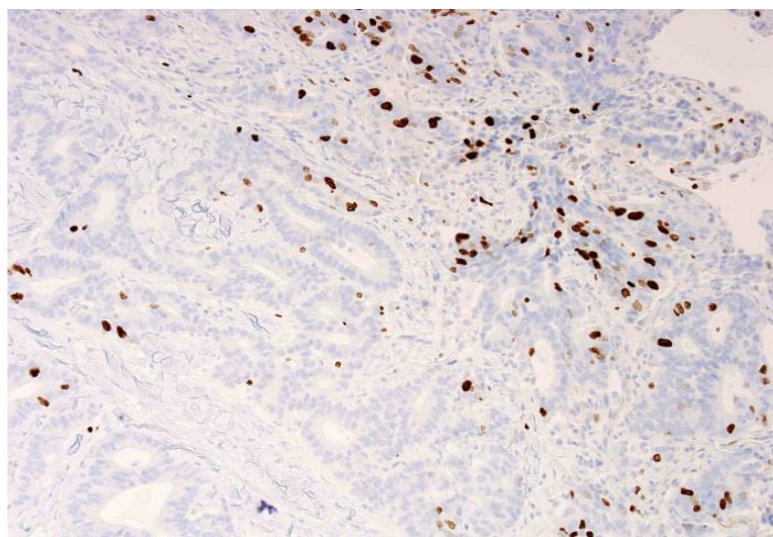
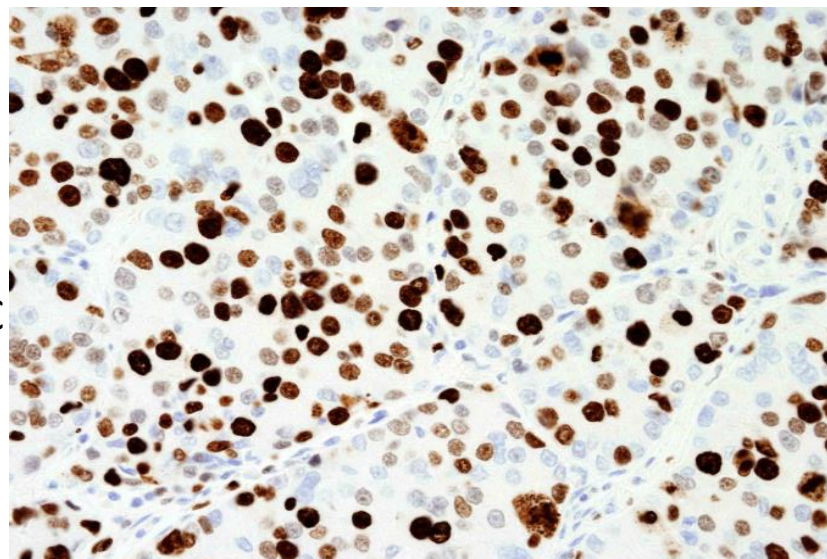
## Индекс Ki-67 в дифференциальной диагностике НЕС

- Carcinoid tumors <20%
- LCNEC 40 – 80%
- SCLC 50 - 100%

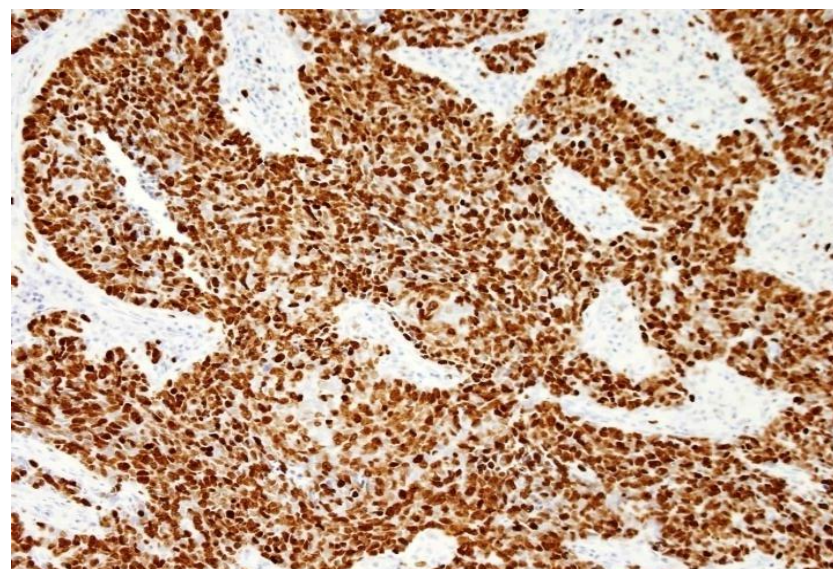
Pelosi G, et al: AJSP 29:179, 2005



TC LCNEC



AC SCLC





## Морфологические особенности нейроэндокринных опухолей.

- Опухоли образуют органоидные, трабекулярные структуры, гнезда и розетки.
- Клетки веретеновидные, овальные, округлые или полигональные.
- Цитоплазма скудная, в виде узкого ободка или не выявляется совсем, что создает впечатление «голых ядер».
- Ядра округлые, овальные или веретенообразные, с неравномерно распределенным, в виде мелких гранул хроматином, гиперхромные.



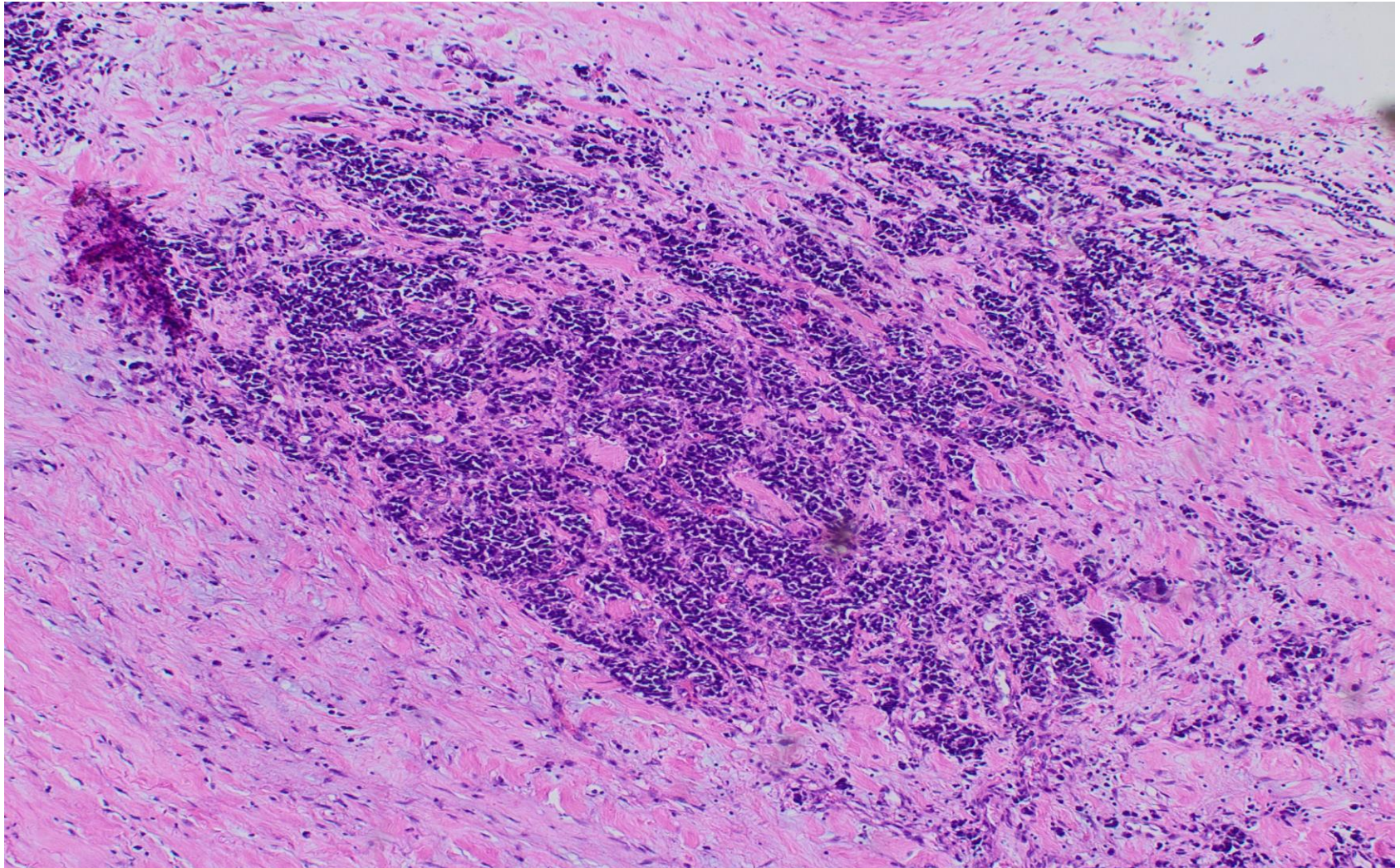
# Small Cell Lung Carcinoma

- Ассоциирована с курением.
- **В 95% случаев имеет центральное расположение.**
- **Часто сопровождается паранеопластическим синдромом.**
- Не имеет характерной для нейроэндокринной опухоли морфологической картины, растет сплошными пластами, иногда с образованием структуры, напоминающие розетки.
- Клетки круглые, овальные или веретеновидные со скудной цитоплазмой.
- Ядра с гранулярным хроматином по типу «соль с перцем». Ядрышки отсутствуют или едва заметны.
- Многочисленные митозы – более 10 в 2 мм<sup>2</sup> (медиана 70)
- Характерно наличие обширных некрозов.



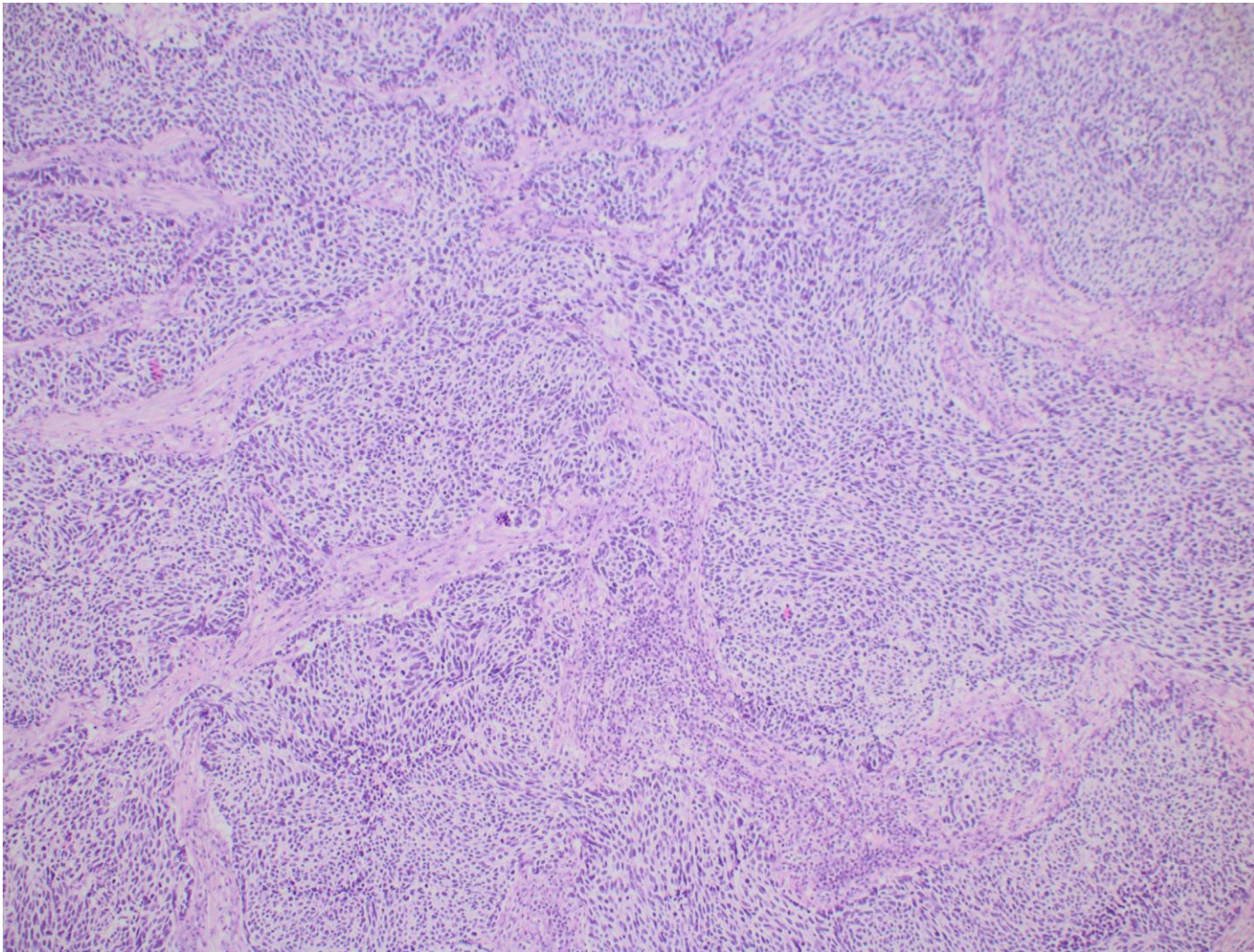


# Small Cell Lung Carcinoma



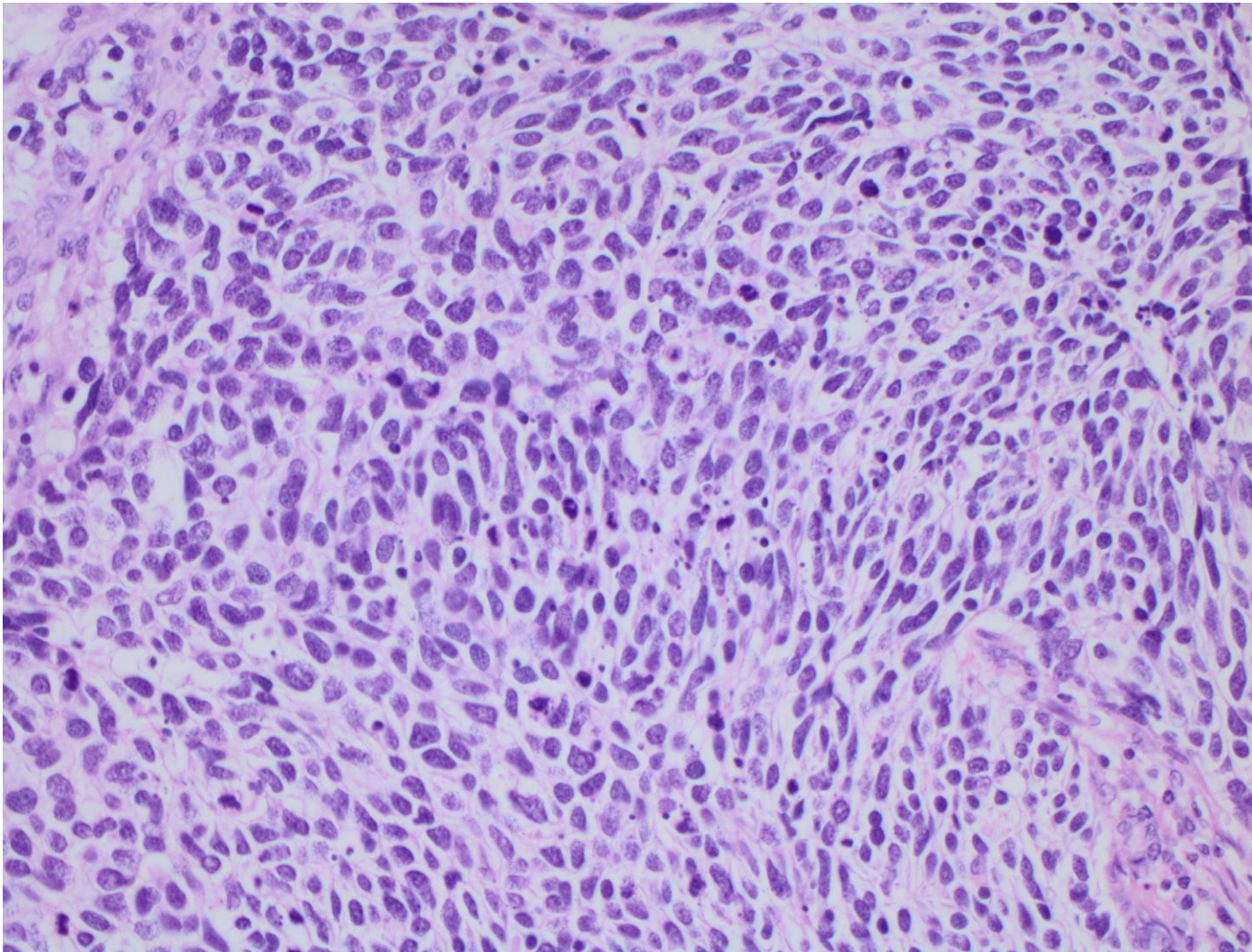


# Small Cell Lung Carcinoma





# Small Cell Lung Carcinoma



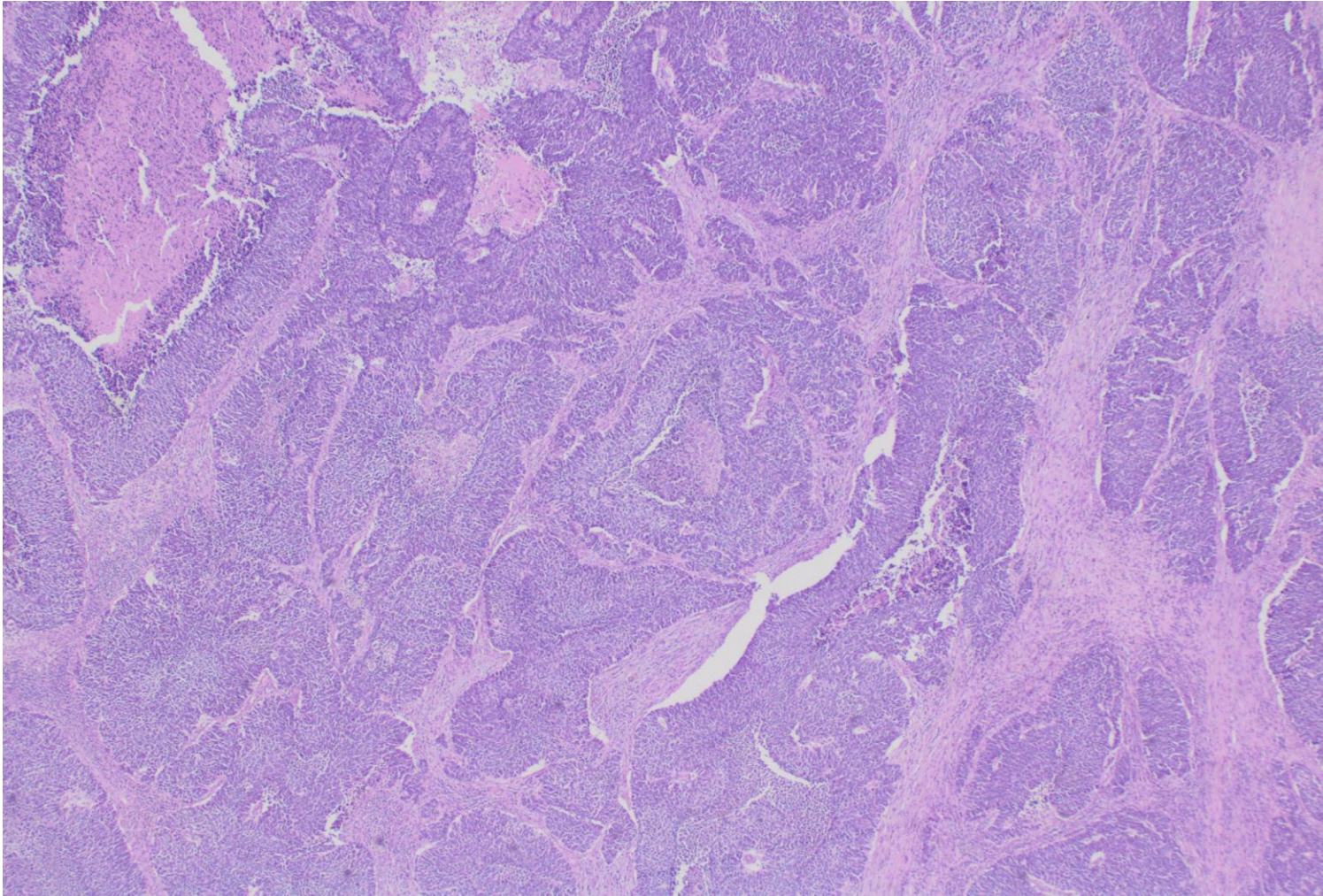


# Large Cell Neuroendocrine Carcinoma

- Ассоциирована с курением.
- **В 90% случаев имеет периферический рост.**
- **Паранеопластический синдром не характерен.**
- Имеет характерную для нейроэндокринной опухоли гистоархитектонику.
- Клетки опухоли крупные (более чем в 3-5 раз больше размера малого лимфоцита) со скудной цитоплазмой.
- Ядрышки крупные, выступающие.
- Митозы  $> 10$  в  $2 \text{ мм}^2$  (медиана 80).

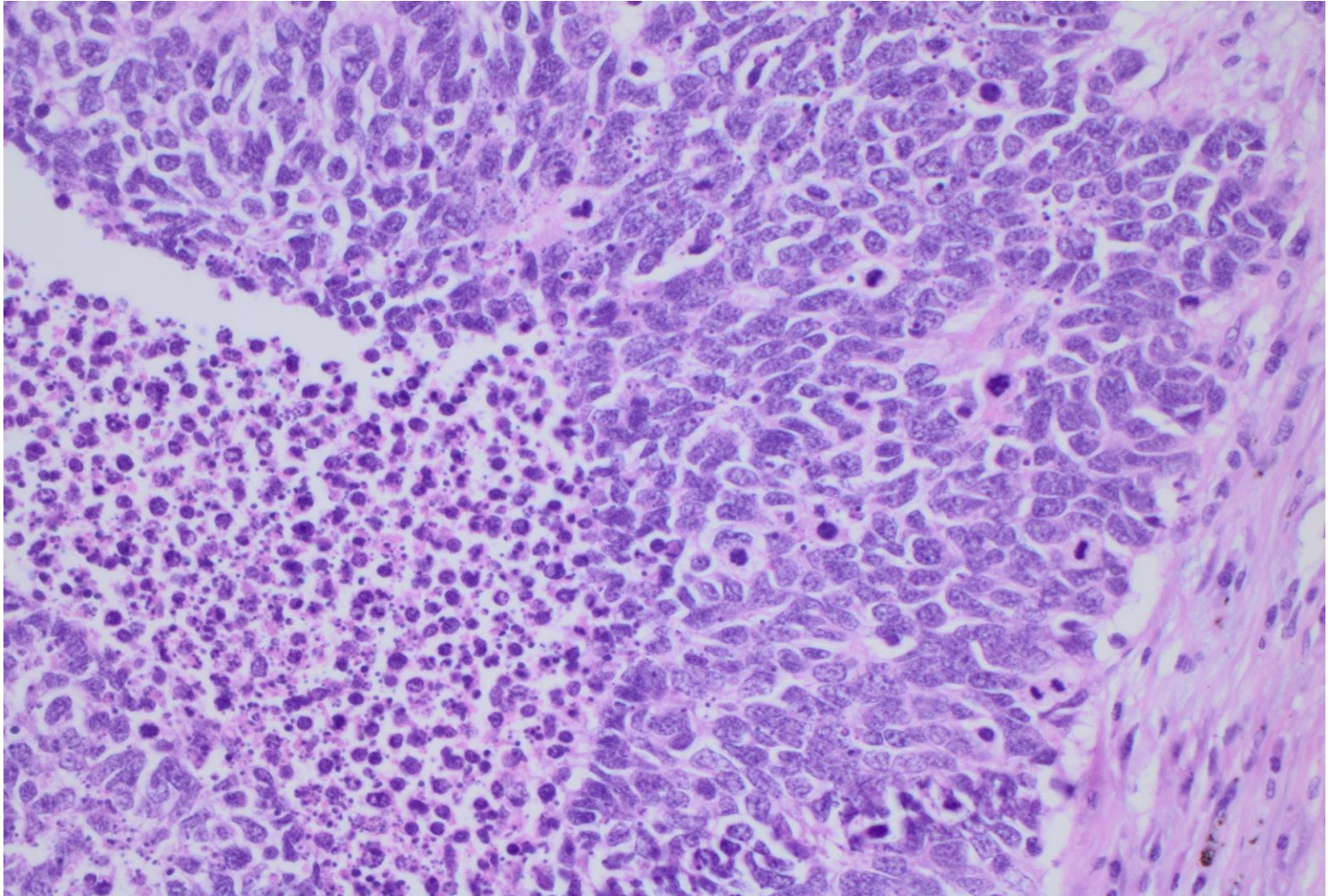


# Large Cell Neuroendocrine Carcinoma



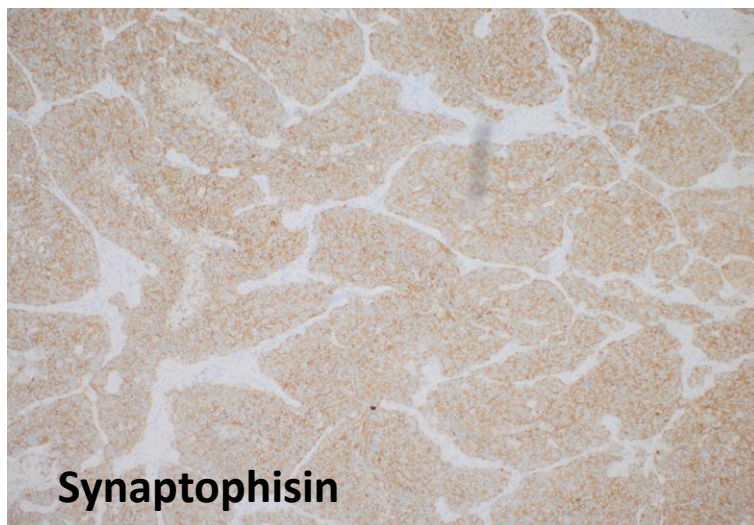


# Large Cell Neuroendocrine Carcinoma





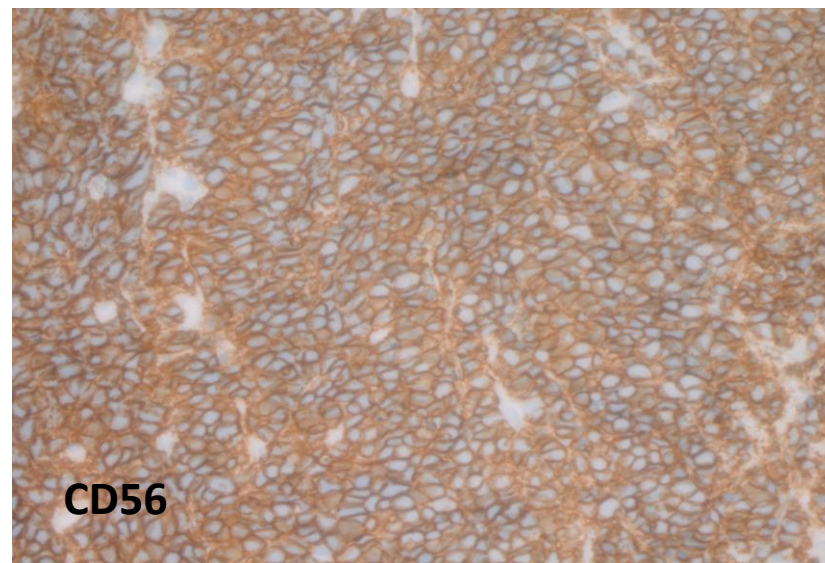
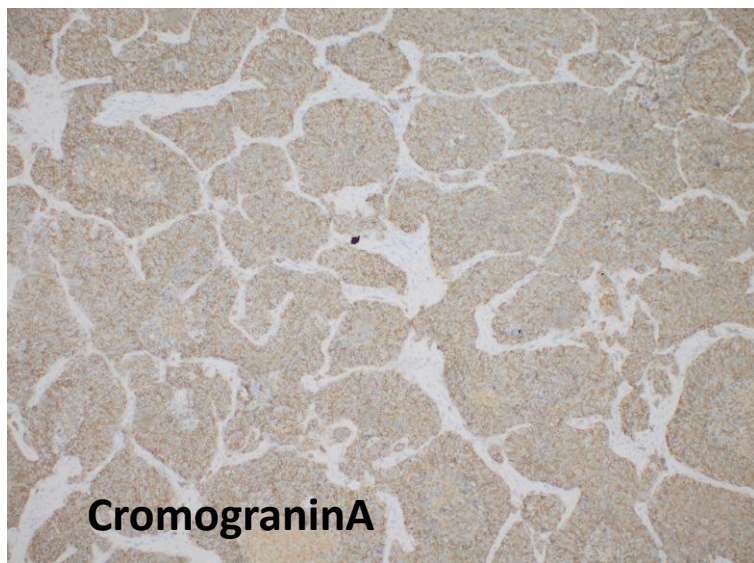
# Дифференциальная диагностика LCNEC и LCLC



**Synaptophysin – 50-60%**

**CromograninA – 80-85%**

**CD56 – 92-100%**





# Carcinoid tumors

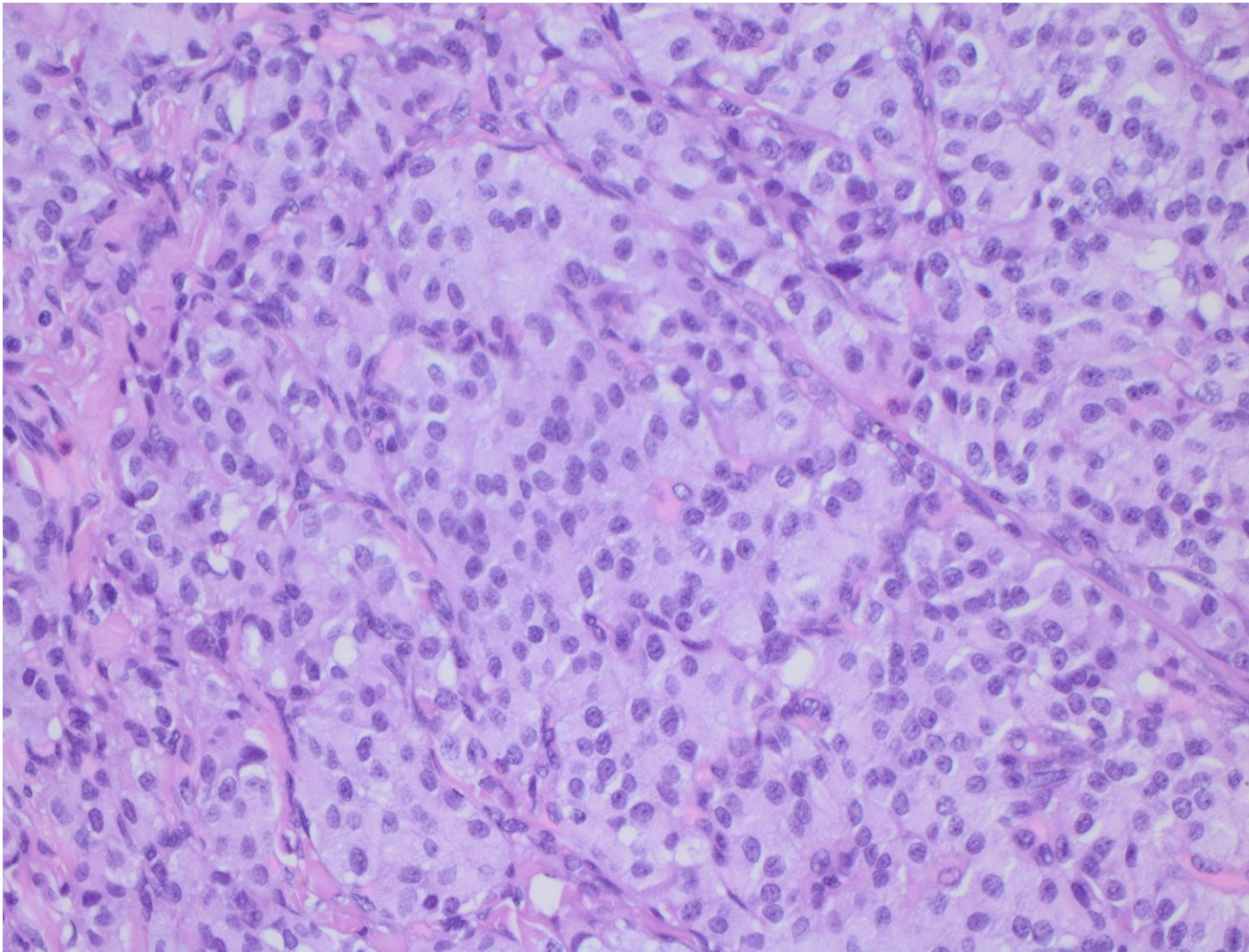
- Имеют характерную нейроэндокринную морфологию, иногда с псевдогландулярным или папиллярным типами роста.
- Клетки одинаковые, овальной или полигональной формы.

| Typical Carcinoid                                 | Atypical Carcinoid |
|---|--------------------|
| Матозы 0-2 в 2мм2                                 | Митозы 2-10 в 2мм2 |
| отсутствуют                                       | характерны         |
| Характерны отложения гиалина и очаги оссификации. |                    |



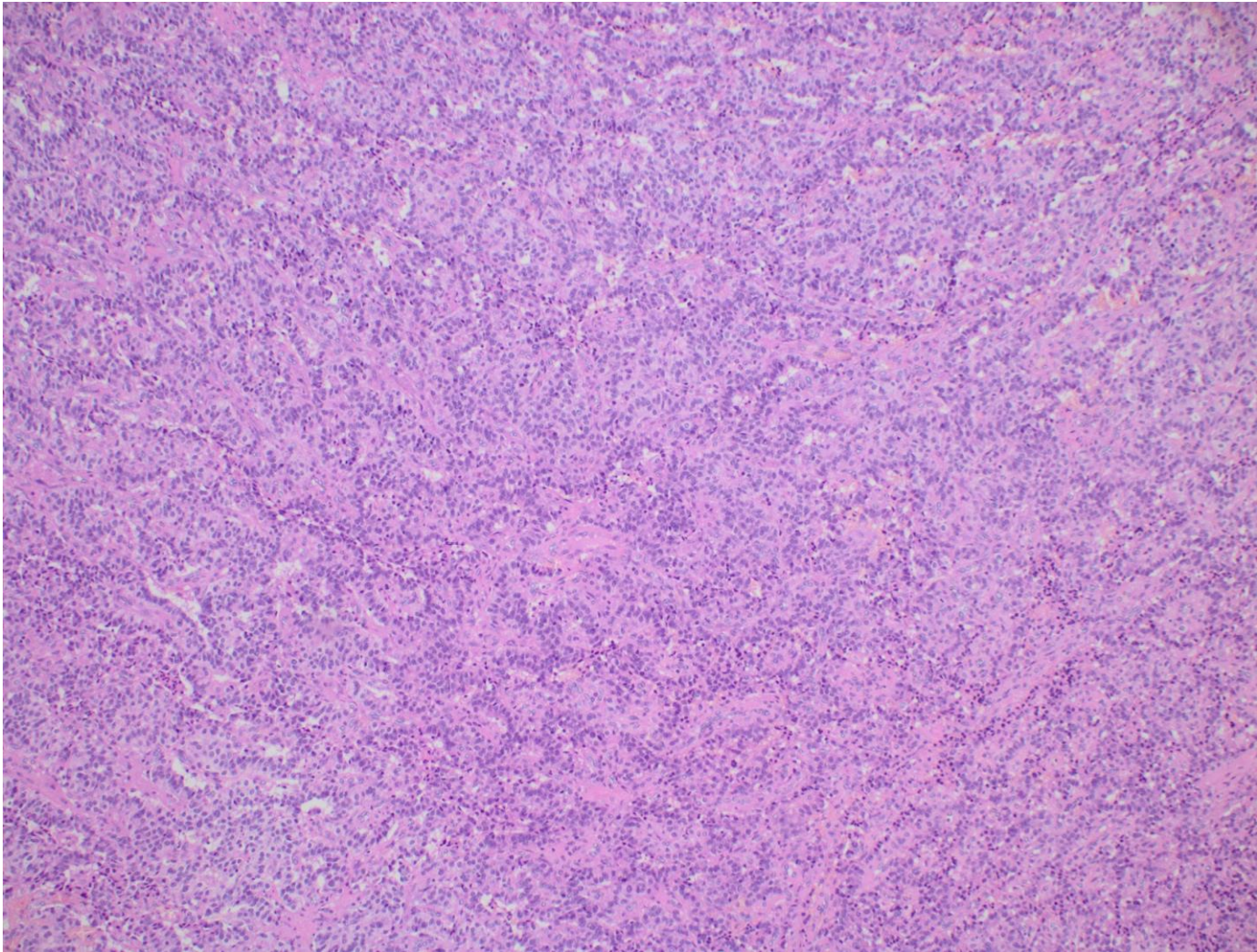


# Typical Carcinoid



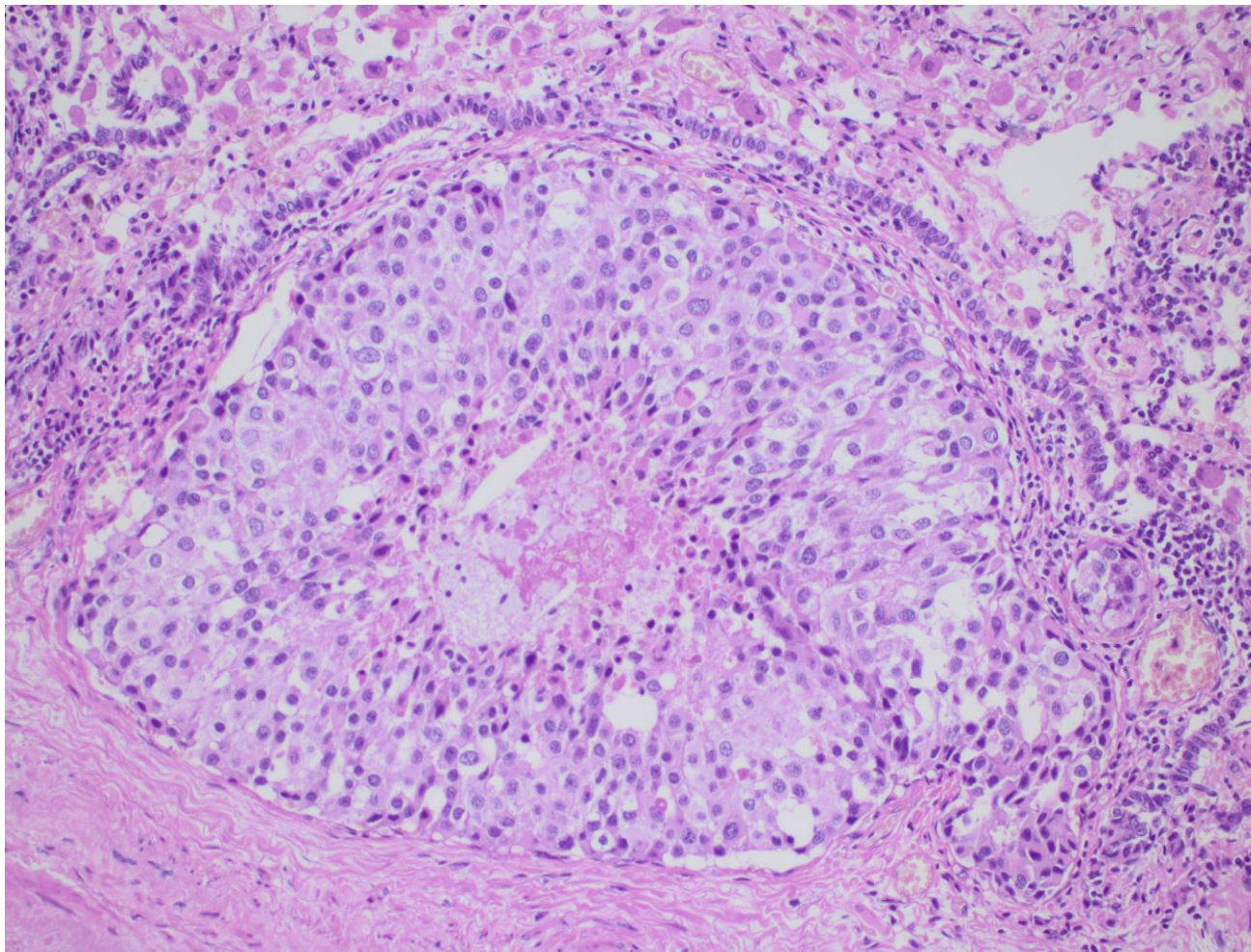


# Atypical Carcinoid



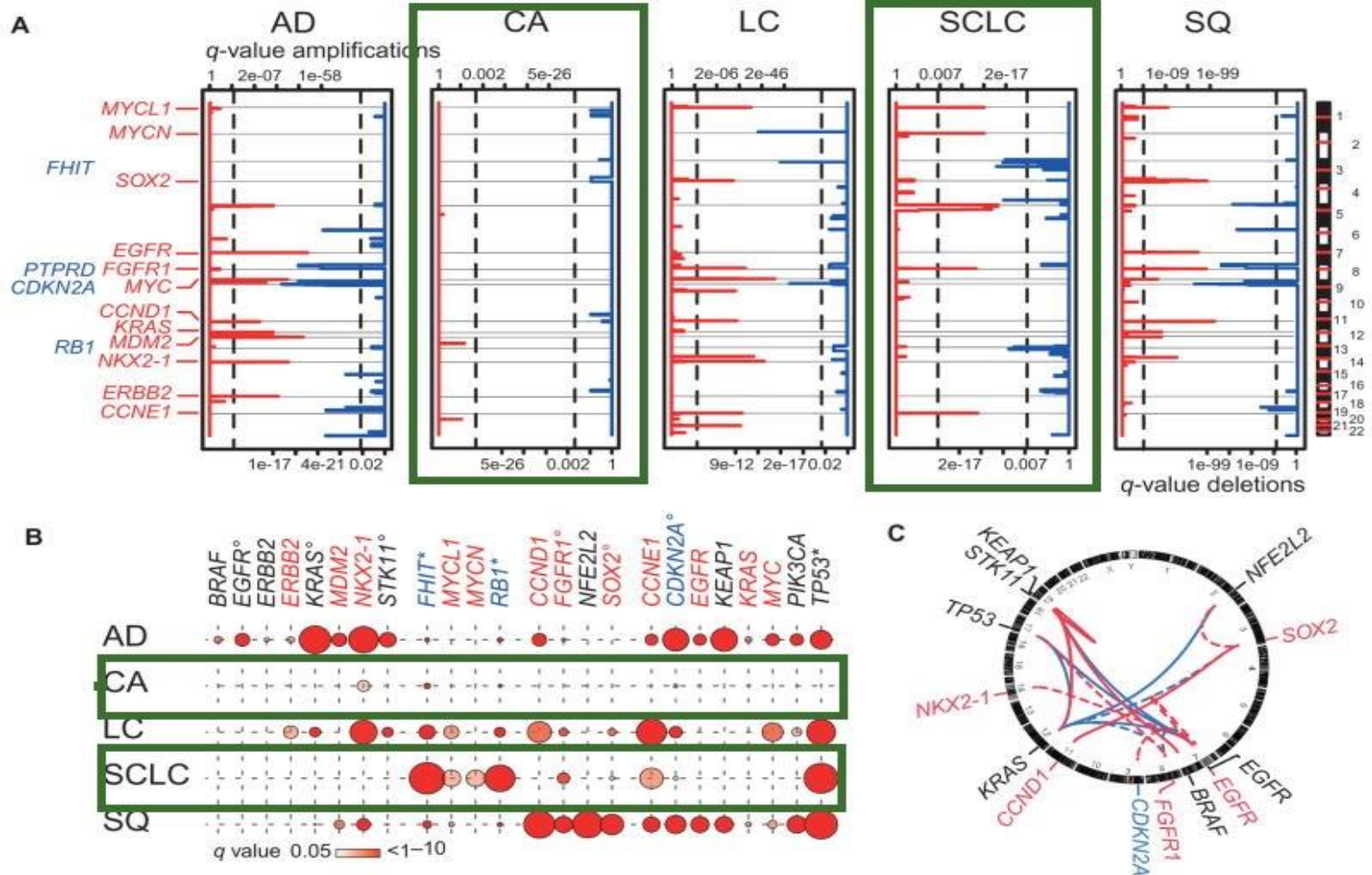


# Atypical Carcinoid





# Genomic alterations in histological subgroups of lung cancer



[Sci Transl Med. 2013 Oct 30; 5\(209\): 209ra153.](https://doi.org/10.1126/scitranslmed.1250000)



**Спасибо за внимание**