

# **PATHOLOGY OF ENDOMETRIAL CANCER**

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Hospital U de Bellvitge, IDIBELL***

# Summary

- Pathologic Classification
- Molecular Classification

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- Molecular Classification



WHO Classification of Tumours 5th Edition: Female Genital Tumours  
2nd Editorial Board meeting: 9 May 2019, IARC, Lyon FRANCE





# **Endometrial carcinoma (Histological Classification)**

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- 2- Serous carcinoma**
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- 4- Undifferentiated-Dedifferentiated carcinoma**
- 5- Mixed carcinoma**
- 6- Other**
- 7- Carcinosarcoma**

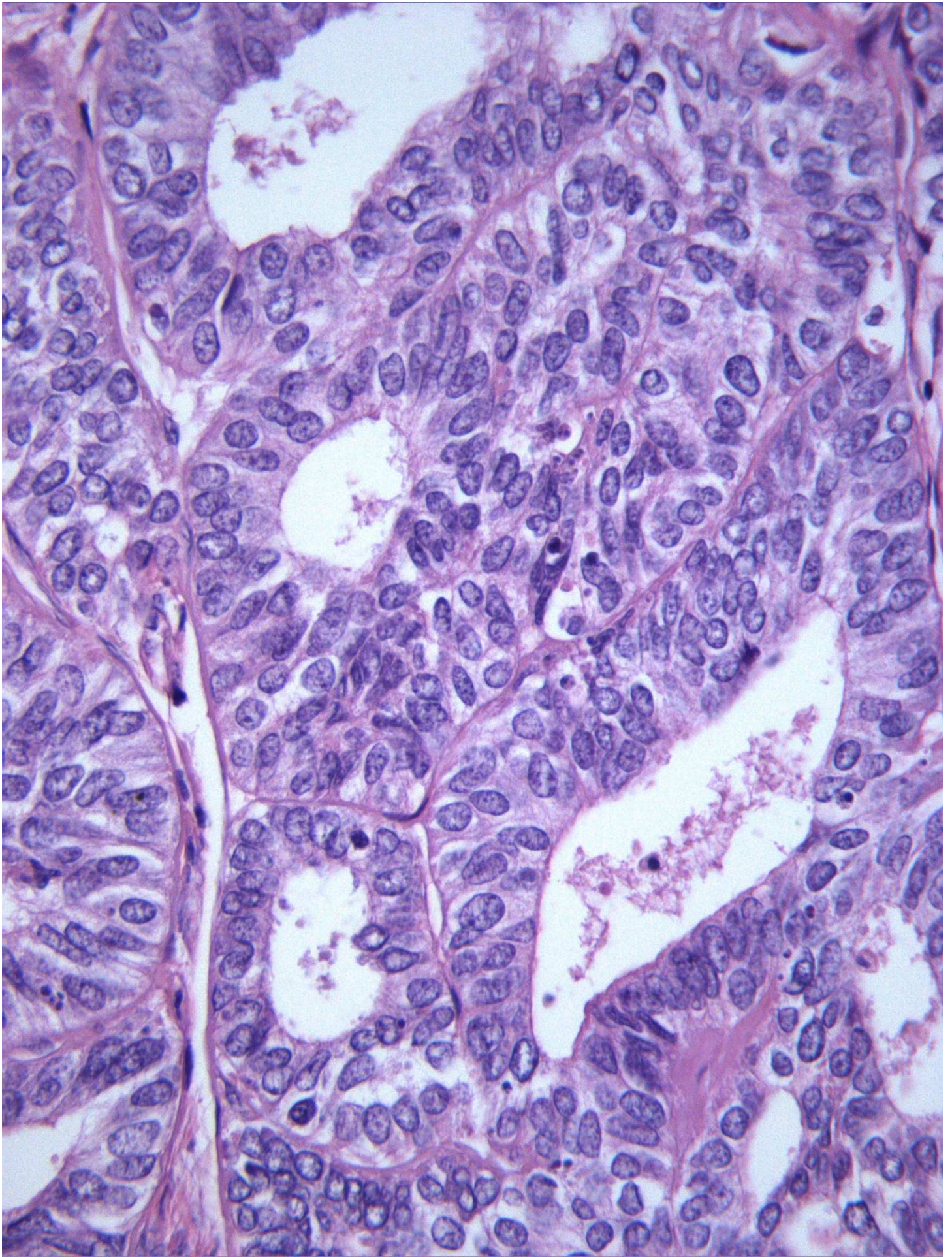
**Neuroendocrine carcinoma**

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**Neuroendocrine carcinoma**

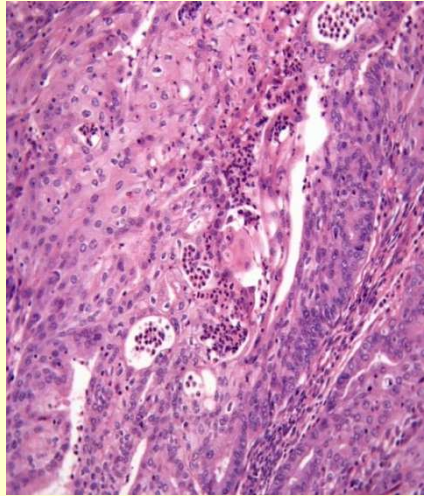




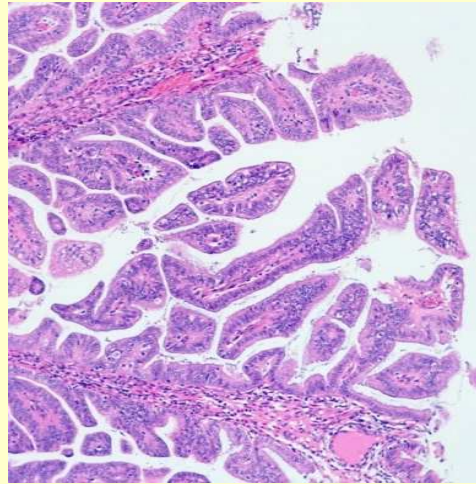


# **Endometrioid carcinoma patterns**

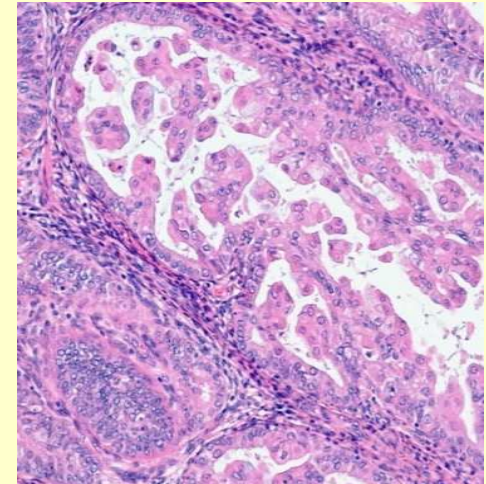
- **Villoglandular**
- **With squamous differentiation**
- **Secretory variant**
- **Small non-villous**
- **Microglandular**
- **Spindle**
- **Sertoliform**
- **Sex-cord-like formation and hyalinization**
- **Mucinous**



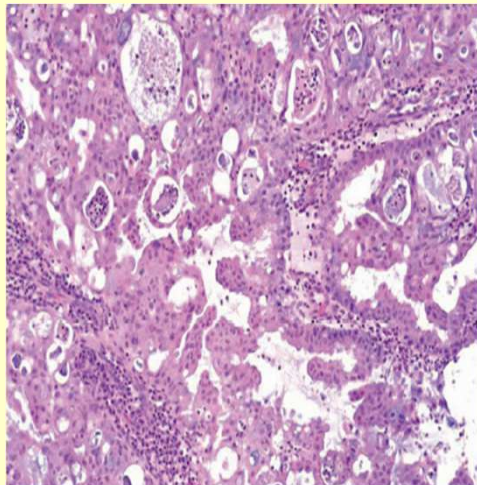
**squamous  
differentiation**



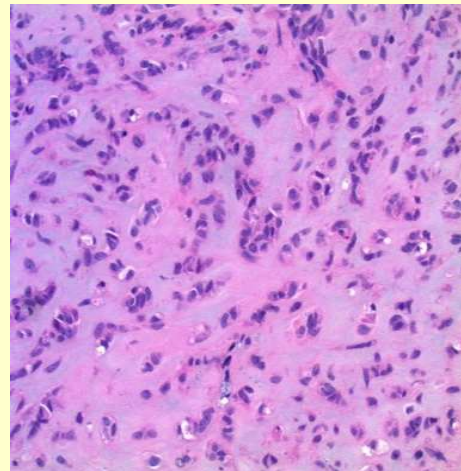
**villoglandular**



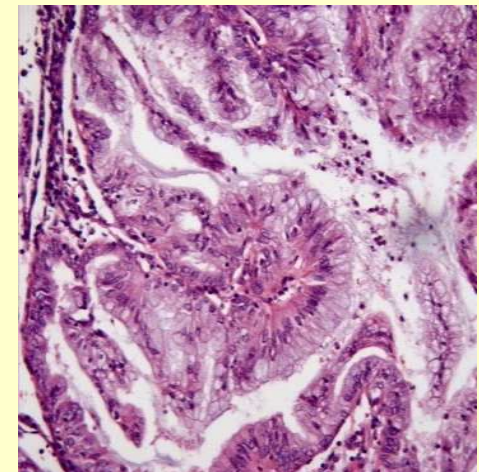
**with small nonvillous  
papillae**



**microglandular**



**sex cord-like  
formations  
hyalinization**



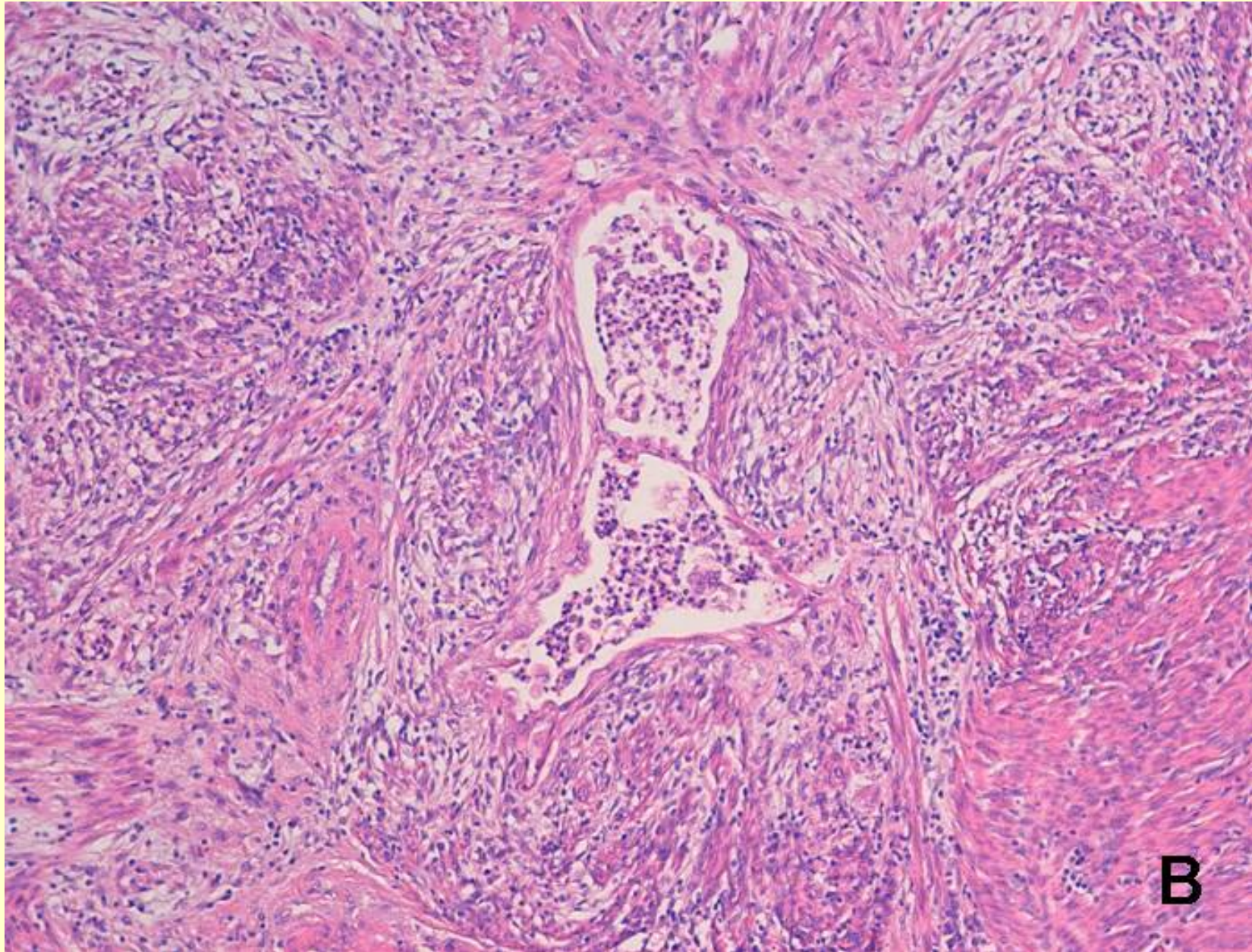
**mucinous**

# **Endometrial carcinoma (Patterns of Myometrial Invasion)**

- Adenoma malignum pattern (diffusely infiltrating)
- MELF (microcystic, elongation, and fragmentation, with a fibromyxoid stroma)

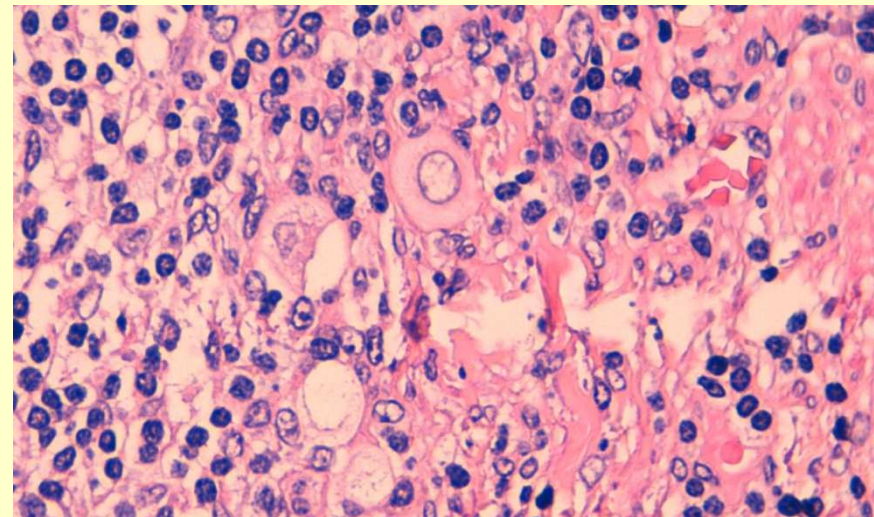
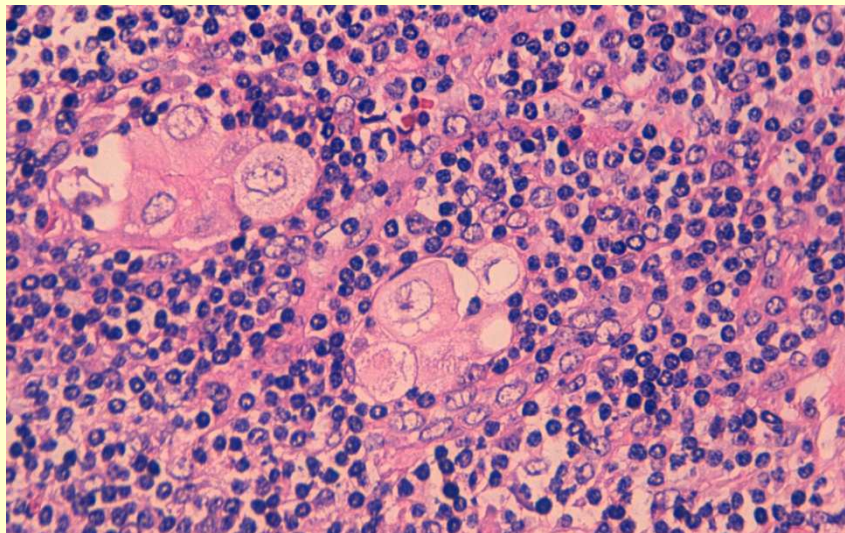
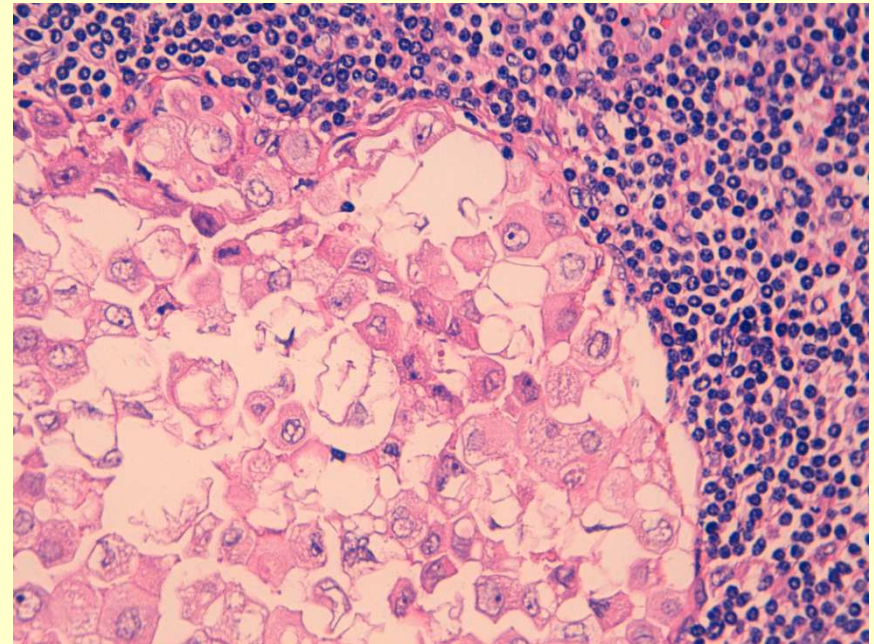
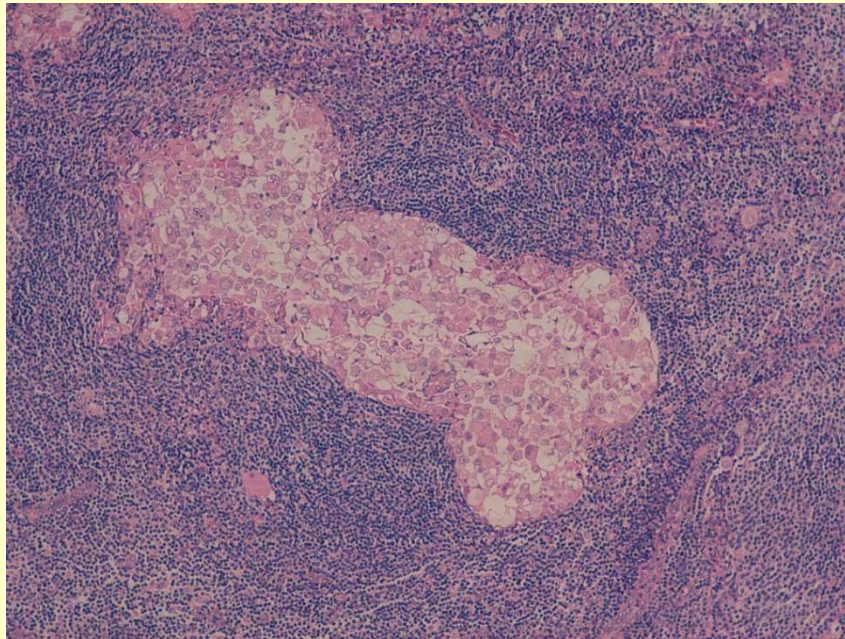


# MELF pattern



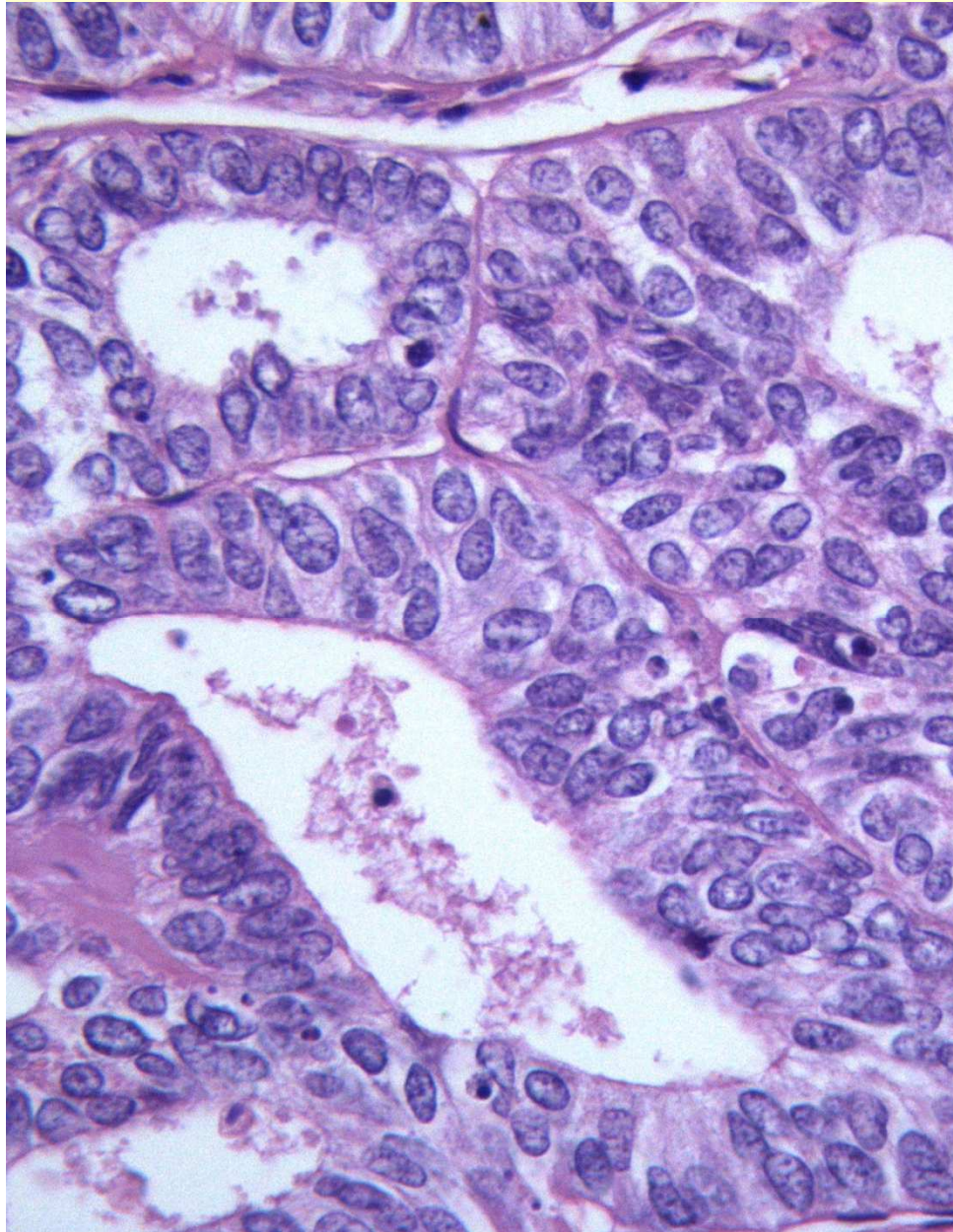


## Histiocyte-like nodal metastasis in low grade EEC with MELF

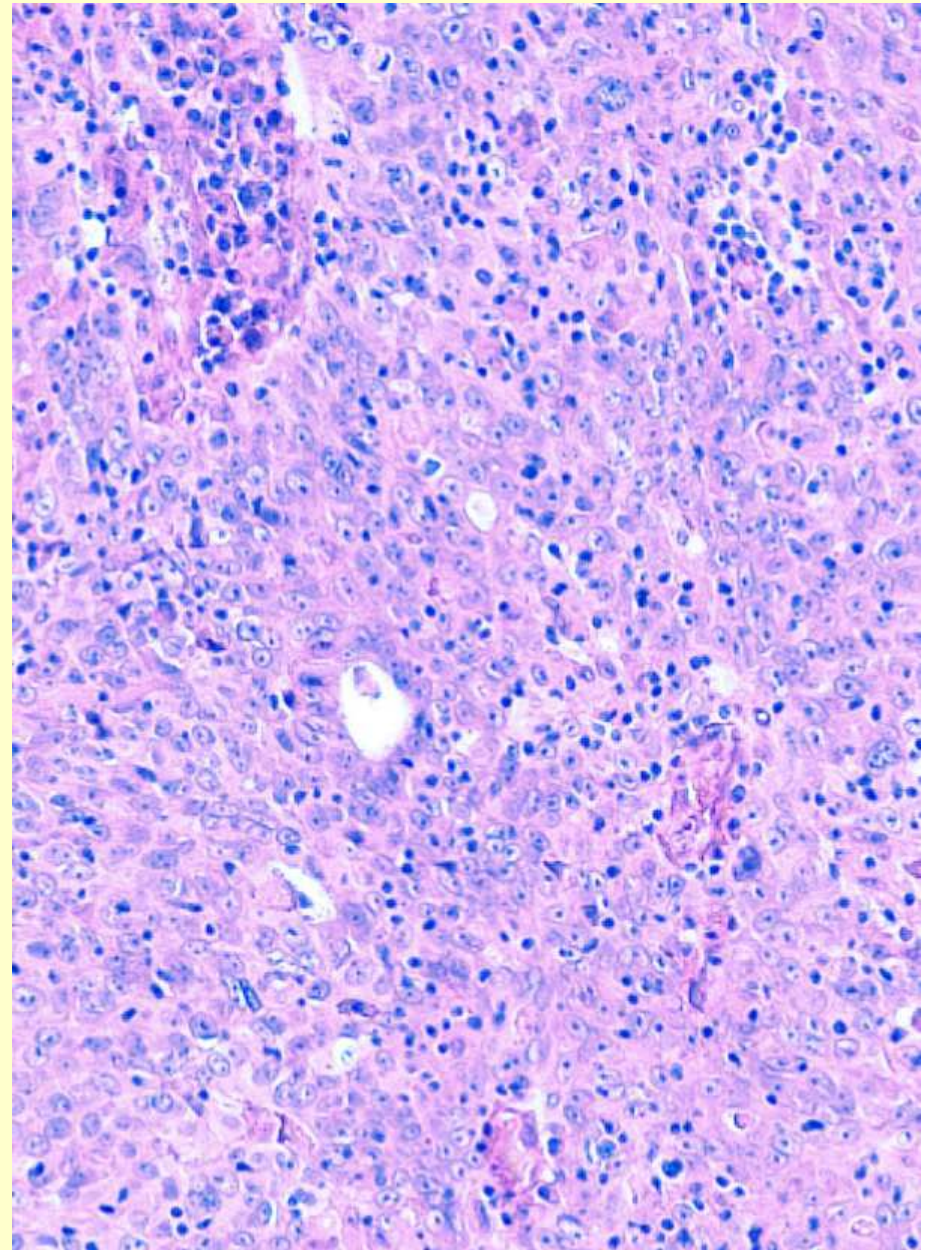




## EEC 1,2



## EEC 3

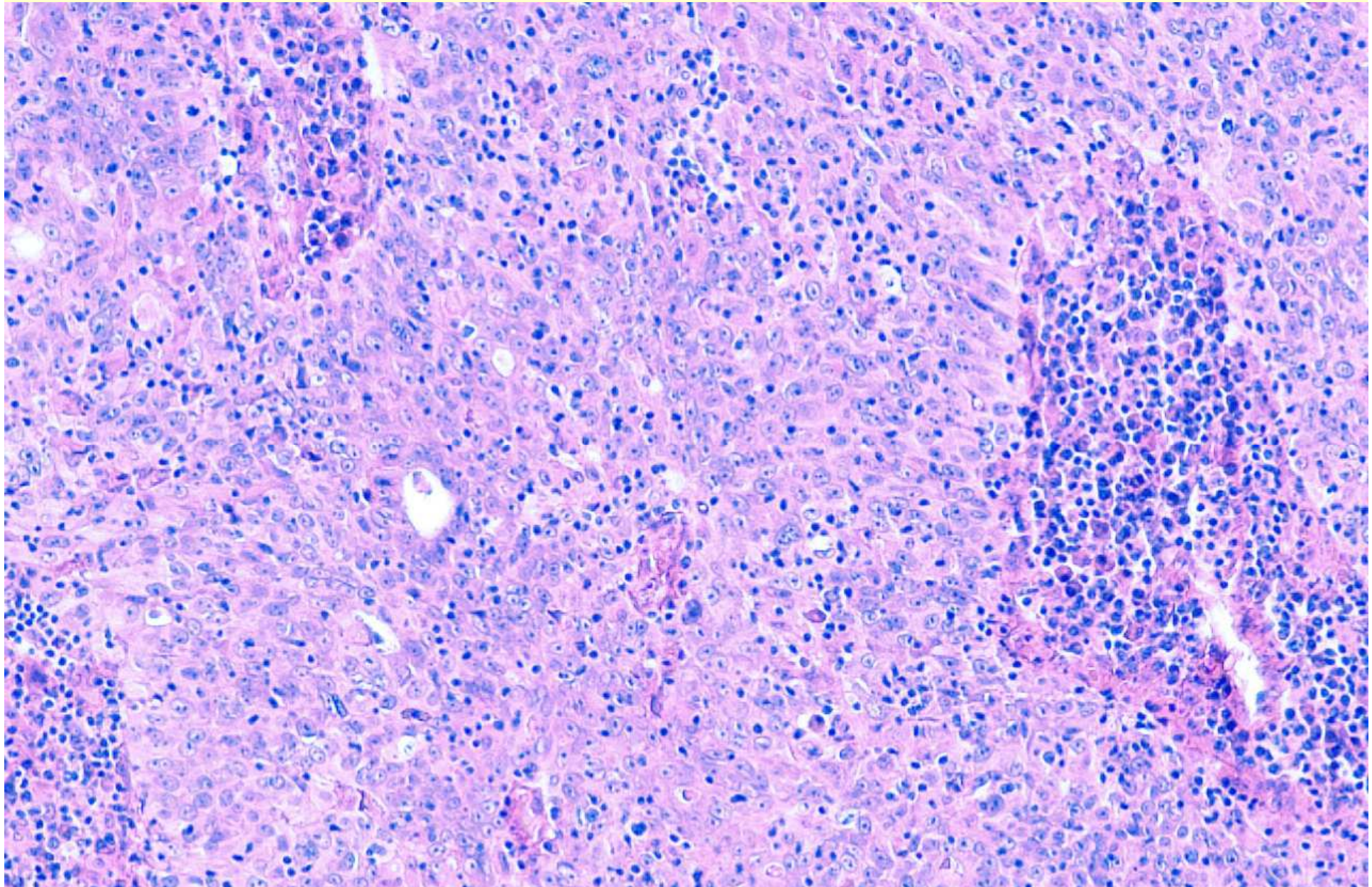


# High-grade endometrioid carcinoma

- **Solid pattern ( $> 50\%$ ) with focal gland formation.**
- **Transition from low-grade endometrioid component**
- **Presence of endometrioid features (mucinous or squamous)**
- **Columnar cells in glandular areas**
- **Occasionally background hyperplasia**



## EEC 3 with focal glandular differentiation

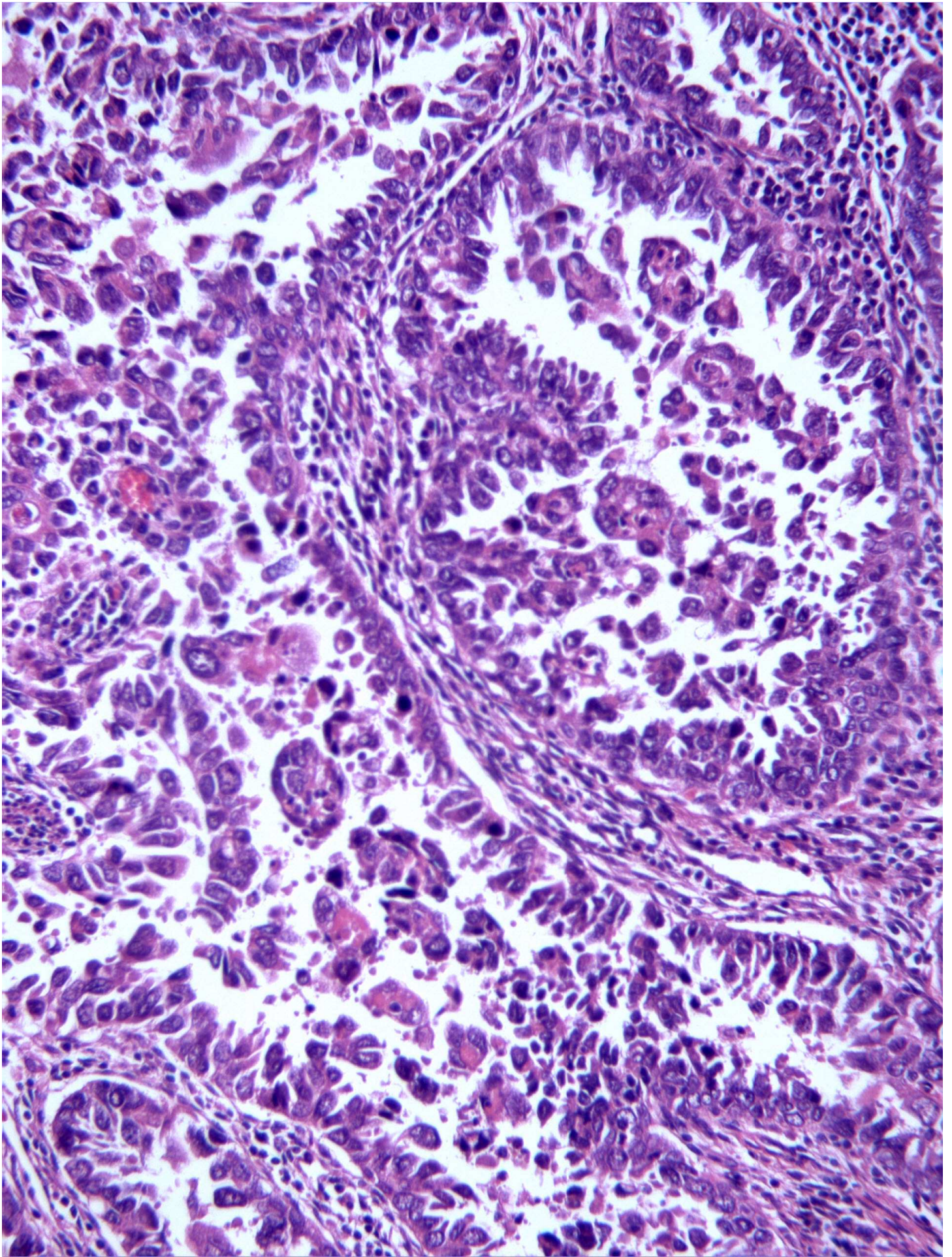


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**Neuroendocrine carcinoma**

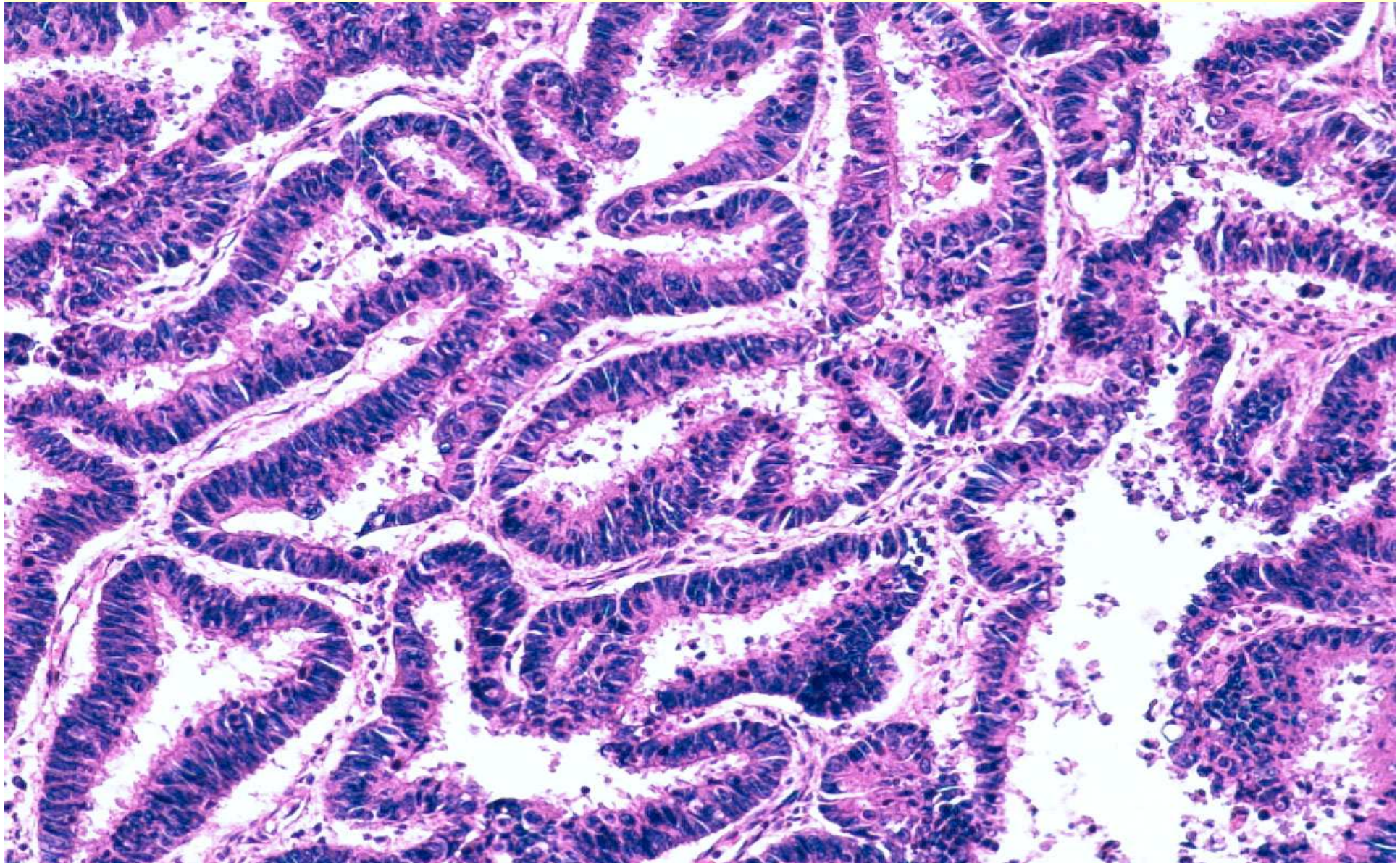




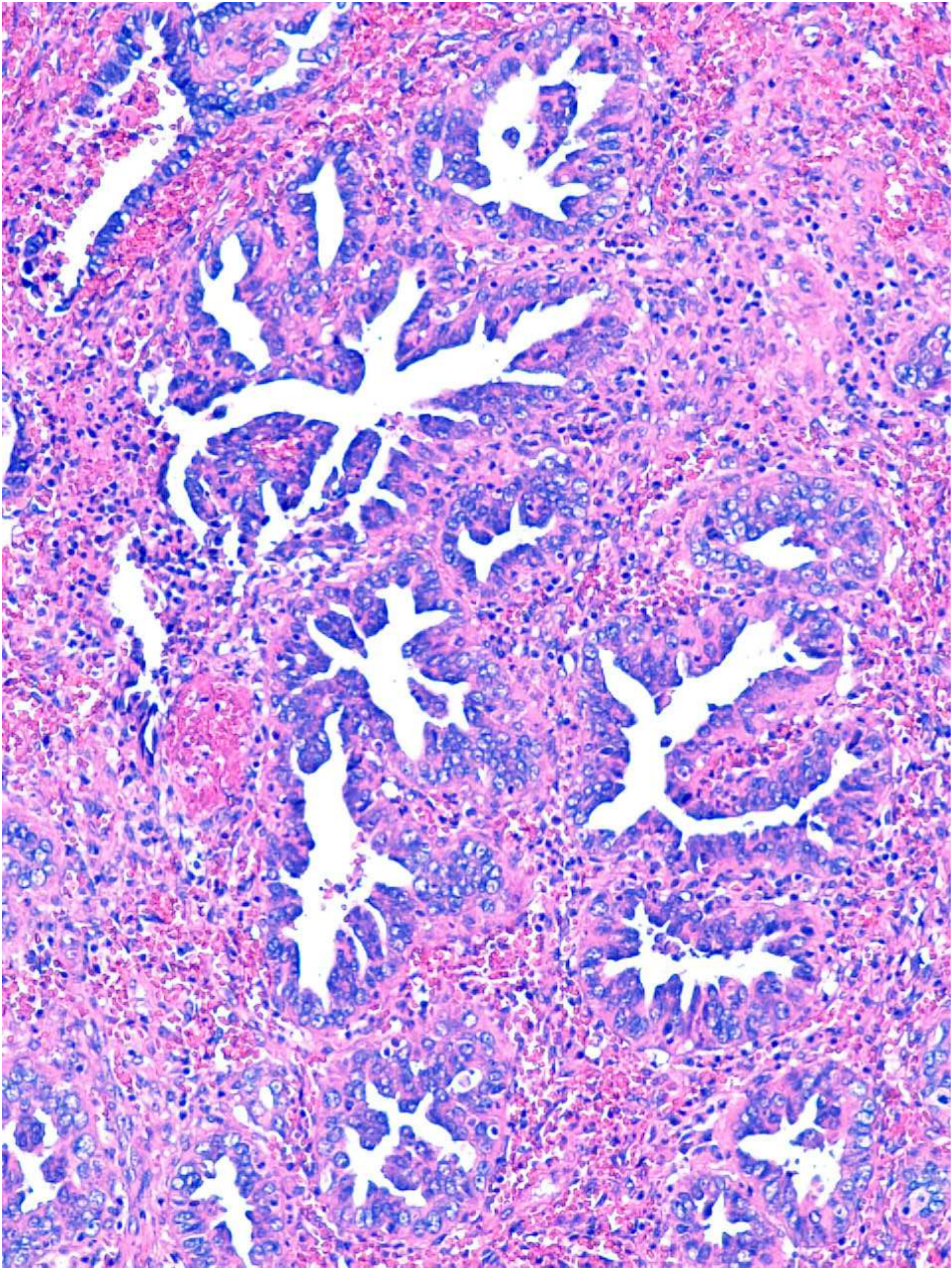


# **Serous carcinoma with glandular pattern**

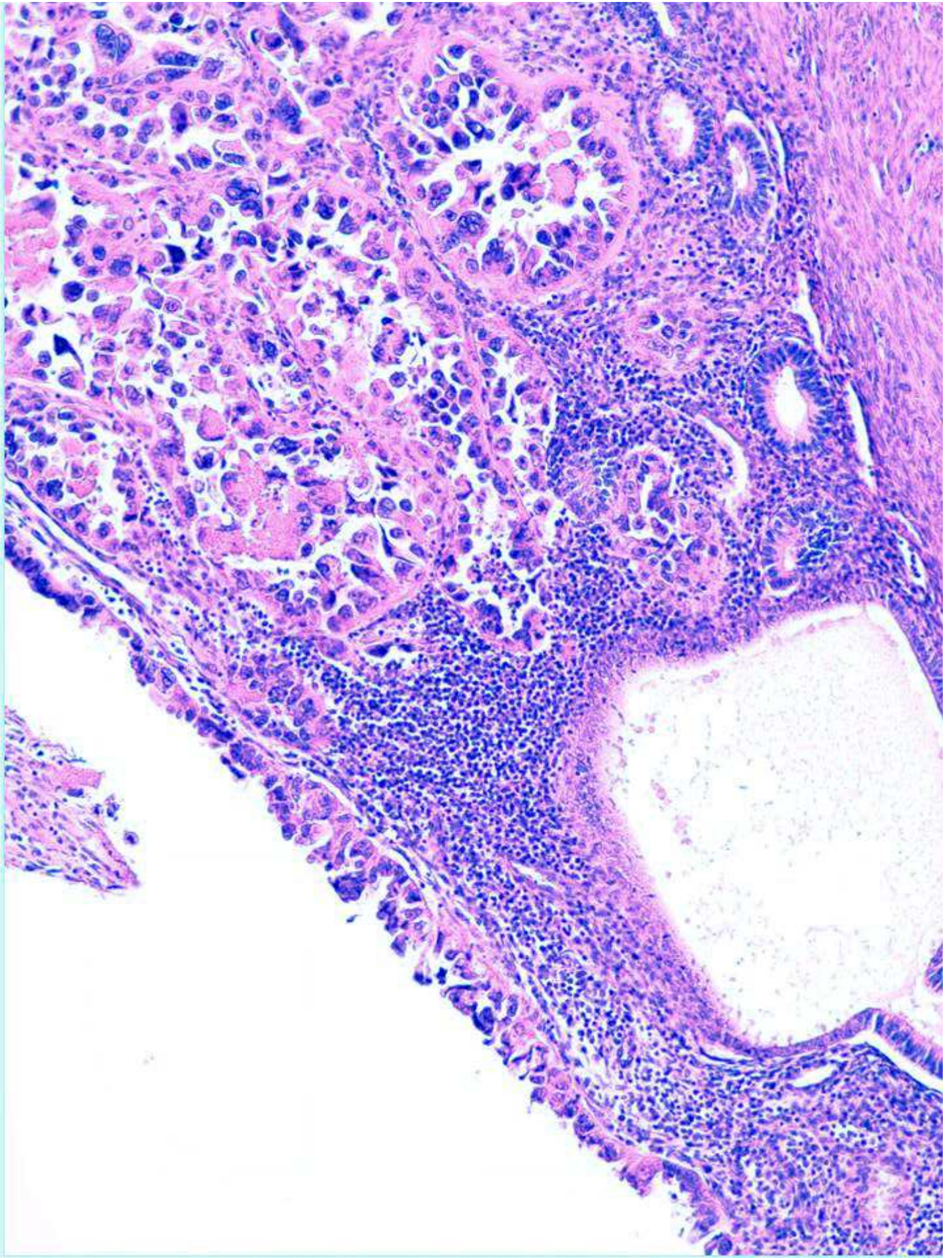
## **Discordant architecture/cytology**







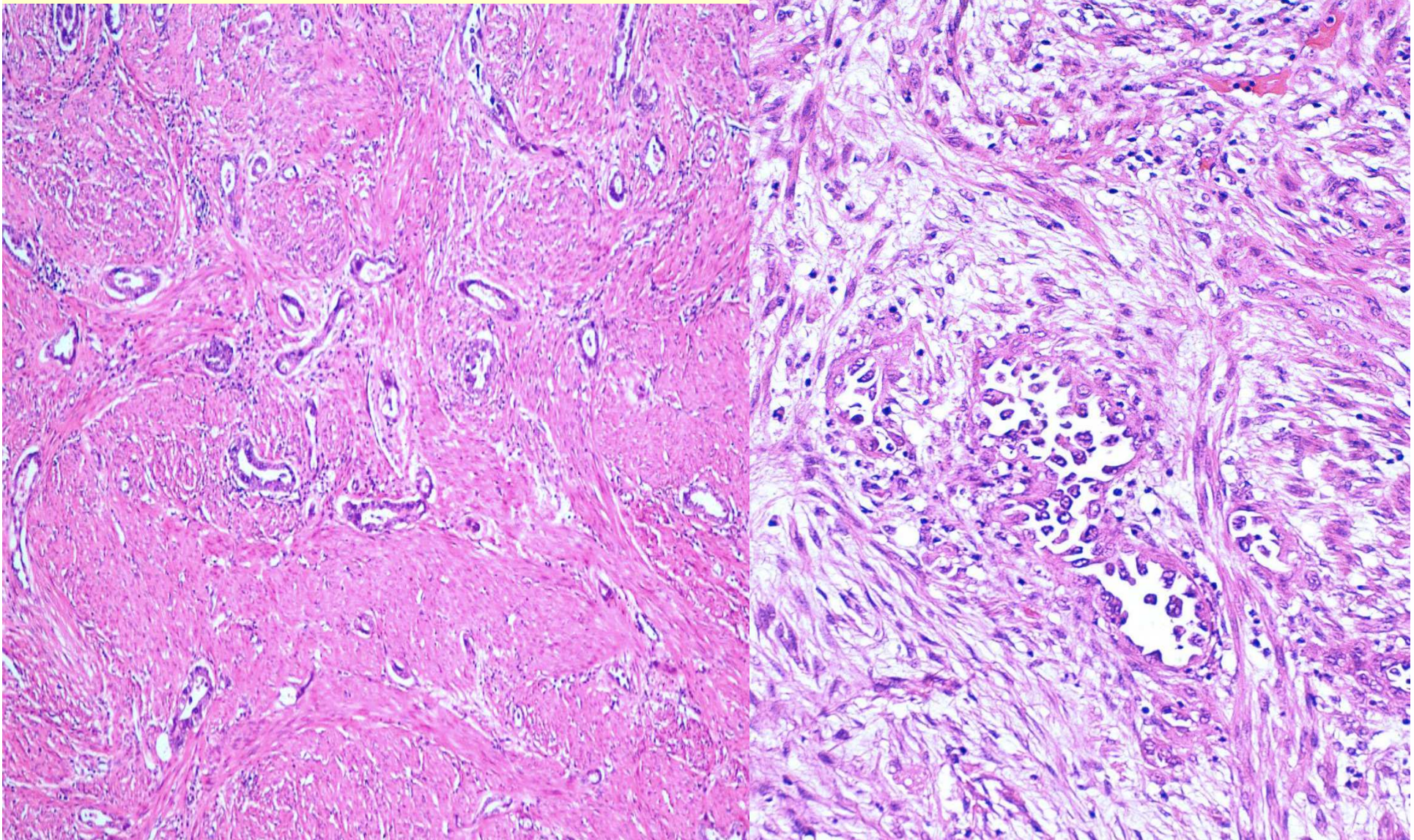






# Myometrial invasion front

## Gaping gland pattern/serous





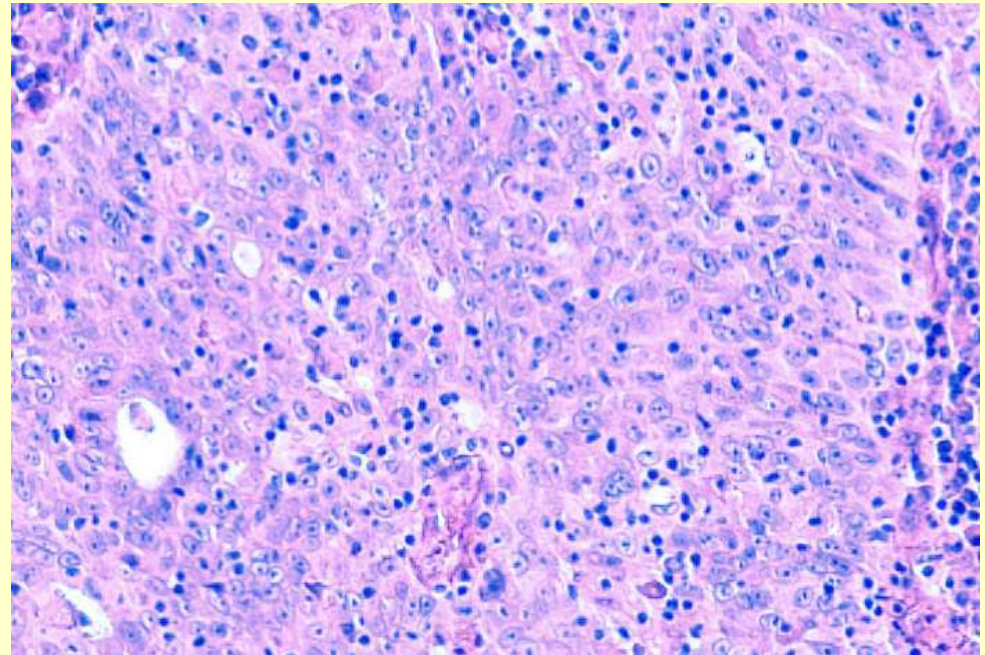
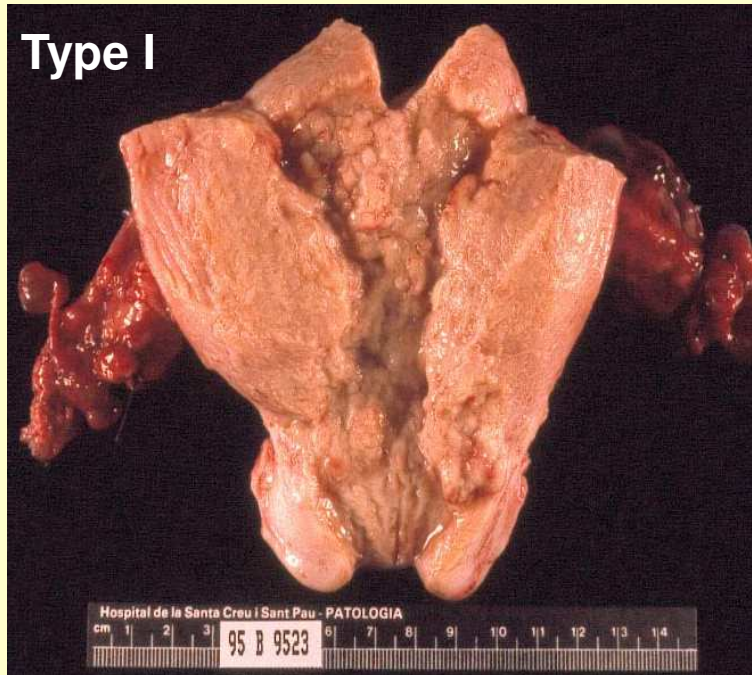
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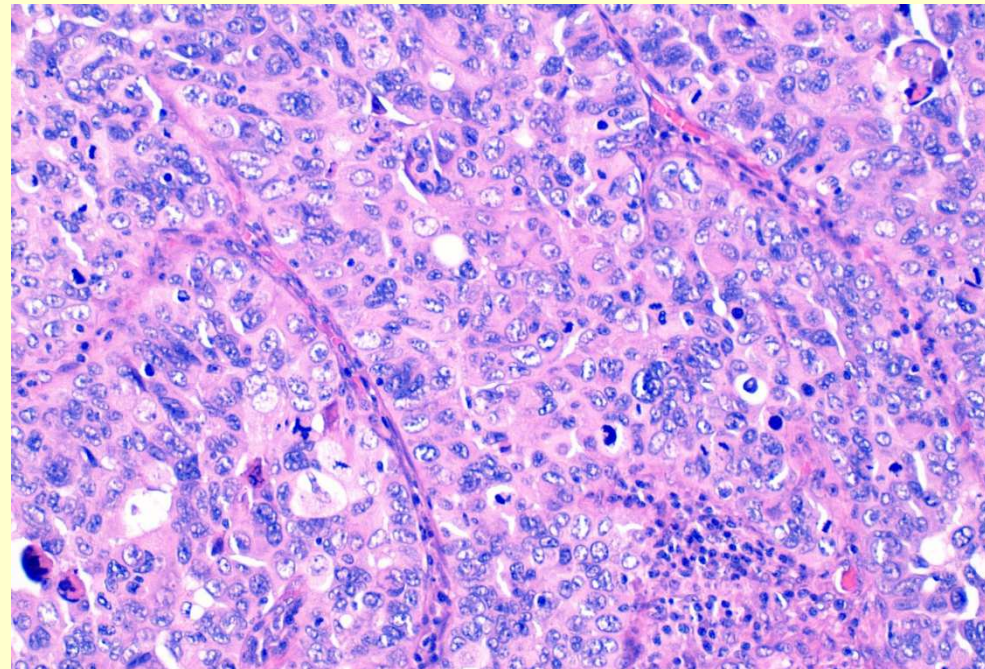
**Neuroendocrine carcinoma**



Type I



Type II



# Serous Versus EEC 3

## IHC Profiles

	Serous	Endometrioid 3	Pattern of staining (Serous)
	%	%	
p53	70-90%	35%	All (< 75%) or Nothing
p16	90%	10-30%	Diffuse Cytoplasmic
ER/PR	20-50%	40-80%	Nuclear
IMP2	80-95%	20%	Diffuse Cytoplasmic
IMP3	60-90 %	20%	Diffuse Cytoplasmic
PTEN loss	0-5%	50-70%	Retained Expression
ARID1A loss	0-20%	40 %	Retained Expression
β-catenin	100%	90%	Positive Membranous
HMGA-2	46-91 %	20-40 %	Positive Nuclear
FOLR-1	50-70%	30%	Positive Cytoplasmic

# **High-grade endometrioid carcinoma versus Serous**

- **Presence of obvious endometrioid or serous features (sampling is important)**
- **Immunohistochemistry (p53, p16, mismatch repair, PTEN, ARID 1A)**
- **Molecular pathology useful in occasional cases**

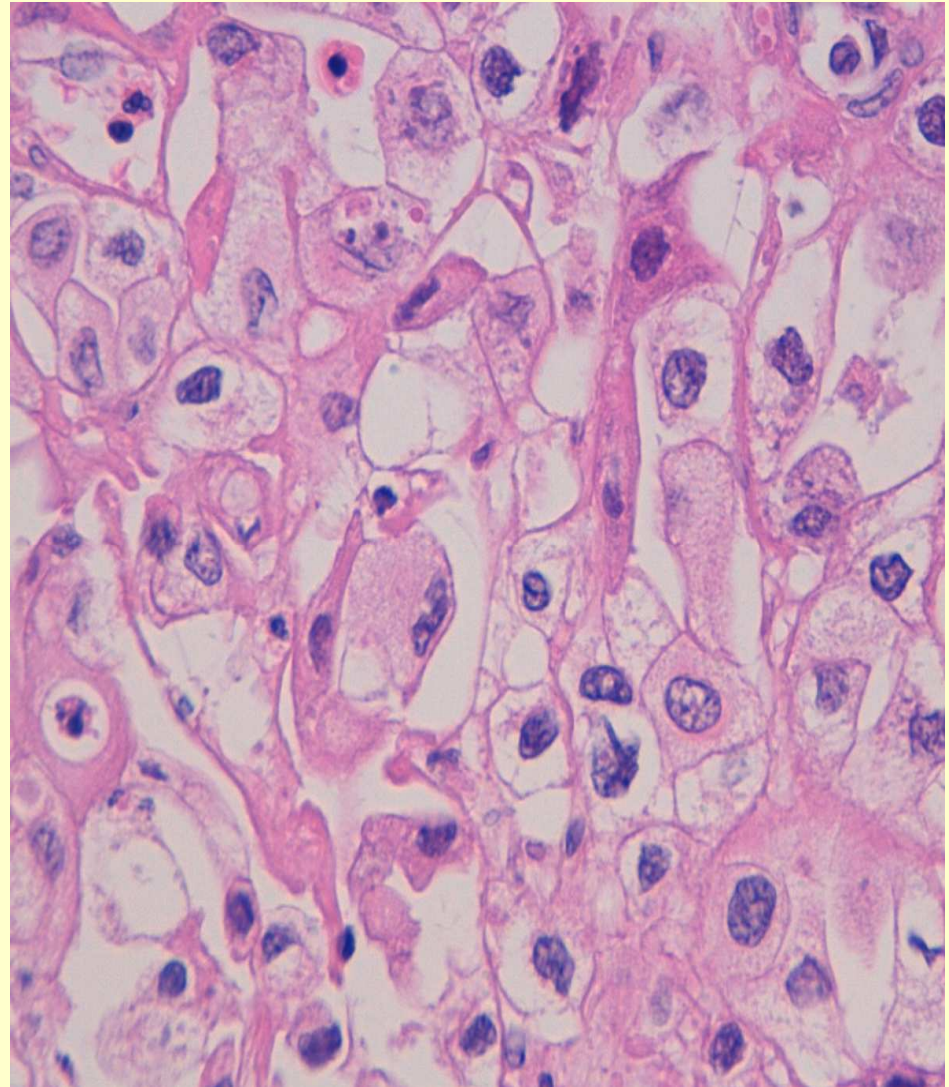


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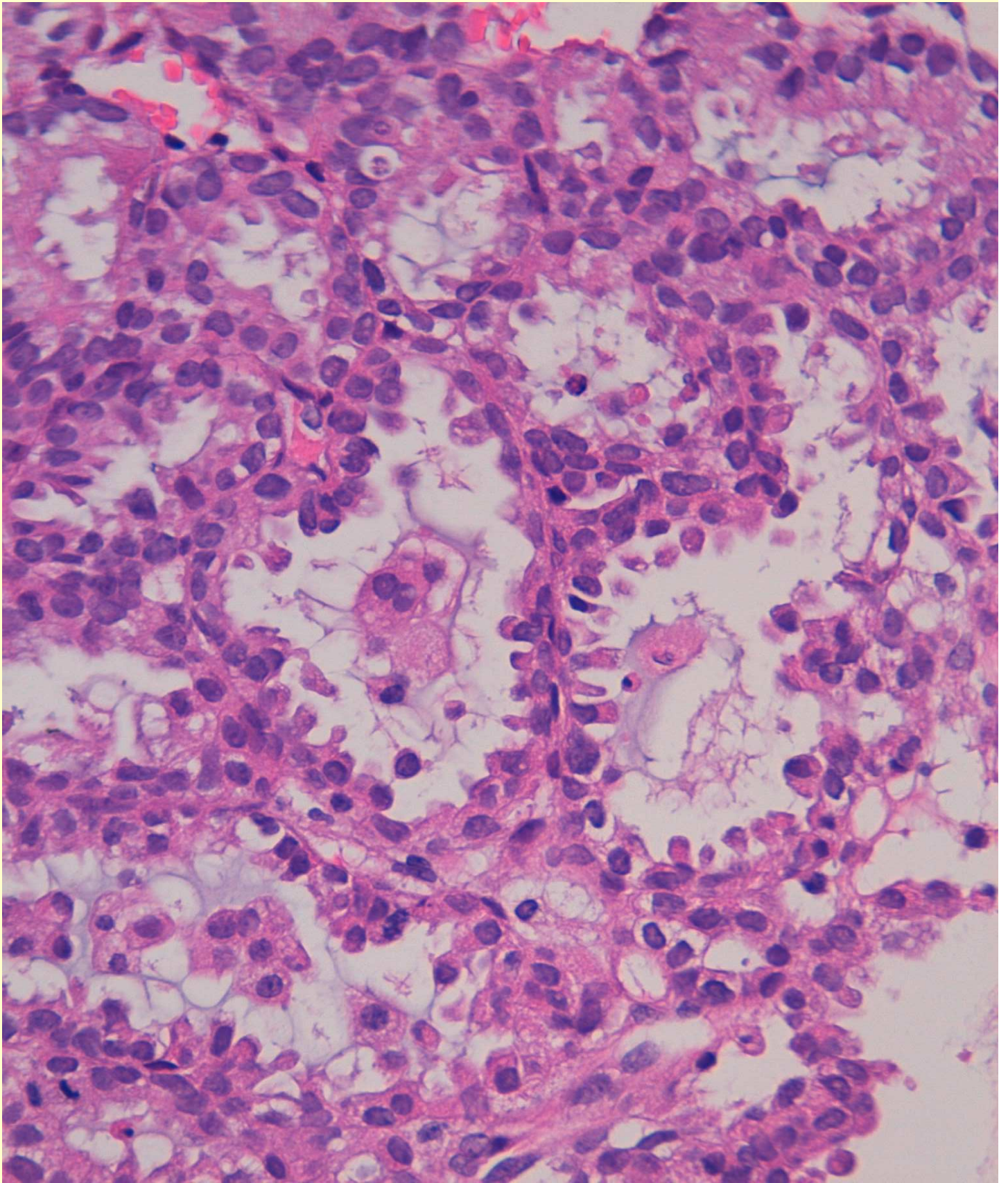
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**Neuroendocrine carcinoma**

# Clear cell Carcinoma of the Endometrium





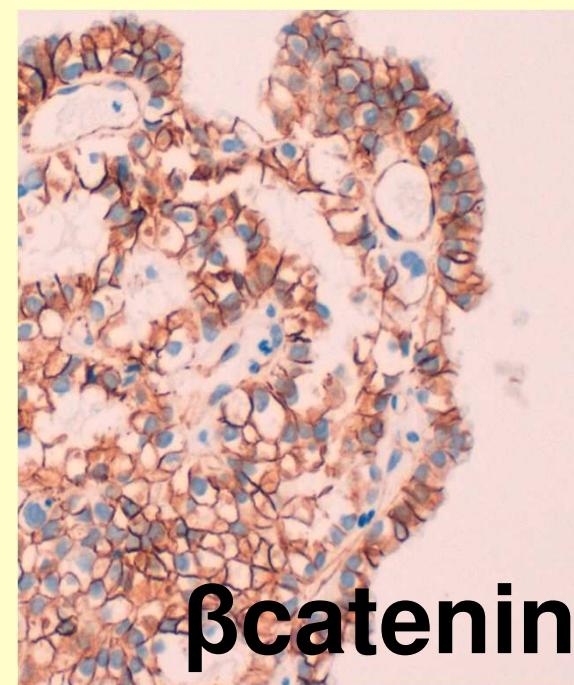
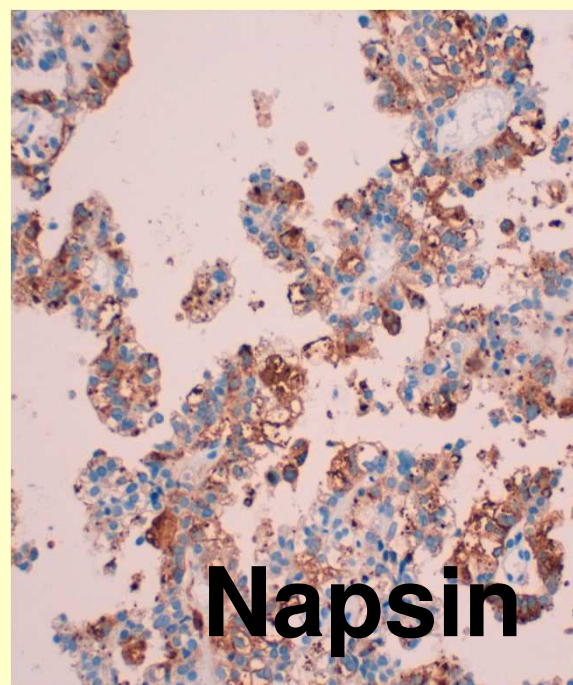
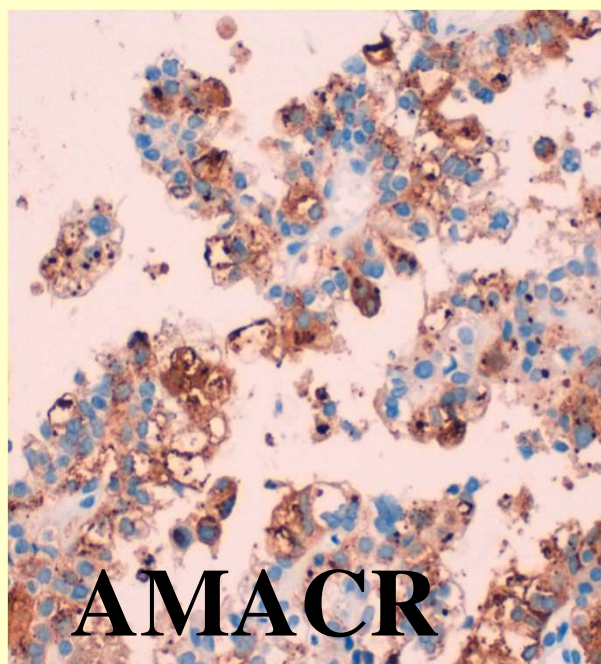
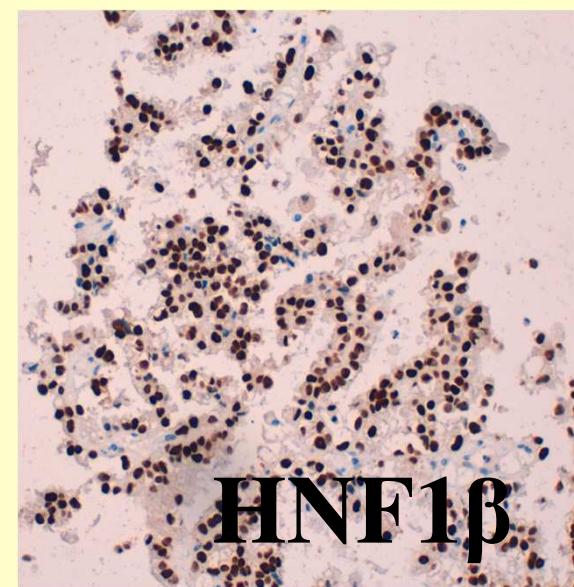
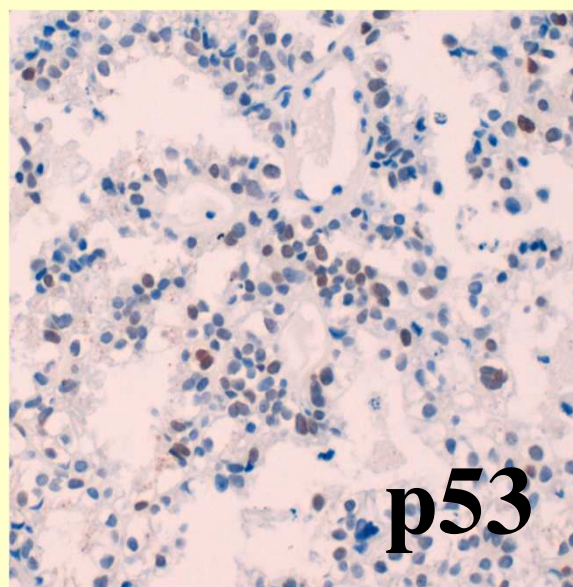
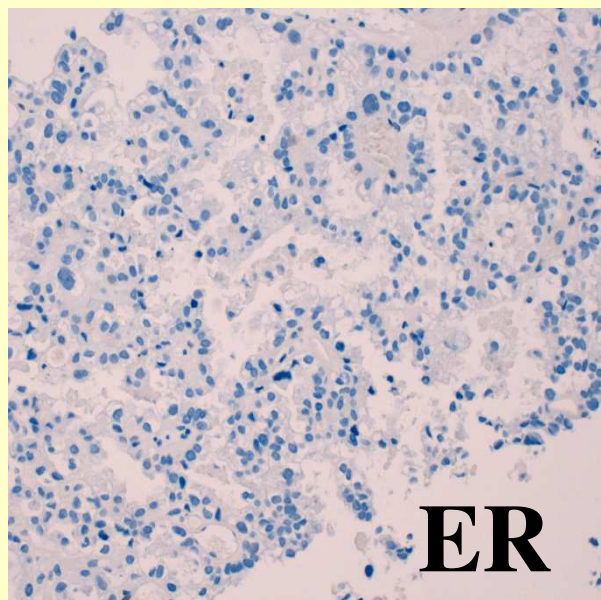




# Clear Cell carcinoma of the endometrium

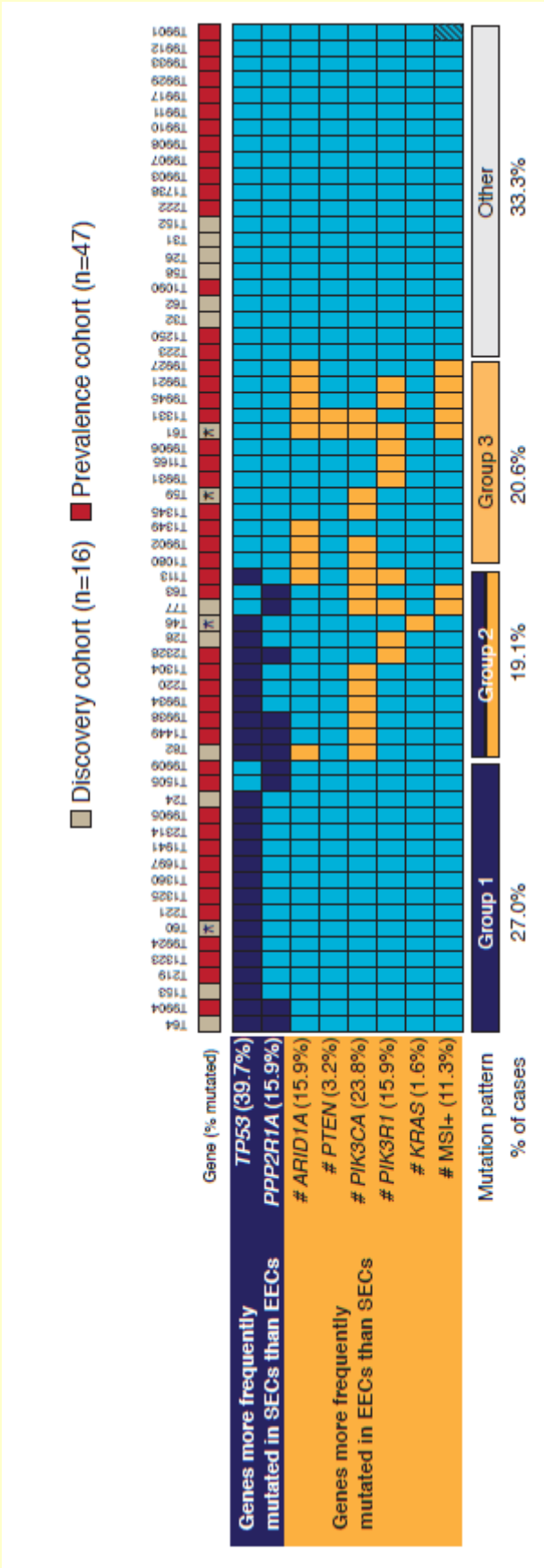
- Admixture of patterns (glandular, papillary, solid, cystic)
- Clear cells and eosinophilic cells
- Low mitotic index
- Cell stratification unusual
- Hyaline bodies, hyaline papillae, hobnail cells

*Fadare O, Am J Cancer Res 2013*



# Somatic Mutation Profiles of Clear Cell Endometrial Tumors Revealed by Whole Exome and Targeted Gene Sequencing

Matthieu Le Gallo, PhD<sup>1</sup>; Meghan L. Rudd, MS<sup>1</sup>; Mary Ellen Urlick, PhD<sup>1</sup>; Nancy F. Hansen, PhD<sup>1</sup>; Suiyuan Zhang, MS<sup>2</sup>; NISC Comparative Sequencing Program<sup>3</sup>; Fred Lozy, PhD<sup>1</sup>; Dennis C. Sgroi, MD<sup>4,5,6</sup>; August Vidal Bel, MD [ID](#)<sup>7,8</sup>; Xavier Matias-Guiu, MD, PhD<sup>8,9</sup>; Russell R. Broadus, MD, PhD<sup>10</sup>; Karen H. Lu, MD<sup>10</sup>; Douglas A. Levine, MD<sup>11</sup>; David G. Mutch, MD<sup>12</sup>; Paul J. Goodfellow, PhD<sup>13</sup>; Helga B. Salvesen, MD, PhD<sup>14,15†</sup>; James C. Mullikin, PhD<sup>1,3</sup>; and Daphne W. Bell, PhD [ID](#)<sup>1</sup>





# **Endometrial carcinoma (Histological Classification)**

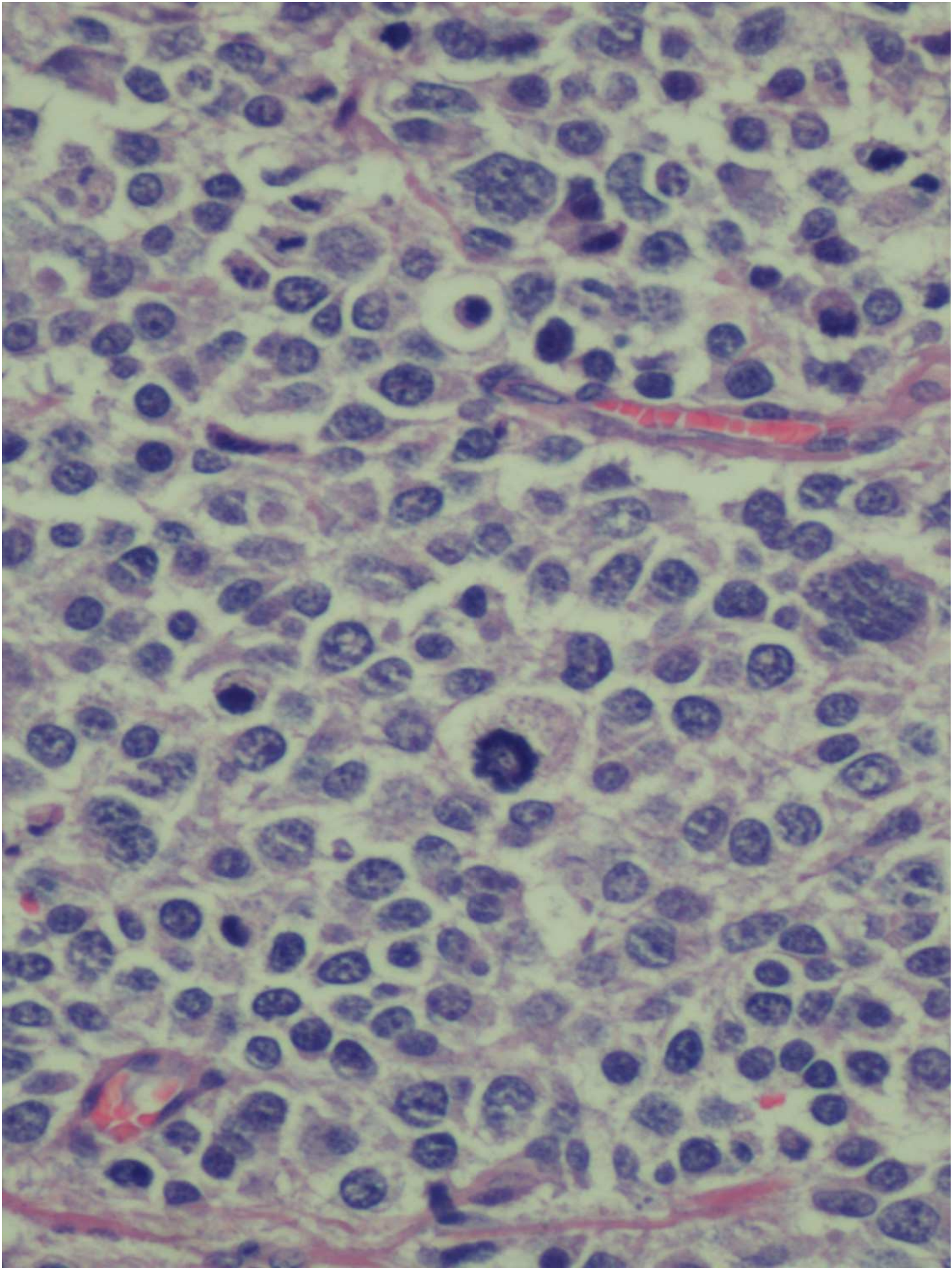
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**Neuroendocrine carcinoma**

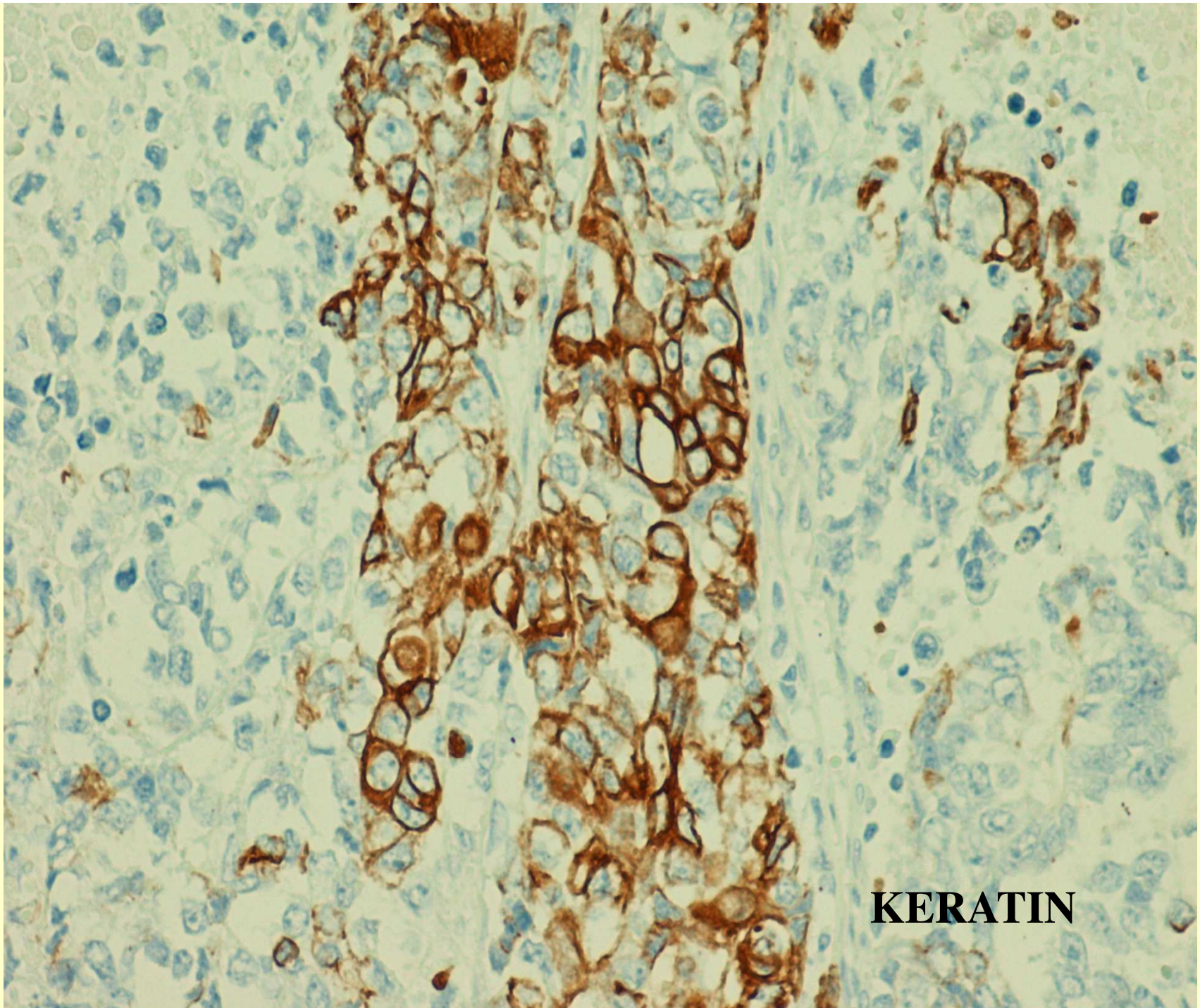


# **Undifferentiated Carcinoma of the Endometrium**

- **Unusual**
- **Solid sheets of epithelial cells, sometimes plasmacytoid-like**
- **Necrosis, mitosis**
- **Monotonous or pleomorphic**
- **5-10% positive for keratins; Positivity for EMA,**
- **Negative for E-cadherin, PAX8**
- **Frequent mismatch repair deficiency**





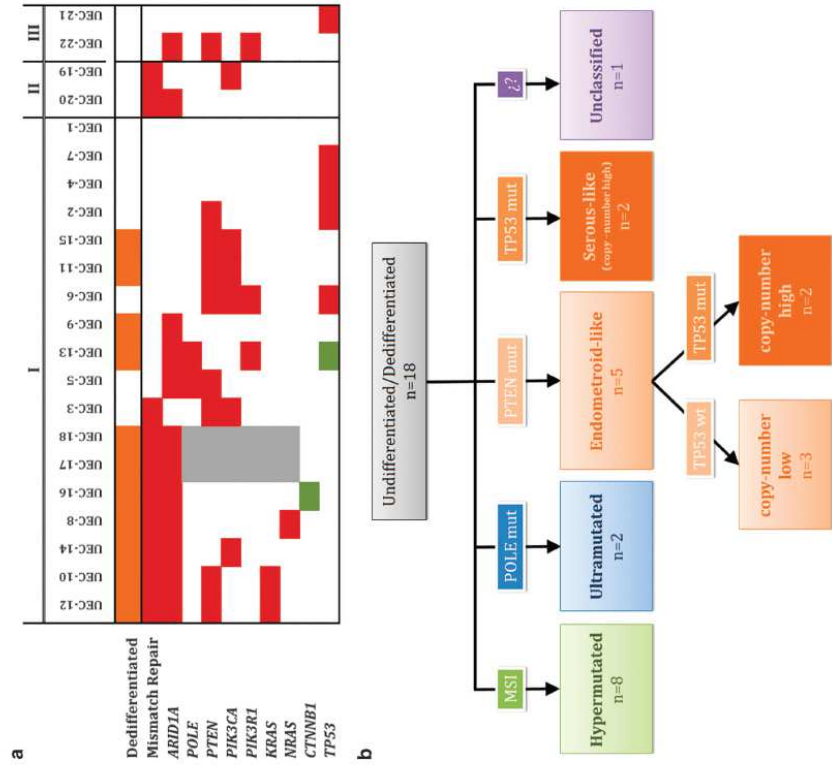
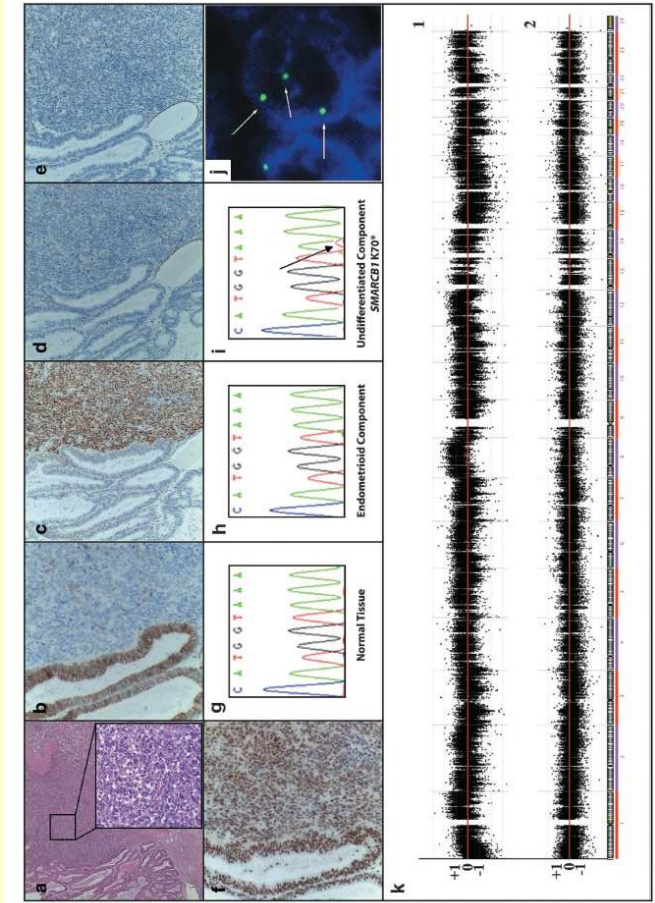


**KERATIN**



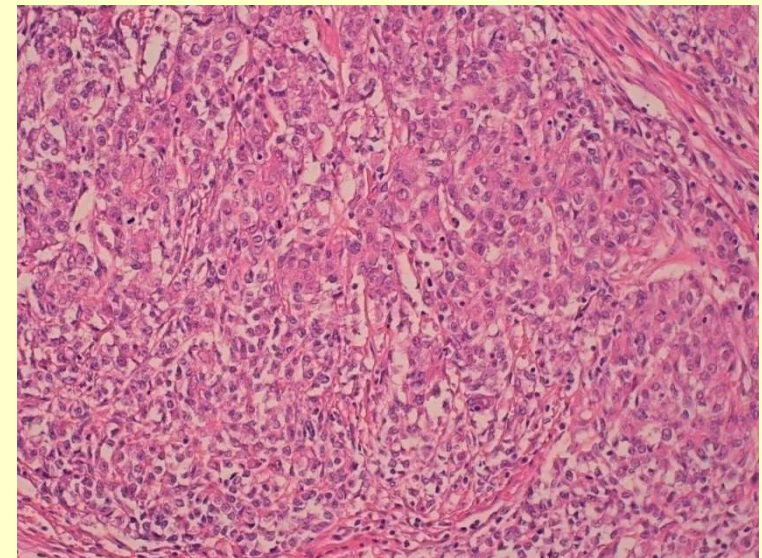
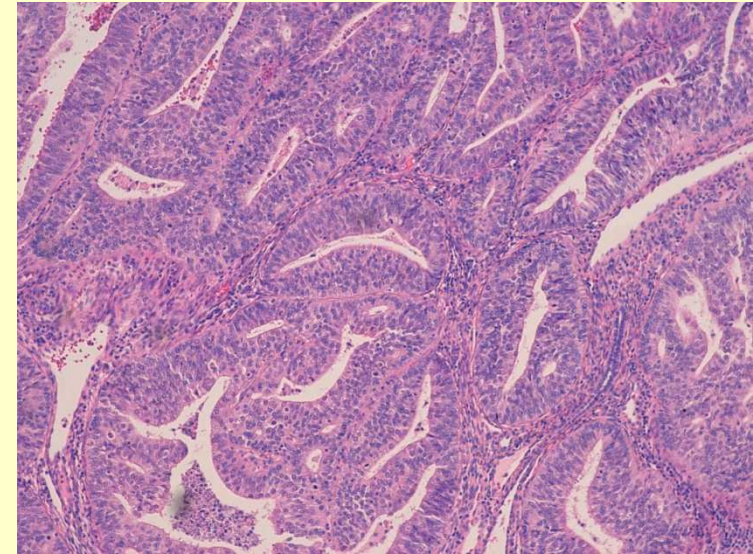
# Molecular genetic heterogeneity in undifferentiated endometrial carcinomas

Juan M Rosa-Rosa<sup>1</sup>, Susanna Leskelä<sup>1</sup>, Eva Cristóbal-Lana<sup>1</sup>, Almudena Santón<sup>1</sup>, Ma Angeles López-García<sup>2</sup>, Gloria Muñoz<sup>3</sup>, Belen Pérez-Mies<sup>1</sup>, Michele Biscuola<sup>2</sup>, Jaime Prat<sup>4</sup>, Oliva E Esther<sup>5</sup>, Robert A Soslow<sup>6</sup>, Xavier Matias-Guiu<sup>7,8</sup> and Jose Palacios<sup>1</sup>





In De-Differentiated carcinoma, both endometrioid and undifferentiated components are clonal.



**Kuhn E, Ayhan A, Bahadirli-Talbott A, Zhao C, Shih leM. Molecular characterization of undifferentiated carcinoma associated with endometrioid carcinoma. Am J Surg Pathol. 2014. 38:660-5**

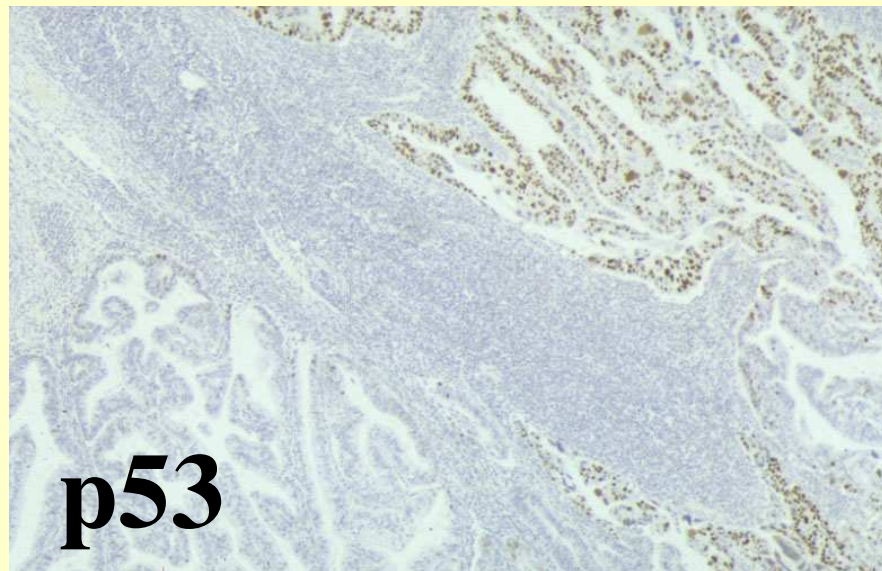
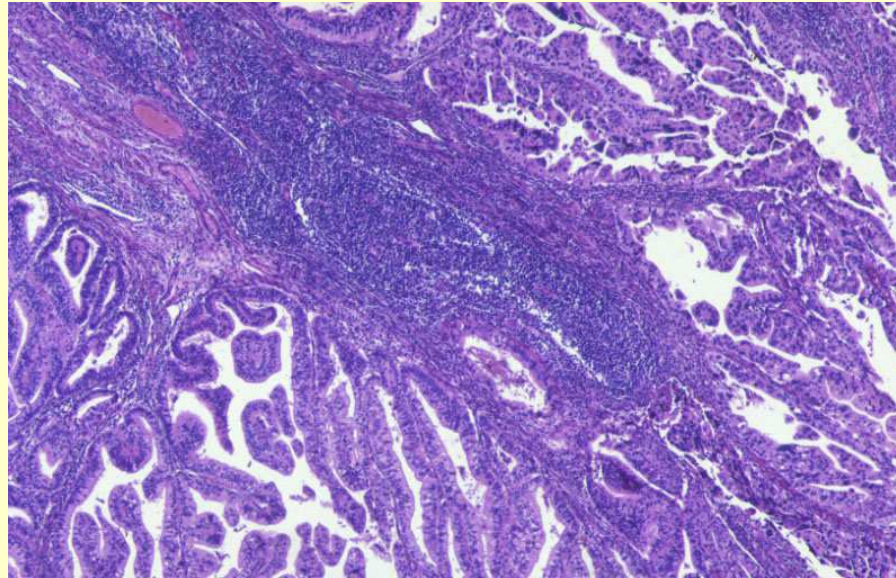
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**Neuroendocrine carcinoma**



# Mixed Endometrioid-Serous carcinomas



# **Mutation profile and clinical outcome of mixed endometrioid-serous endometrial carcinomas are different from that of pure endometrioid or serous carcinomas**

L. Coenegrachts • D. A. Garcia-Dios • J. Depreeuw • M. Santacana •  
S. Gätius • M. Zikan • P. Moerman • L. Verbist • D. Lambrechts •  
Xavier Matias-Guiu • Frédéric Amant



	<b>EEC in mixed</b>	<b>Pure EEC</b>	<b>SC in mixed</b>	<b>Pure SC</b>
PTEN	11.8 %	19.6%	7.1%	2.9%
p53	8.8%	1.7%	14.3%	17.1%

Hussein Y, Weigelt B, Levine D, Schoolmeester JK, Dao LN, Balzer BL, Liles G, Karlan B, Köbel M, Lee C, Soslow RA

Clinicopathological analysis of endometrial carcinomas harboring somatic POLE exonuclease domain mutations

Mod Pathol 2015 28:505-14

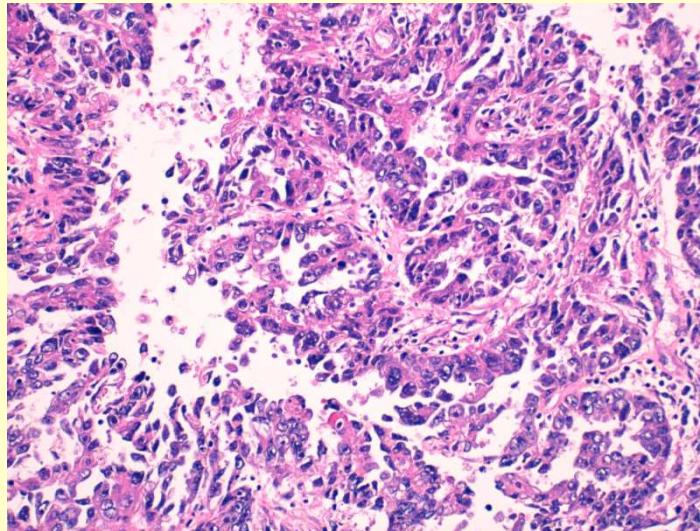
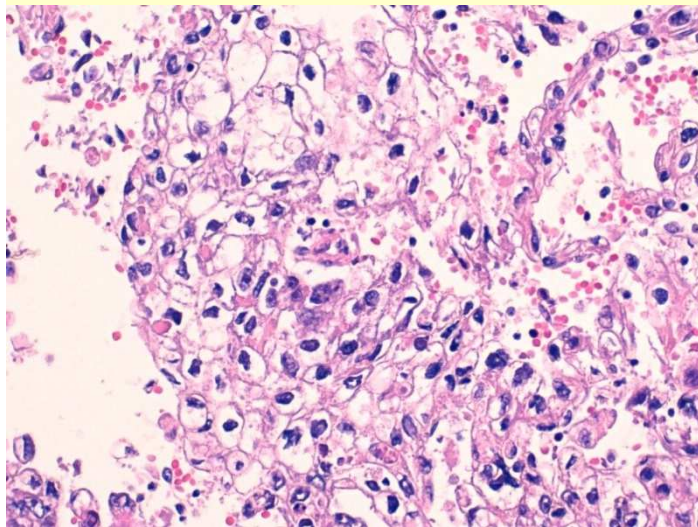
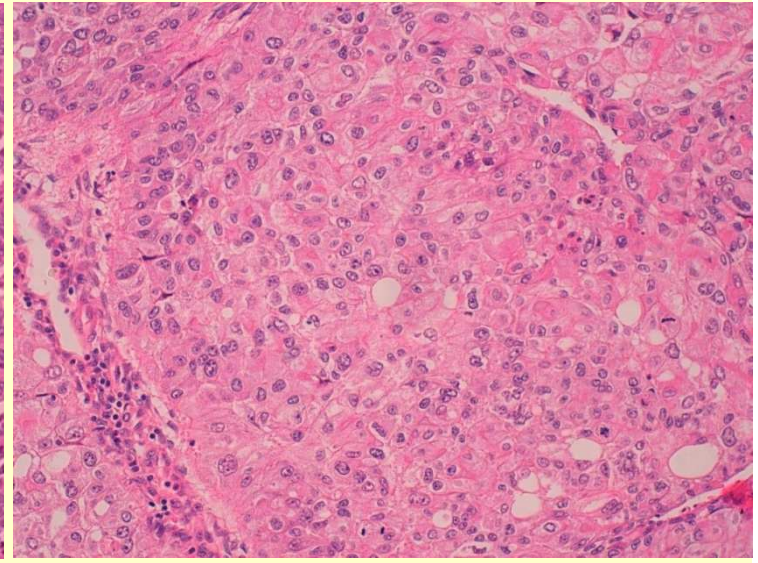
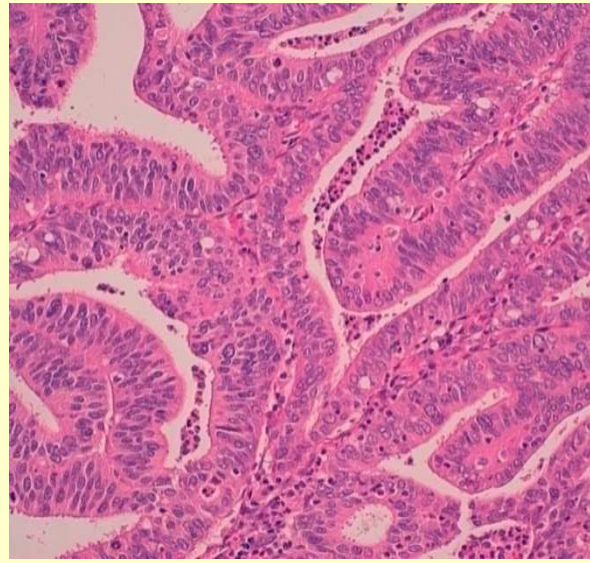
Conlon N, Da Cruz A, Ashley C, Segura S, De Brot L, M da Silva E, Soslow RA, Weigelt B, DeLair D:

Endometrial Carcinomas with a "Serous" Component in Young Women Are Enriched for DNA Mismatch Repair Deficiency, Lynch Syndrome, and POLE Exonuclease Domain Mutations

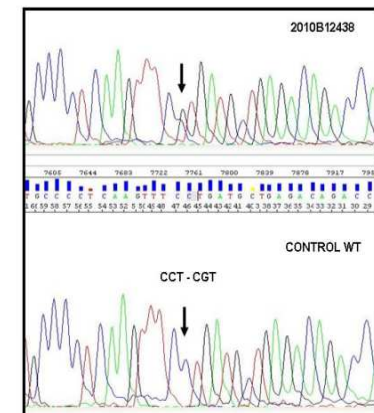
Am J Surg Pathol . 2020 44:641-648



# Heterogenous POLE-mutated EC



POL E exon 9 P286R

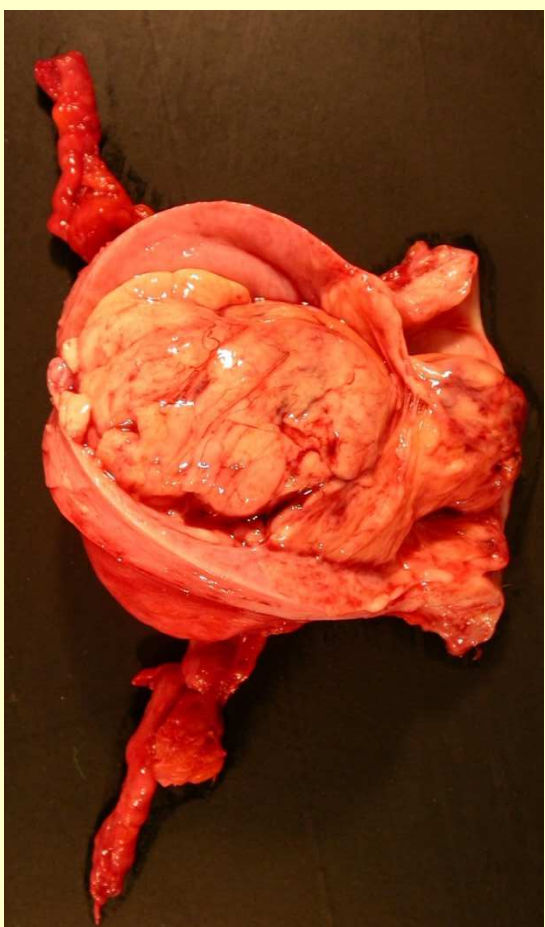
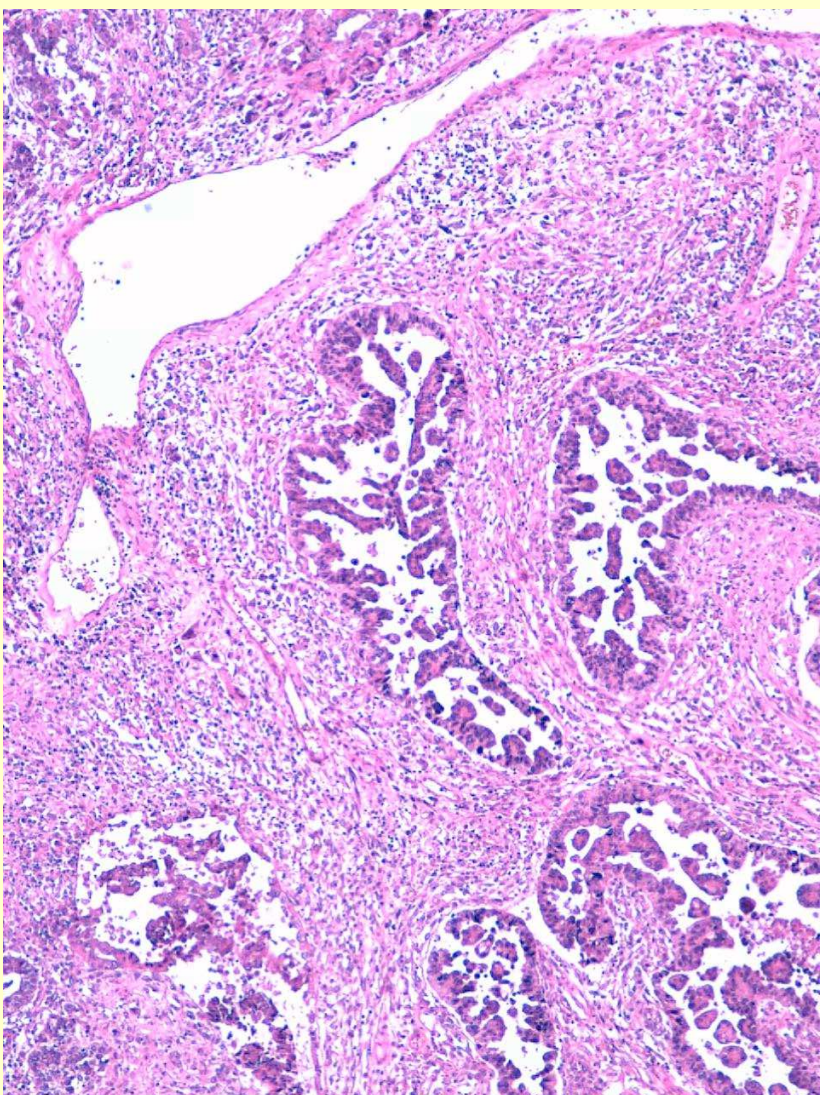


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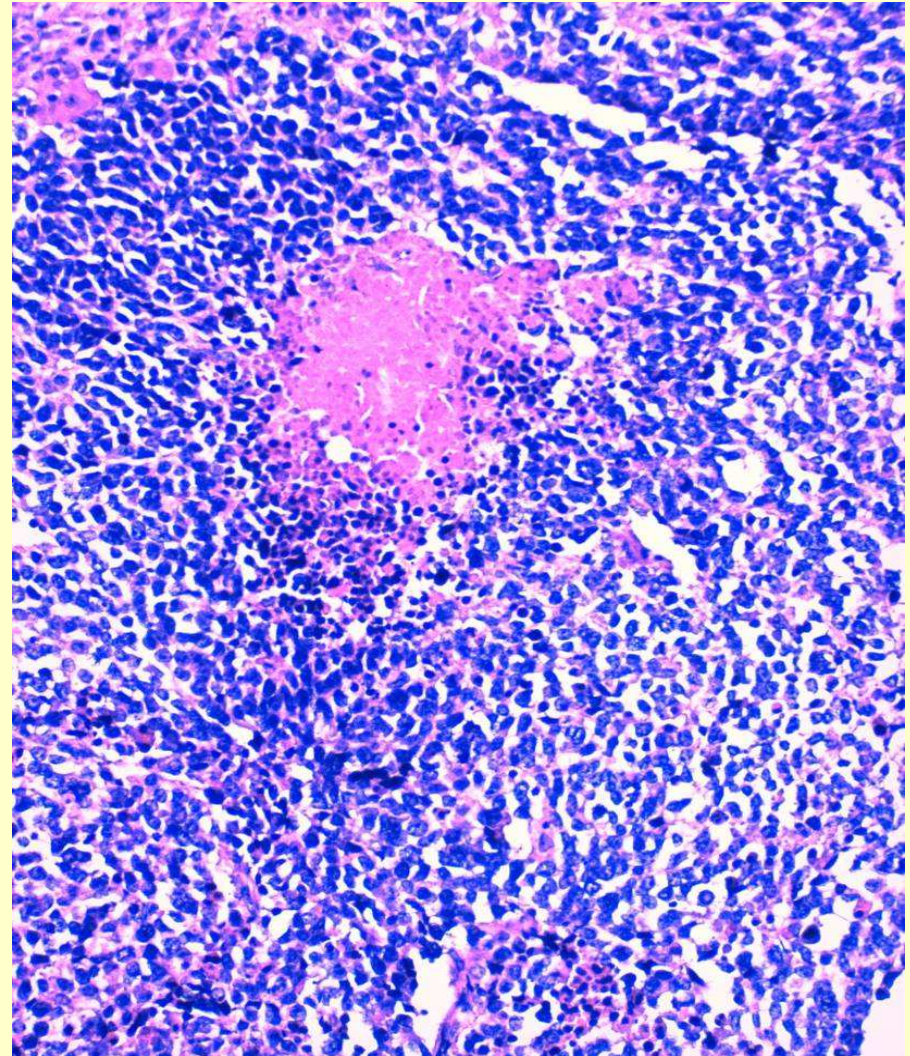
**Neuroendocrine carcinoma**



# **Neuroendocrine Carcinoma of the Endometrium**

- **Pure or mixed, most often with endometrioid carcinoma**
- **Large cell, small cell, mixed**
- **Positive for Synaptophysin, chromogranin A or CD56), and may be negative for keratins**
- **p16 and CD117 may be positive**
- **Mismatch repair deficiency in some cases**
- **Some overlap with undifferentiated ca**
- **50% of patients died of disease.**

# Neuroendocrine Carcinoma of the Endometrium





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**Neuroendocrine carcinoma**

# Endometrial cancer (Emerging Entities)

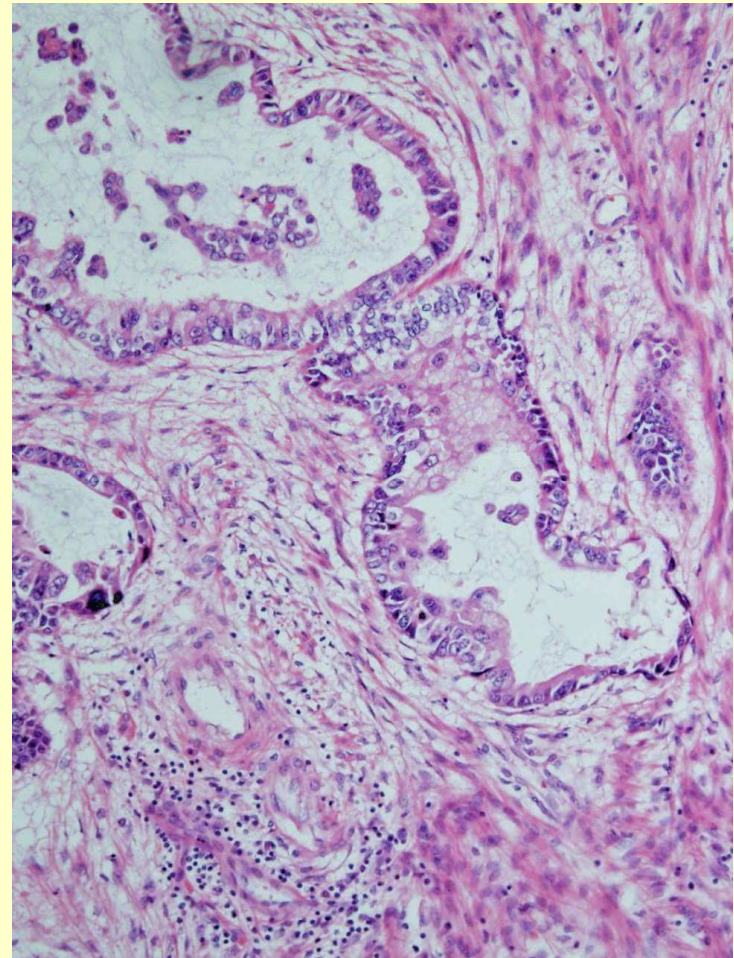
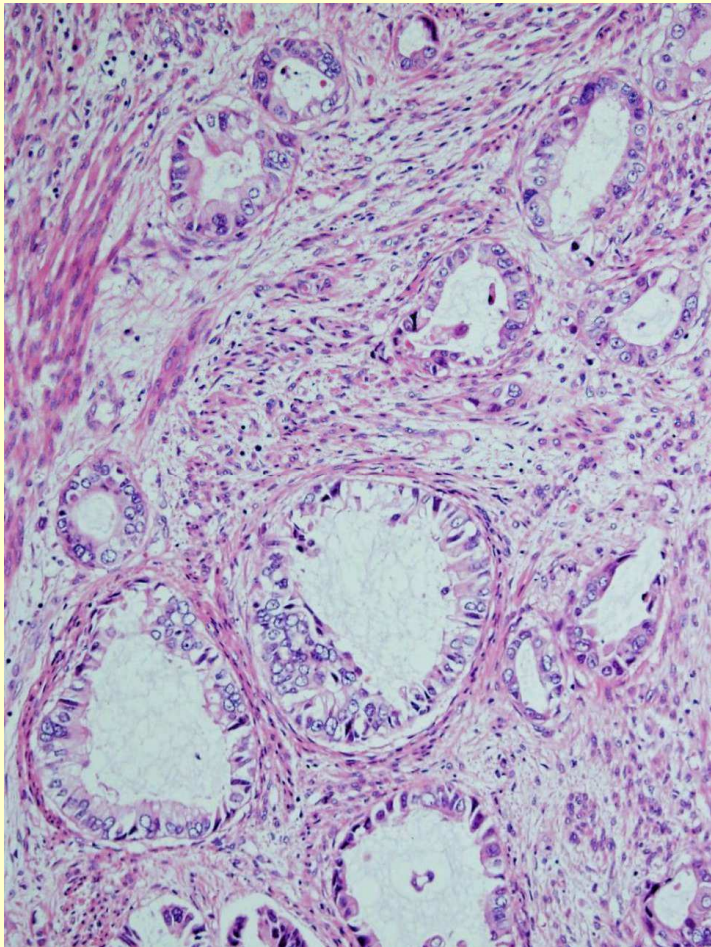
- Gastric-Type adenocarcinoma
- Mesonephric-like adenocarcinoma



# Gastric- type adenocarcinoma of the endometrium

- Similar to the cervical tumor
- A few cases described in Japan and USA
- Cells with mucinous appearance, distinct cytoplasmic borders, gastro-intestinal differentiation
- Worse behaviour than mucinous “endometrioid” tumors.
- Deep myoinvasion, positive LNs.

# Gastric- type adenocarcinoma of the endometrium

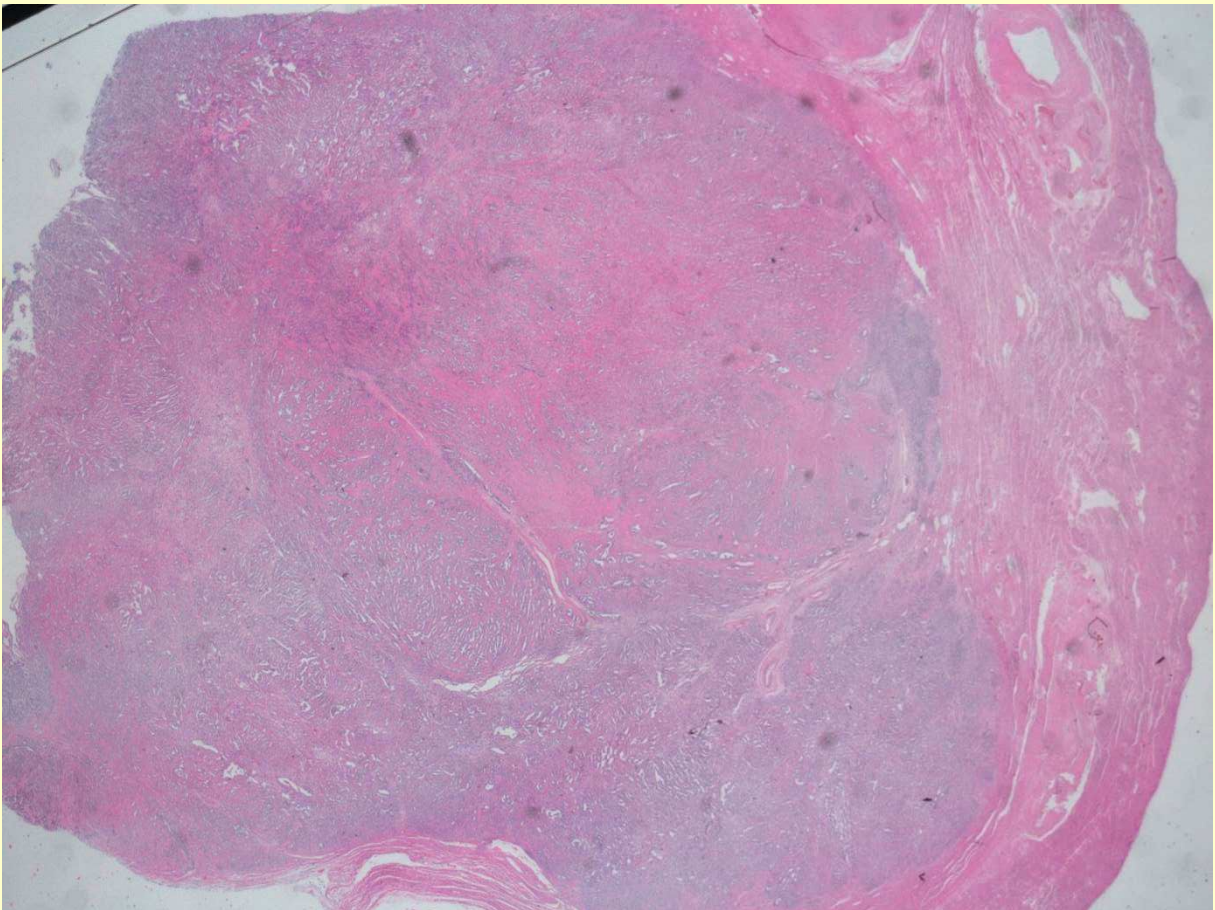
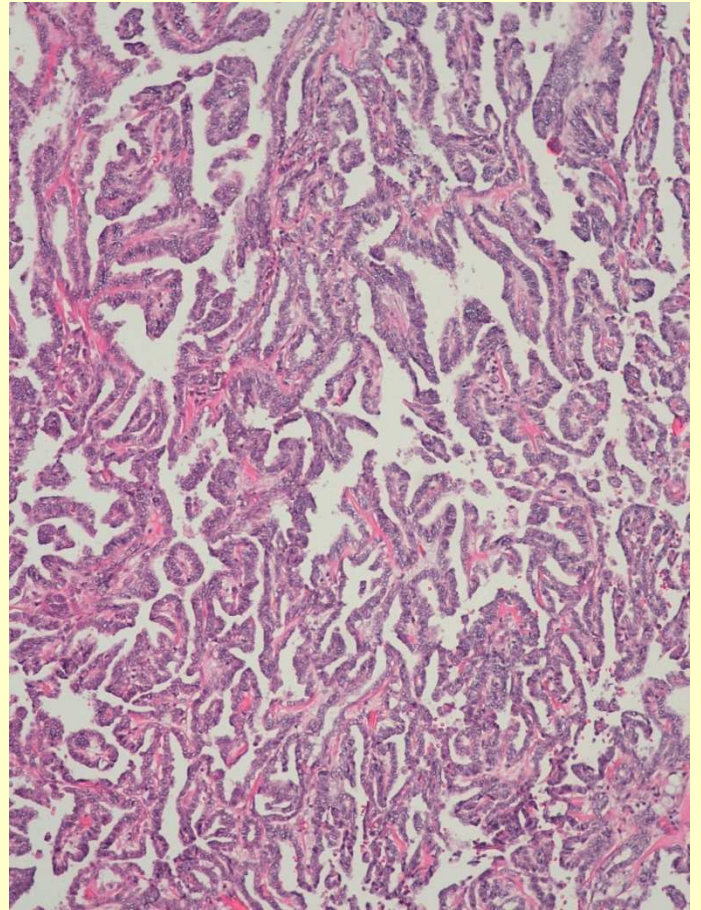
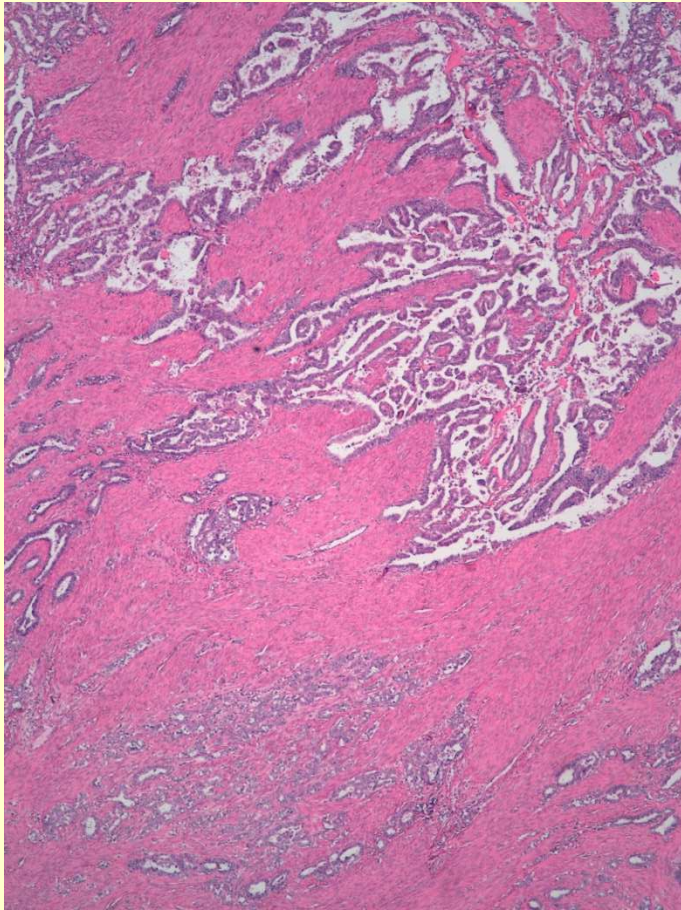




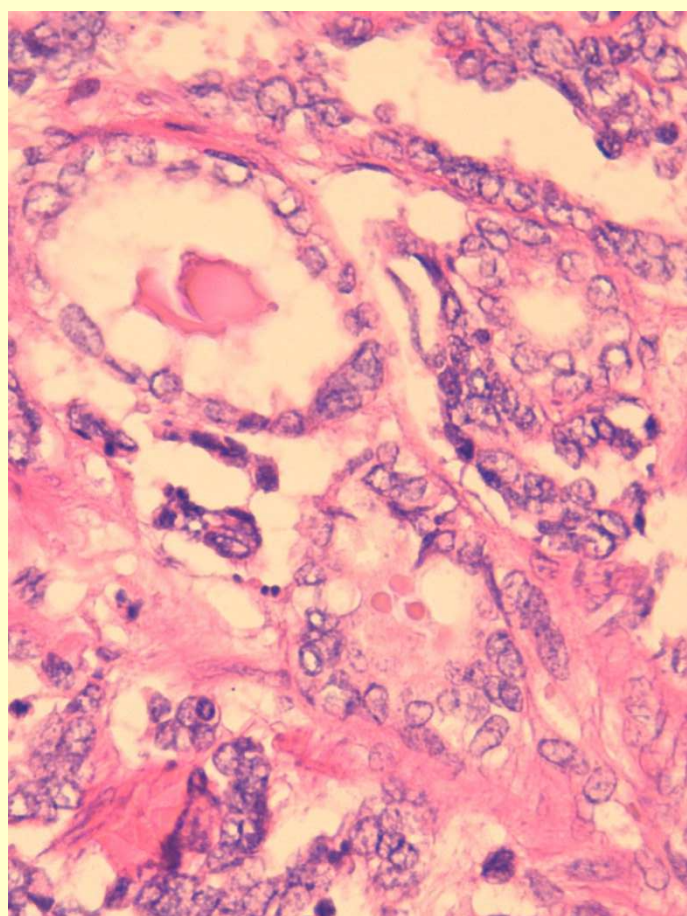
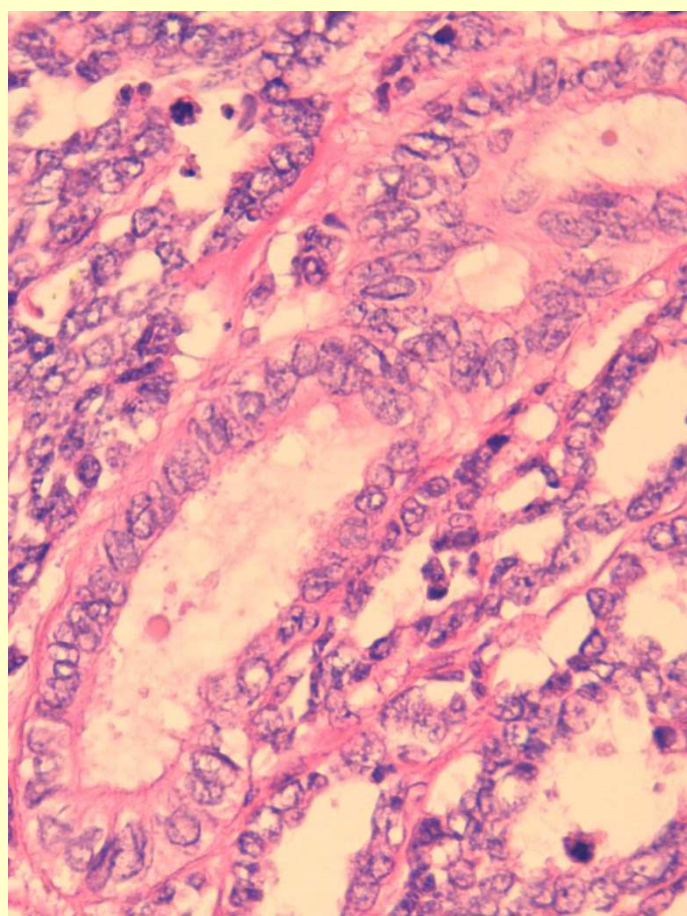
# Mesonephric-like adenocarcinoma of the endometrium

- Similar to the cervical mesonephric carcinoma
- Admixture of architectural patterns (small tubules/glands, colloid-like material, papillary, solid) (similar to thyroid carcinomas)
- Positive for PAX8, TTF1, CD10, GATA3, calretinin
- Negative for ER/PR, WT1
- p53 wild-type,
- Visceral metastasis









# Pathologic classification strenghts

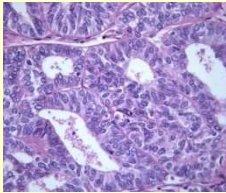
- Different types of tumors with different morphologic features, precursor lesions, natural histories, and molecular features
- Pathologic classification allows distinction between low grade (70%) and high grade tumors (30%) , which is prognostically relevant.



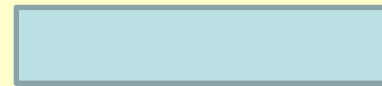
# LOW GRADE AND HIGH GRADE ENDOMETRIAL CARCINOMAS



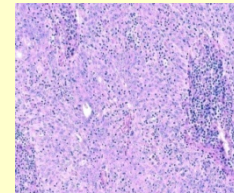
70%  
EEC 1,2



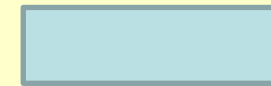
**LOW-GRADE**



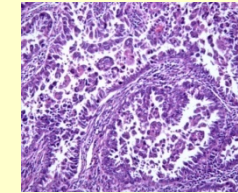
17%  
EEC 3



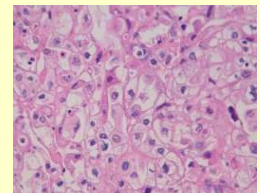
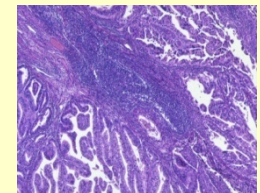
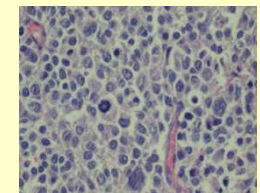
**HIGH-GRADE**



10%  
SC



3%  
other  
Undiff  
Mixed  
Clear  
Cell



# Pathologic classification limitations

1-Poor interobserver reproducibility in high grade carcinomas

2- Some histotypes are heterogenous regarding prognosis (grade 3 EEC)

3- In the high grade group, maybe histologic typing is not as relevant as in the low grade group



# Summary

- Pathologic Classification
- Molecular Classification

# Endometrial carcinoma

## TCGA, 2013

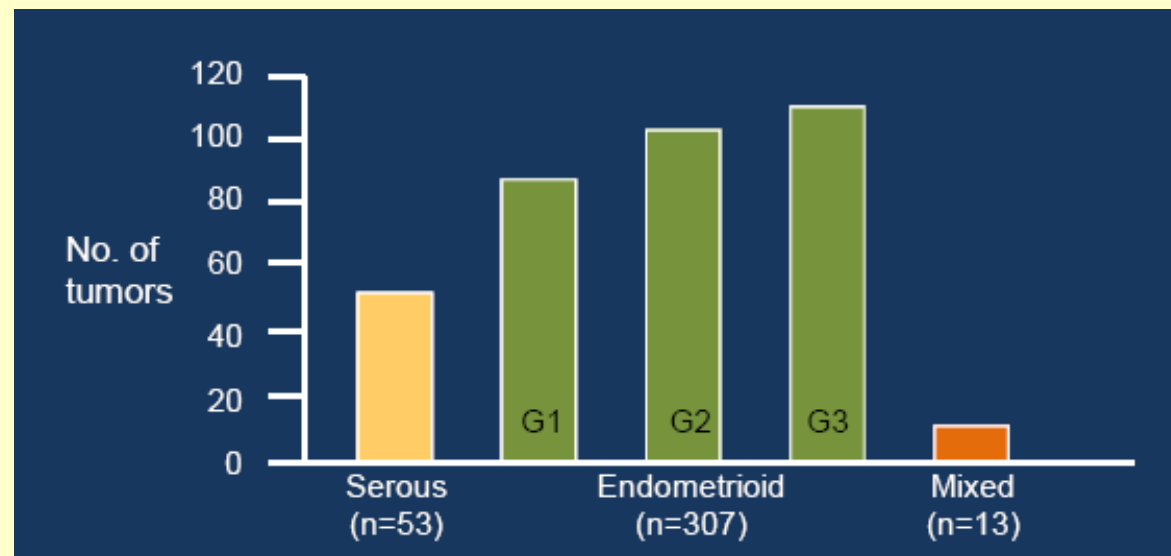
ARTICLE

OPEN

doi:10.1038/nature12113

## Integrated genomic characterization of endometrial carcinoma

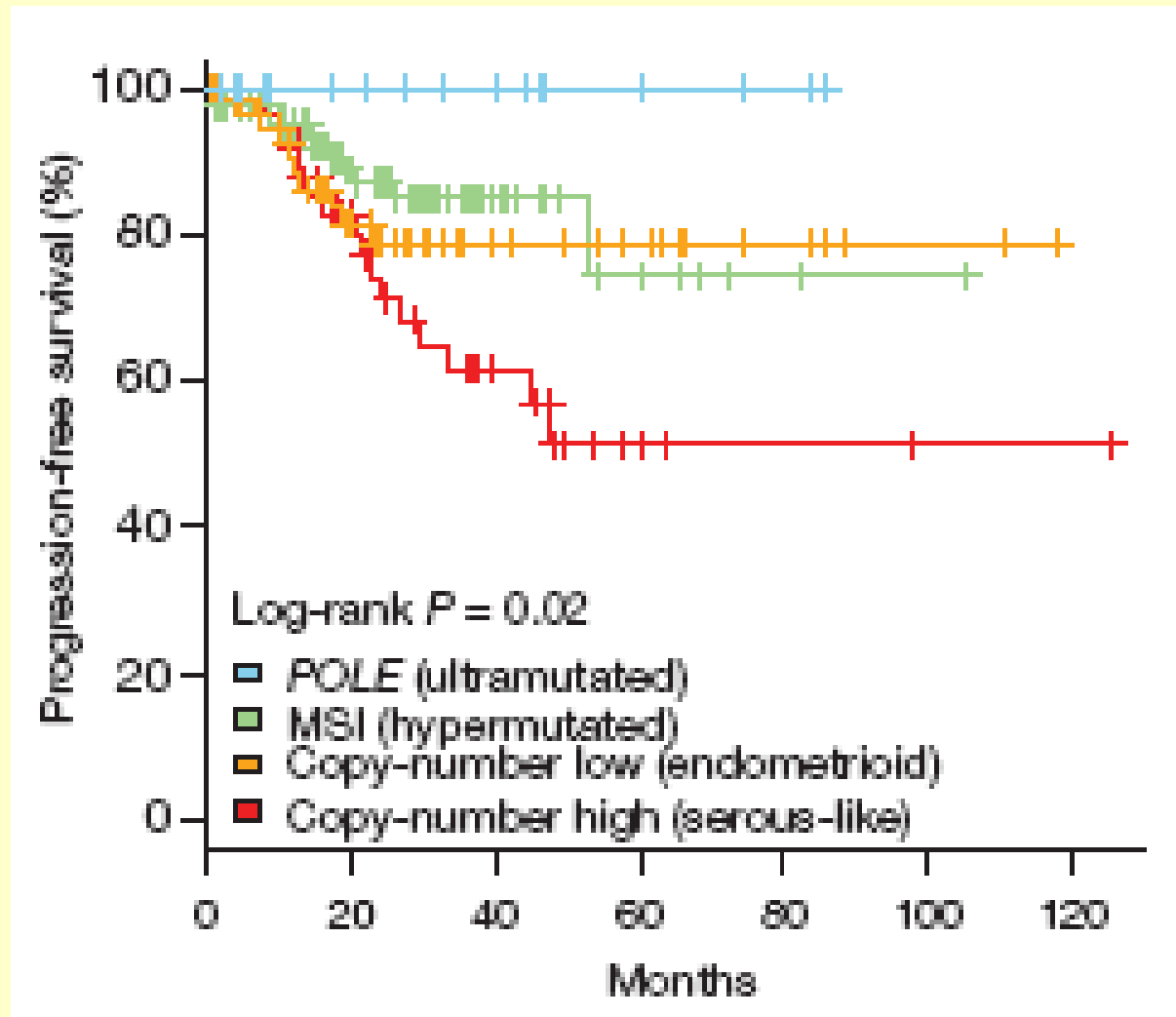
The Cancer Genome Atlas Research Network\*





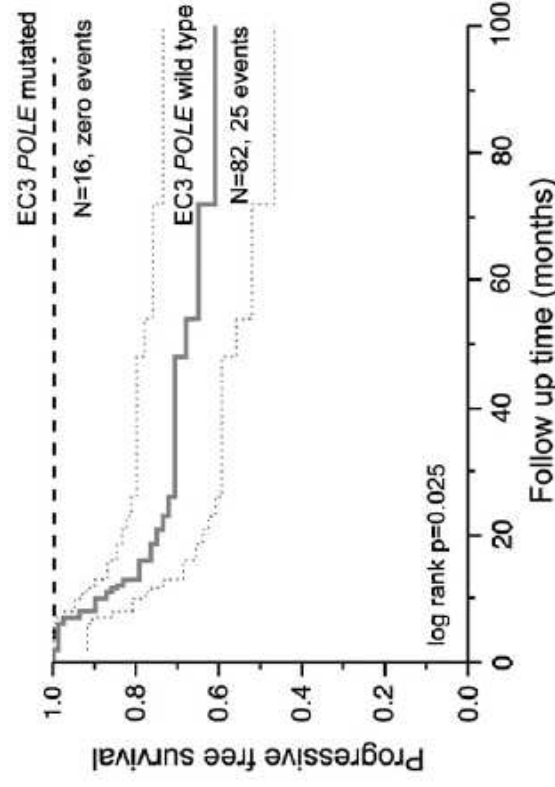
# Endometrial carcinoma

## TCGA, 2013

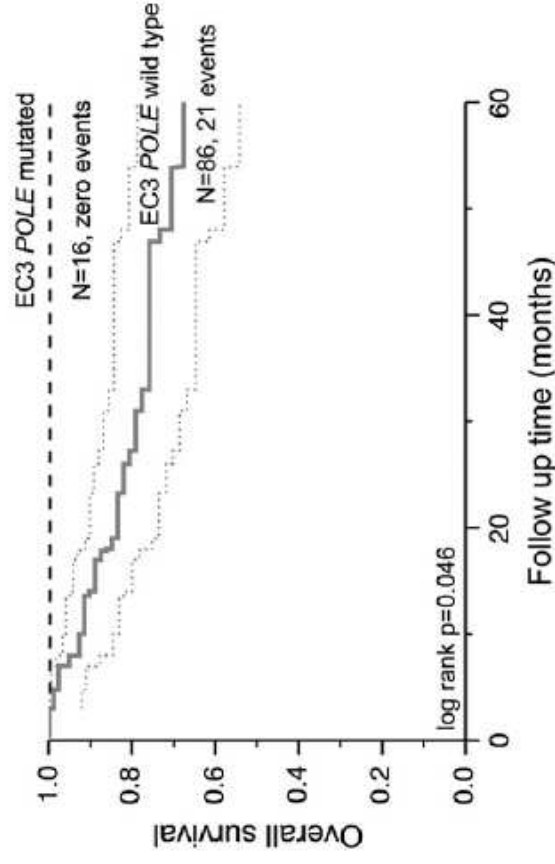


# *POLE* exonuclease domain mutation predicts long progression-free survival in grade 3 endometrioid carcinoma of the endometrium

Bo Meng<sup>a</sup>, Lien N. Hoang<sup>b</sup>, John B. McIntyre<sup>c</sup>, Máire A. Duggan<sup>d</sup>, Gregg S. Nelson<sup>e</sup>,  
Cheng-Han Lee<sup>a\*,1</sup>, Martin Köbel<sup>d,1</sup>



**Fig. 1.** Progression-free survival analysis in grade 3 endometrial endometrioid-type carcinoma stratified based on *POLE* exonuclease domain mutation status in combined HGEC and TCGA [5] cohorts. EC3, grade 3 endometrioid carcinoma. Dotted lines, 95% confidence intervals.

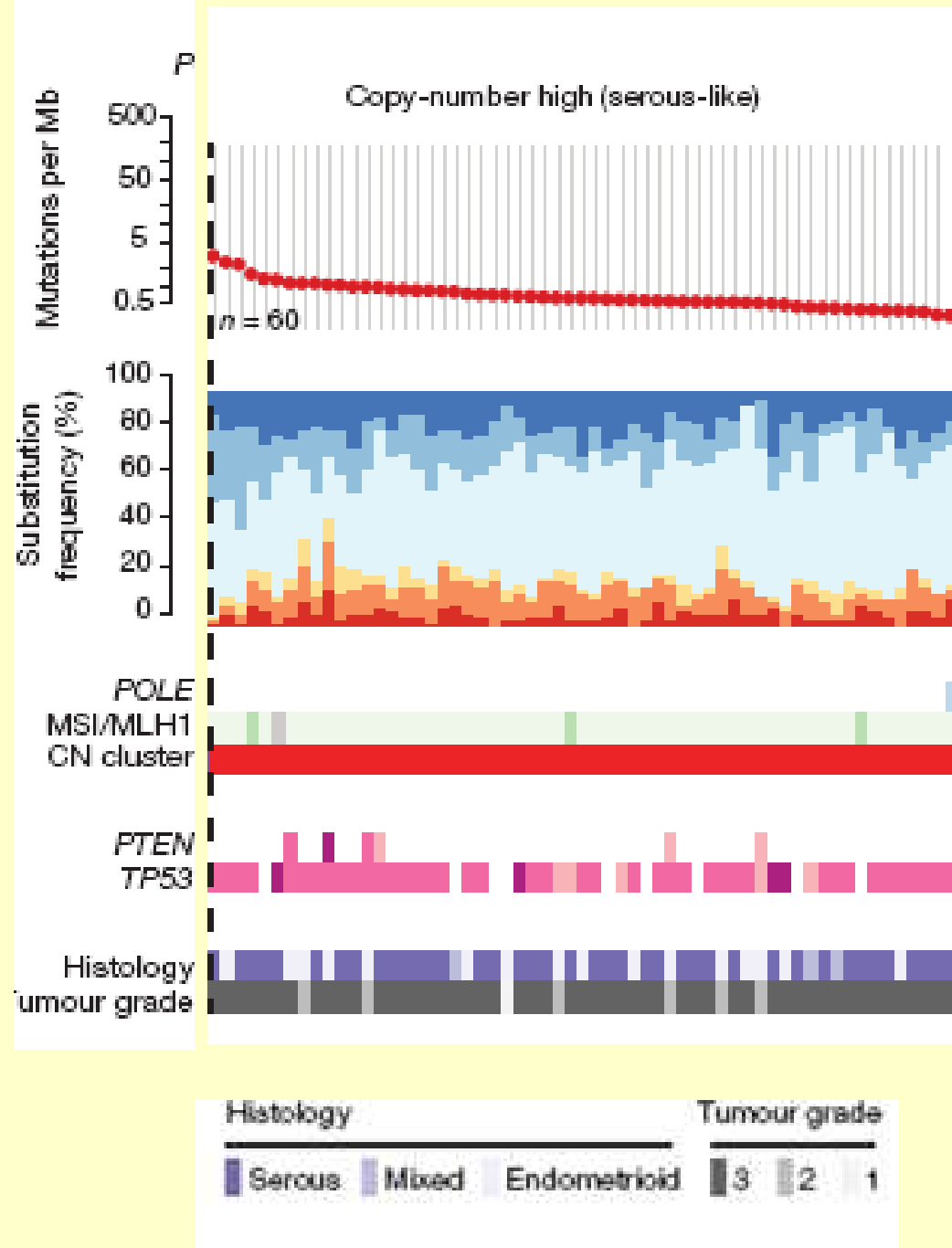


**Fig. 3.** Overall survival analysis in grade 3 endometrial endometrioid carcinoma stratified based on *POLE* exonuclease domain mutation status in combined HGEC and TCGA [5] cohorts. EC3, grade 3 endometrioid carcinoma. Dotted lines, 95% confidence intervals.



## Group 4, Serous-like tumors

Serous (94%),  
mixed ca (62%),  
endometrioid ca  
(12%, usually  
grade 3) with  
p53 mutations  
and recurrent  
amplifications  
(MYC, ERBB2,  
CCNE1, FGFR3,  
SOX17)



# Bringing TCGA subtyping into pathology in high-grade endometrial carcinomas

**POLE mutation  
(hypermuted)**

**POLE mutated EC**

**POLE wild-type, p53 abnormal expression:**

**Serous-like EC**

**POLE wild-type, p53 wild-type pattern,  
abnormal mismatch repair:**

**EEC with  
microsatellite instability**

**POLE wild-type, p53 wild-type pattern,  
normal mismatch repair**

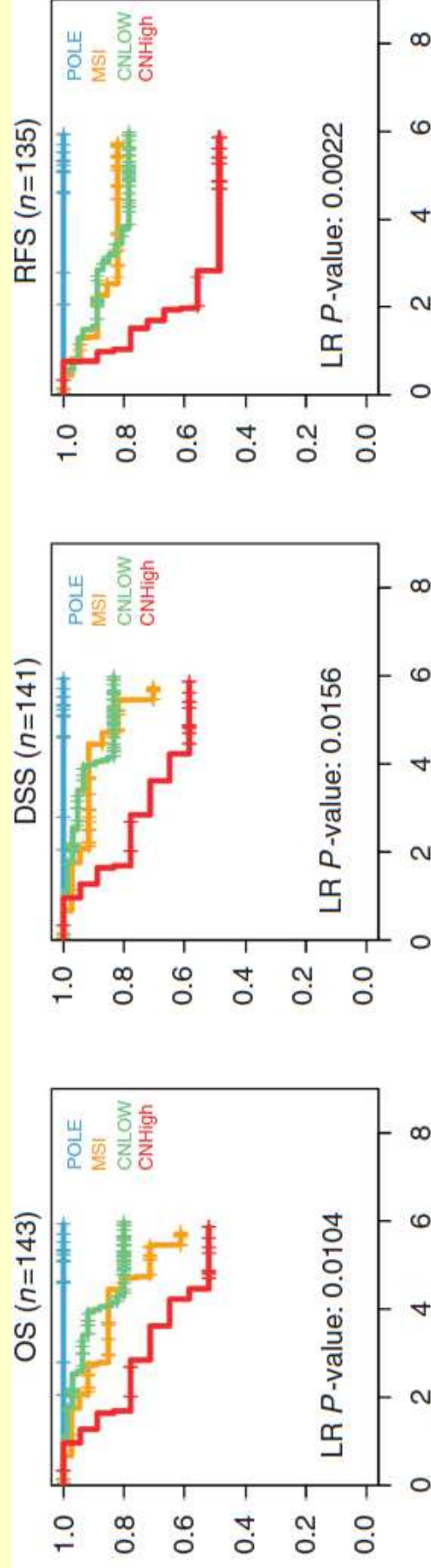
**EEC with low copy  
number alterations**



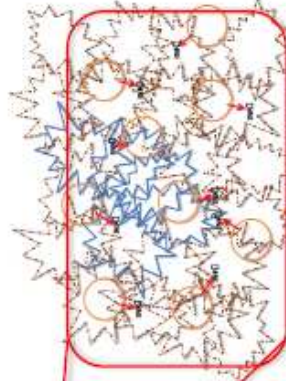
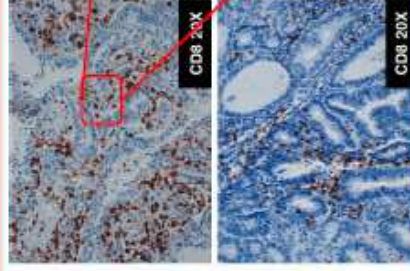
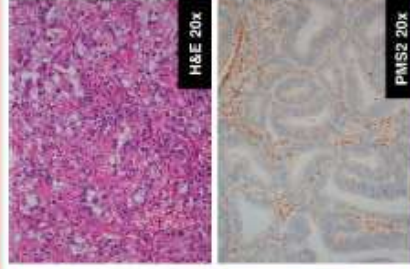
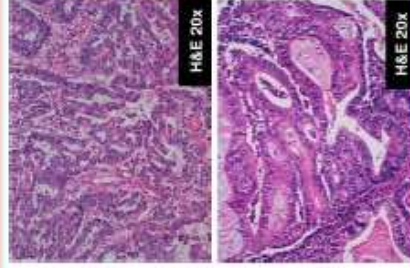
# A clinically applicable molecular-based classification for endometrial cancers

A Talhouk<sup>1</sup>, M K McConechy<sup>1</sup>, S Leung<sup>2</sup>, H H Li-Chang<sup>1,3</sup>, J S Kwon<sup>4</sup>, N Melnyk<sup>1</sup>, W Yang<sup>1</sup>, J Senz<sup>1</sup>, N Boyd<sup>1</sup>, A N Karnezis<sup>1</sup>, D G Huntsman<sup>1</sup>, C B Gilks<sup>1</sup> and J N McAlpine<sup>\*,4</sup>

British Journal of Cancer (2015) 113, 299–310

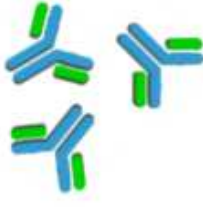


**POLE**  
Ultramutated



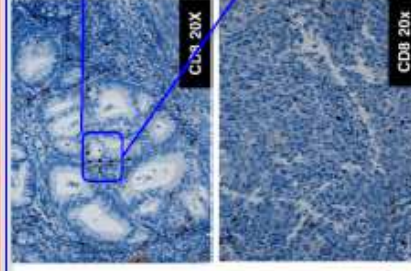
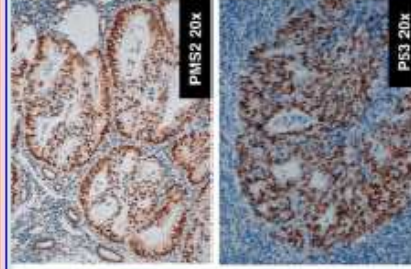
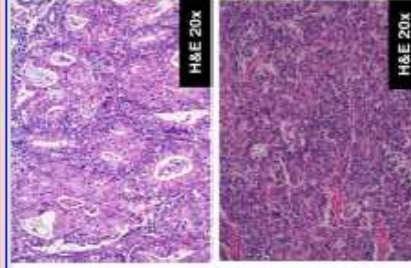
**Adaptive  
Immune resistance**

**Treatment:**



Anti-PD1

**Low Copy  
Number**



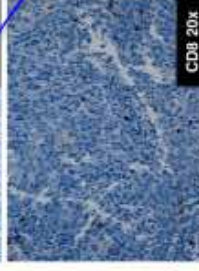
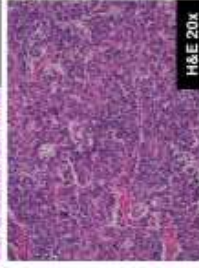
**Immunosuppression?**

**Treatment:**



Combinations?

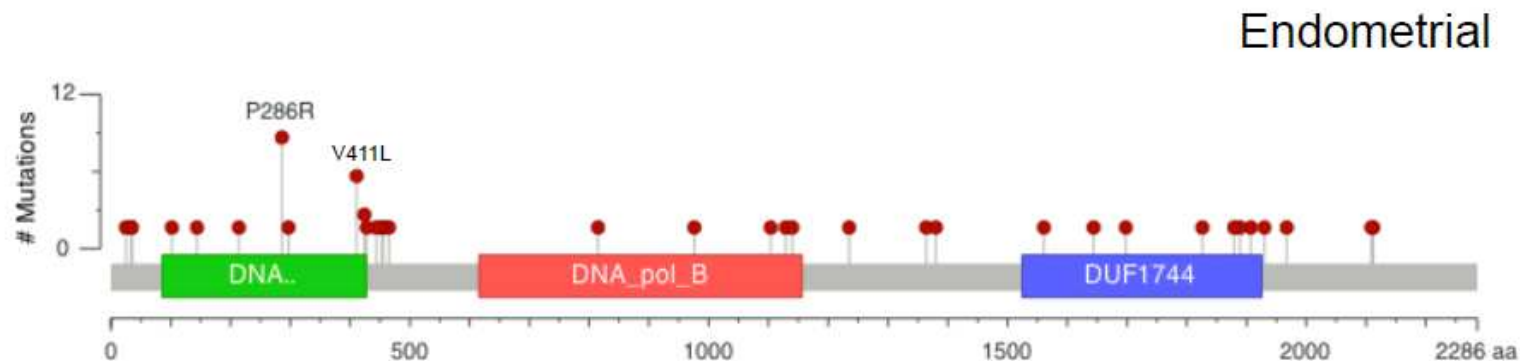
**Serous-Like**





# TCGA-based surrogate limitations

1-POLE mutation analysis is not available in all laboratories. Not all POLE mutations are associated with ultramutated status and good prognosis.



*Eve Shinbrot, HGSC; cBIO Portal*

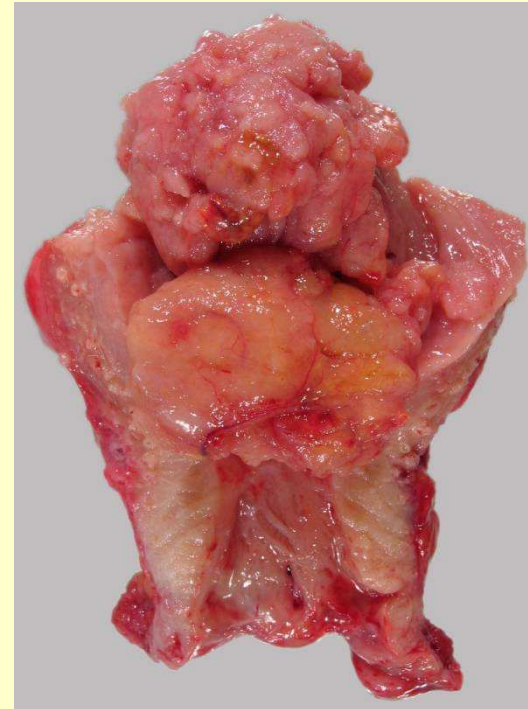
# Interpreting POLE mutations

- Functional mutations occur in the exonuclease domain, but not all mutations in the exonuclease domain are functional.
- Very unfrequently, mutations outside the exonuclease domain are functional.
- Functional mutations are: **P286R, V411L**, S297F, S459F, A456P, F367S, L424I, M295R, P436R, M444K, D368Y, (all of them in exons 9, 11, 13, 14)

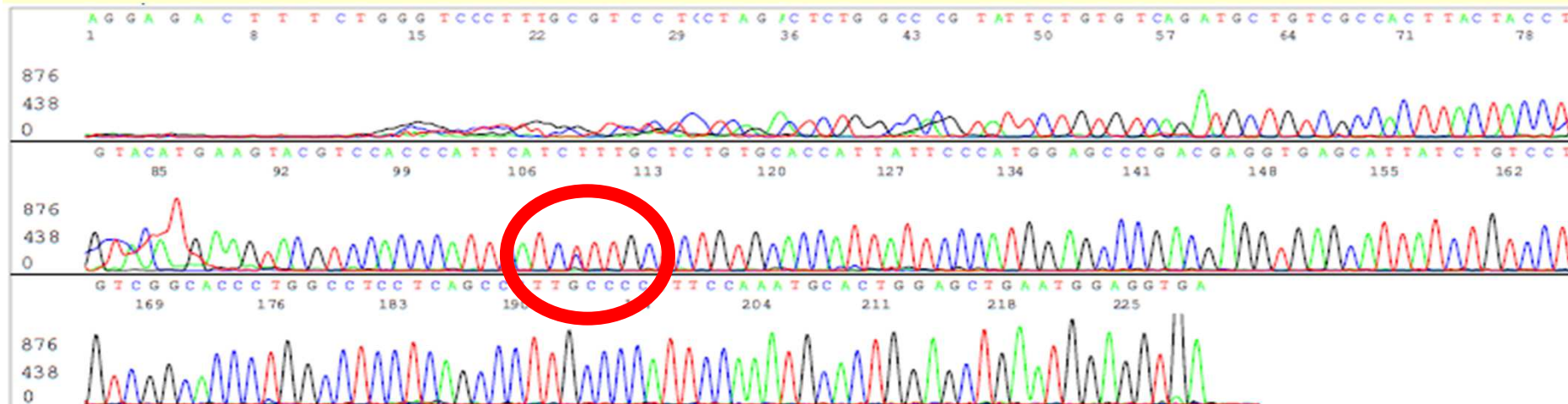
*Leon A,*



## Non functional POLE mutation in the exonuclease domain



POLE , F479L, exon 14



# Clinical outcomes of patients with *POLE* mutated endometrioid endometrial cancer

Marina Stasenکو<sup>a</sup>, Irina Tunnage<sup>a</sup>, Charles W. Ashley<sup>b</sup>, Maria M. Rubinstein<sup>c</sup>, Alicia J. Latham<sup>c,d</sup>, Arnaud Da Cruz Paula<sup>b</sup>, Jennifer J. Mueller<sup>a,d</sup>, Mario M. Leitao Jr.<sup>a,d</sup>, Claire F. Friedman<sup>c,d</sup>, Vicky Makker<sup>c,d</sup>, Robert A. Soslow<sup>b,d</sup>, Deborah F. DeLair<sup>e</sup>, David M. Hyman<sup>c,d</sup>, Dimitriy Zamarin<sup>c,d</sup>, Kaled M. Alektiar<sup>d,f</sup>, Carol A. Aghajanian<sup>c,d</sup>, Nadeem R. Abu-Rustum<sup>a,d</sup>, Britta Weigelt<sup>b,d</sup>, Karen A. Cadoo<sup>c,d,\*</sup>

- In this prospective cohort, 5% of endometrioid endometrial carcinoma have *POLE* EDM.
- 17% of *POLE*-mutant cases developed recurrences.
- Recurrences were observed in uterine-confined G3 disease after adjuvant RT.
- *De novo* metastatic disease was observed.
- Further research is warranted before changes in treatment/management are considered.

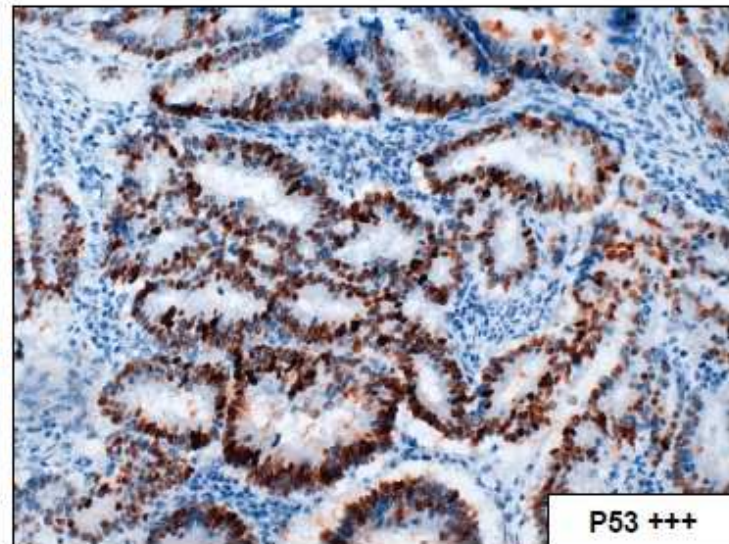
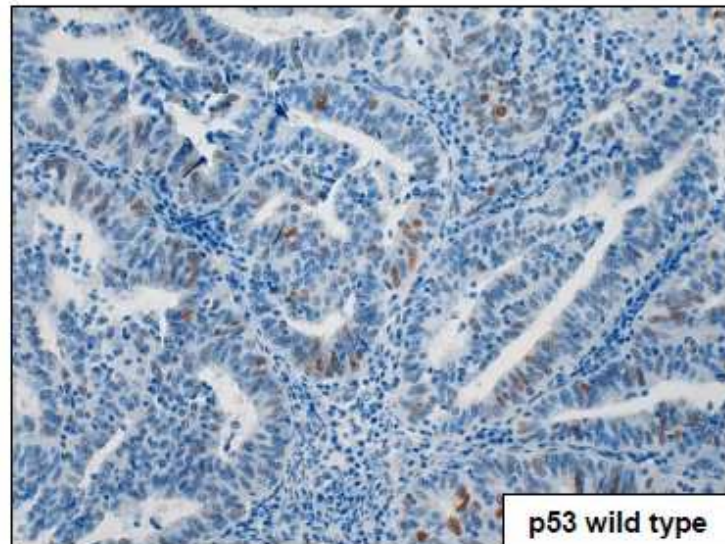
Clinical characteristics of patients with recurrent EEC.

Case	Stage	Grade	Adjuvant treatment	Time to recurrence (m)	Recurrence location	Length of FU (m)	Status at last FU
PE20	IA	3	IVRT & Chemo	146	Rectum	165	NED
PE2	IB	3	IVRT	20	Brain	42	NED
PE18	IB	3	IVRT	21	Chest wall	88	NED
PE17	III	1	IVRT	35	Vagina, liver	165	AWD
PE9	IV	2	Chemo	Progressed	Breast, then brain	33	Deceased

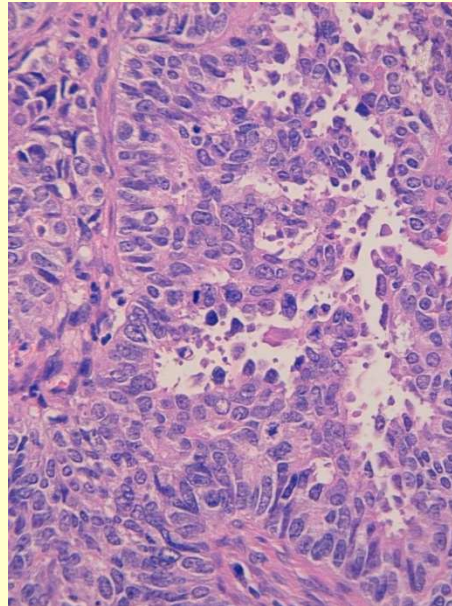
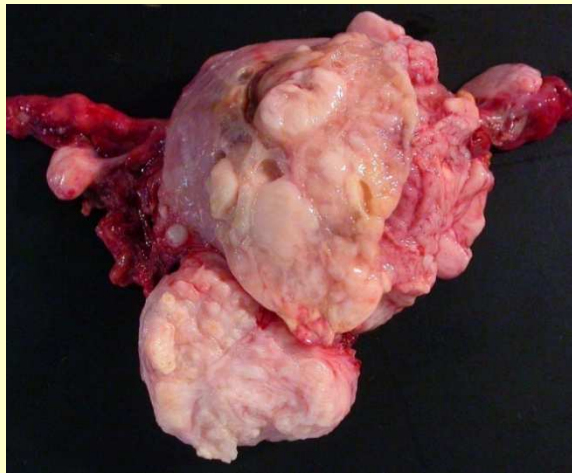


# TCGA-based surrogate limitations

2- p53 immunostaining is not perfect surrogate of p53 mutations, and up to 10% of serous carcinomas are p53 wild-type, p53 is sometimes abnormal in part of a tumor (Tumor heterogeneity)

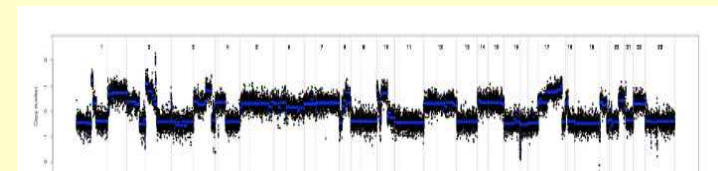


# An example of p53 wild type serous carcinoma



	(MX3TS)	(MX3TC)
ATM E2411*	0.74	0.64
DIS3 R526K	0.66	0.64
EPHA5 C319W	0.66	0.64
DNMT3A C136*	0.44	0.44
ERBB3 R475W	0.41	0.38
CDK4 L120V	0.04	0.12
PIK3R1 M582fs	0.16	0.14
SOX17 P163fs	0.13	0.14
TGFB2 S527I	0.04	

MAFs  
■ >50%  
■ >20-49%  
■ >10-19%  
■ >1-9%  
■ 0%  
☐ LOH



**Microscopy: Serous carcinoma**

**TCGA by exome sequencing: High copy number, serous-like ca**

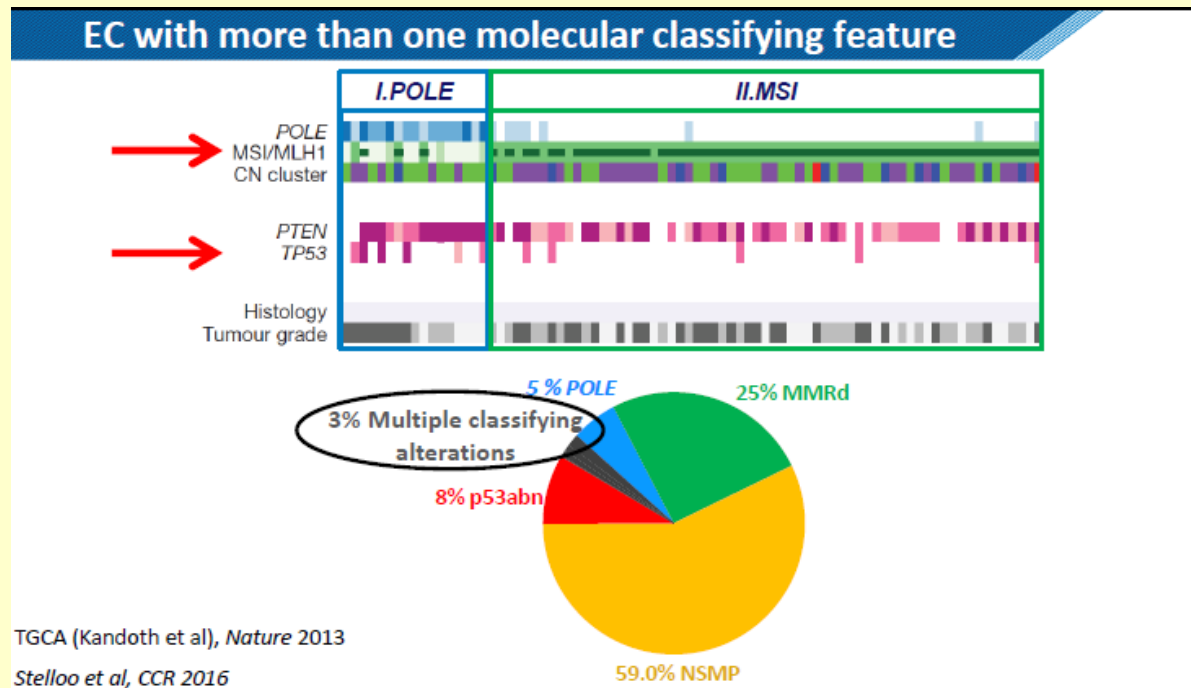
**TCGA by TCGA surrogate: Low copy number EC**

**Conclusion: Serous ca, serous-like but with wild-type p53**



# TCGA-based surrogate limitations

3- Some tumors show more than one classifier  
(Double classifiers)



**Leon A et al,**

# Molecular classification limitations

- 1- Subsets of tumors in the low-copy number group or MMRD have different prognosis.
- 2- Application to low-grade endometrioid carcinomas may be non cost-effective.
- 3- POLE mutation testing and interpretation needs standardization.
- 4- p53 IHC is a good, but not perfect surrogate of high copy number carcinomas.
- 5- Data on clear cell and undifferentiated carcinomas or carcinosarcomas are still immature.
- 6- Prognosis of multiple classifiers is still evolving issue.



# **Molecular classification strenghts**

- 1- Good prognostic risk stratification in general, but in particular in high grade endometrioid carcinoma
- 2- In the high grade group, molecular classification is more important than histologic typing

Original Article

# Equivalent Survival of p53 Mutated Endometrial Endometrioid Carcinoma Grade 3 and Endometrial Serous Carcinoma

Mary Anne Brett, M.D., Eshetu G. Atenafu, Ph.D., Nilanchali Singh, M.D., Prafull Ghatage, M.D.,  
Blaise A. Clarke, M.D., Gregg S. Nelson, M.D., Ph.D., Marcus Q. Bernardini, M.D.,  
and Martin Köbel, M.D.

There was no significant difference in survival between ESC and p53 mutated EEC3 in multivariable analysis.

Although this is so, separate classification should continue due to biological differences that will become important for future targeted therapy.



# **Molecular classification helps in pathologic diagnosis**

- p53 immunostaining in a low-grade endometrioid carcinoma should alert on the possibility of a serous carcinoma with glandular pattern.
- A POLE mutation or MMRd in a serous carcinoma should alert on the possibility of endometrioid carcinoma

# ESGO-ESTRO-ESP Guidelines Endometrial Cancer 2020



Virchows Archiv (2021) 478:153–190  
<https://doi.org/10.1007/s00428-020-03007-z>

## ORIGINAL ARTICLE



### ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma

Nicole Concin<sup>1,2</sup> • Carlen L. Creutzberg<sup>3</sup> • Ignace Vergote<sup>4</sup> • David Cibula<sup>5</sup> • Mansoor Raza Mirza<sup>6</sup> • Simone Marnitz<sup>7</sup> • Jonathan A. Ledermann<sup>8</sup> • Tjalling Bosse<sup>9</sup> • Cyrus Chargari<sup>10</sup> • Anna Fagotti<sup>11</sup> • Christina Fotopoulou<sup>12</sup> • Antonio González-Martin<sup>13</sup> • Sigurd F. Lax<sup>14,15</sup> • Domenica Lorusso<sup>11</sup> • Christian Marth<sup>16</sup> • Philippe Morice<sup>17</sup> • Remi A. Nout<sup>18</sup> • Dearbhaile E. O'Donnell<sup>19</sup> • Denis Querleu<sup>11,20</sup> • Maria Rosaria Raspollini<sup>21</sup> • Jalid Sehouli<sup>22,23</sup> • Alina E. Sturdza<sup>24</sup> • Alexandra Taylor<sup>25</sup> • Anneke M. Westermann<sup>26</sup> • Pauline Wimberger<sup>27</sup> • Nicoletta Colombo<sup>28</sup> • François Planchamp<sup>29</sup> • Xavier Matias-Guiu<sup>30,31</sup>

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#### Abstract

A European consensus conference on endometrial carcinoma was held in 2014 to produce multidisciplinary evidence-based guidelines on selected questions. Given the large body of literature on the management of endometrial carcinoma published since 2014, the European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy & Oncology (ESTRO) and the European Society of Pathology (ESP) jointly decided to update these evidence-based guidelines and to cover new topics in order to improve the quality of care for women with endometrial carcinoma across Europe and worldwide. ESGO/ESTRO/ESP nominated an international multidisciplinary development group consisting of practicing clinicians and researchers who have demonstrated leadership and expertise in the care and research of endometrial carcinoma (27 experts across Europe). To ensure that the guidelines are evidence-based, the literature published since 2014, identified from a systematic search was reviewed and critically appraised. In the absence of any clear scientific evidence, judgment was based on the professional experience and consensus of the development group. The guidelines are thus based on the best available evidence and expert agreement. Prior to publication, the guidelines were reviewed by 191 independent international practitioners in cancer care delivery and patient representatives. The guidelines comprehensively cover endometrial carcinoma staging, definition of prognostic risk groups integrating molecular markers, pre- and intra-operative work-up, fertility preservation, management for early, advanced, metastatic, and recurrent disease and palliative treatment. Principles of radiotherapy and pathological evaluation are also defined.

# DEFINITION OF PROGNOSTIC RISK GROUPS INTEGRATING MOLECULAR MARKERS

- Histopathological type, grade, myometrial invasion and LVSI (no/focal/substantial) should be recorded in all patients with endometrial carcinoma [V, A].
- The definition of prognostic risk groups is presented in the Figure 3 for both situations, when Molecular Classification is known or unknown.



## PROGNOSTIC RISK GROUPS

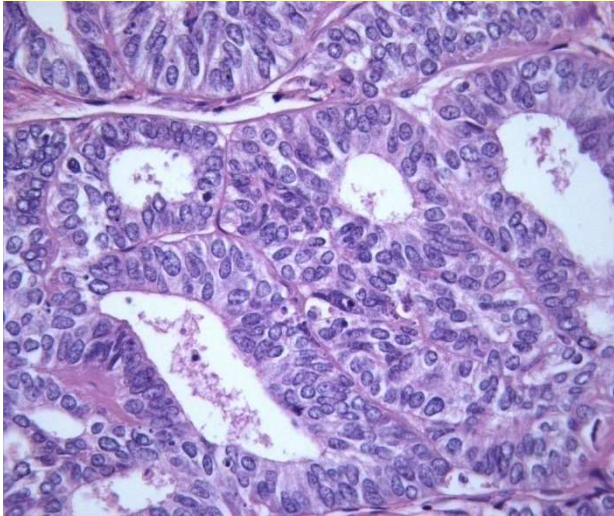
Stage	POLE	MMRd Endometriod	NSMP Endometriod	MMRd / NSMP* Serous, undifferentiated carcinosarcoma	P53abn*
IA Low grade LVSI neg/focal	Low	Low		High	High
IA High grade LVSI neg/focal		Intermediate**			
IB Low grade LVSI neg/focal					
IB High grade LVSI any		High intermediate			
Any I with LVSI					
II		High			
III***					
IVA***					

\*With myometrial invasion

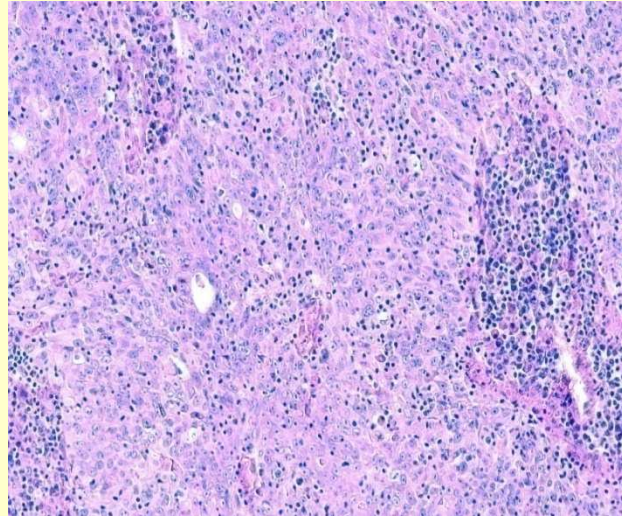
\*\*Stage IA p53abn and/or non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) without myometrial invasion

\*\*\*No residual disease

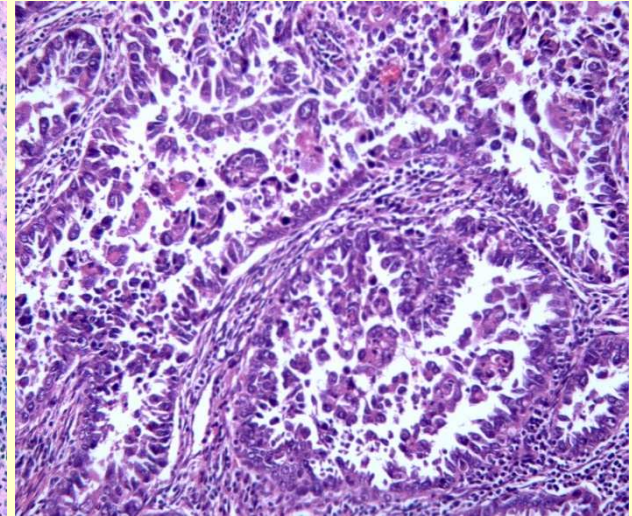
## TCGA-BASED MOLECULAR CLASSIFICATION IS APPLICABLE TO ALL HISTOLOGIC SUBTYPES OF ENDOMETRIAL CARCINOMA



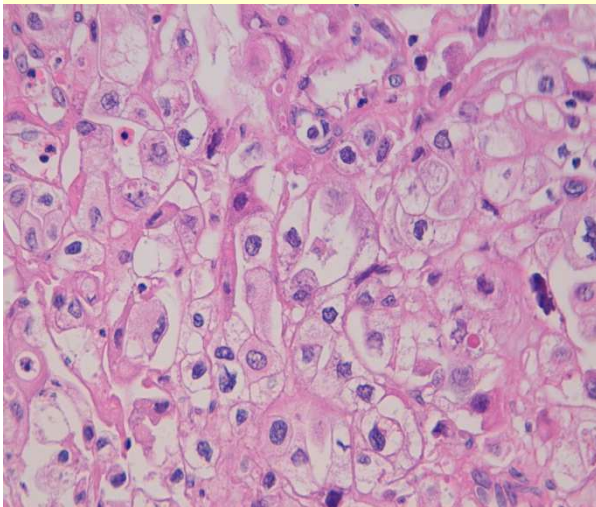
EEC 1,2



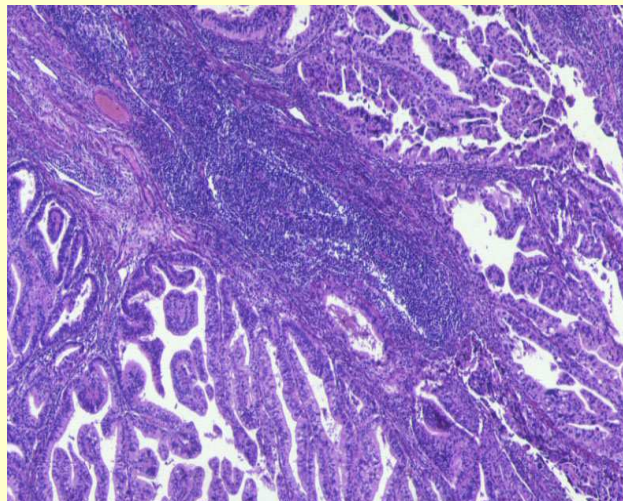
EEC 3



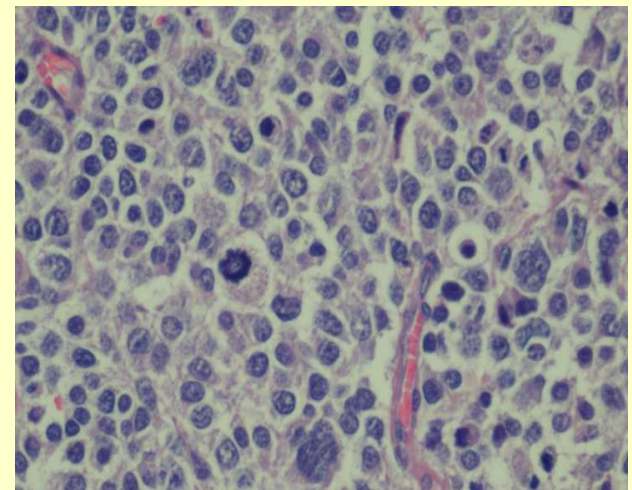
Serous



Clear Cell



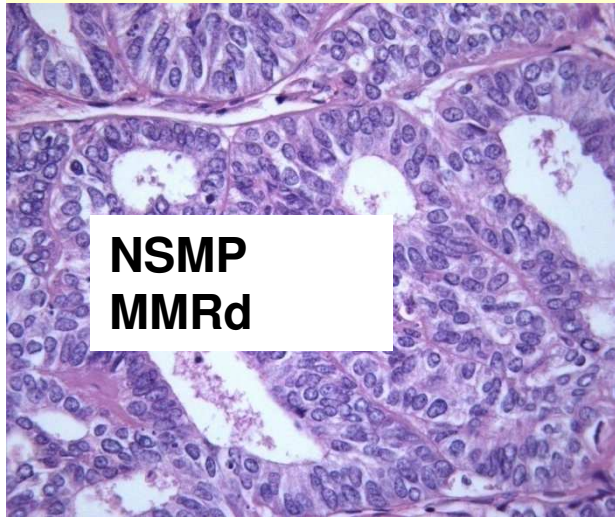
Mixed



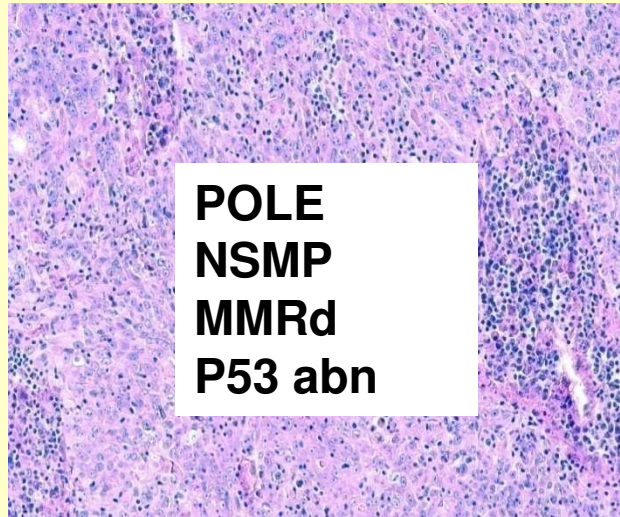
Undiff



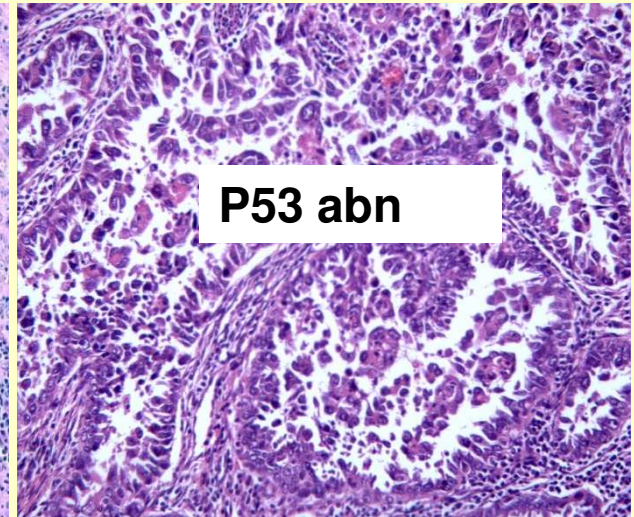
## TCGA-BASED MOLECULAR CLASSIFICATION IS APPLICABLE TO ALL HISTOLOGIC SUBTYPES OF ENDOMETRIAL CARCINOMA



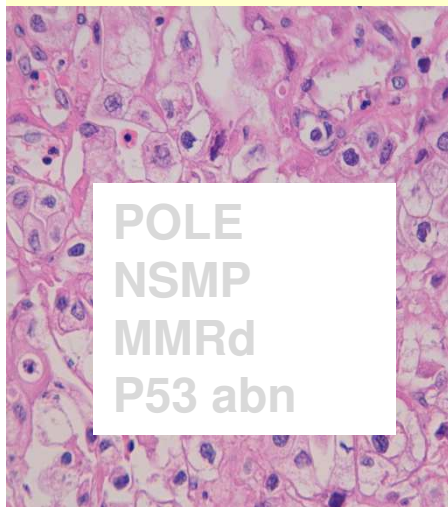
EEC 1,2



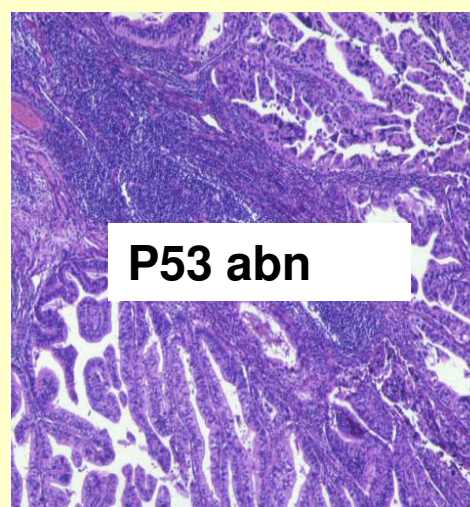
EEC 3



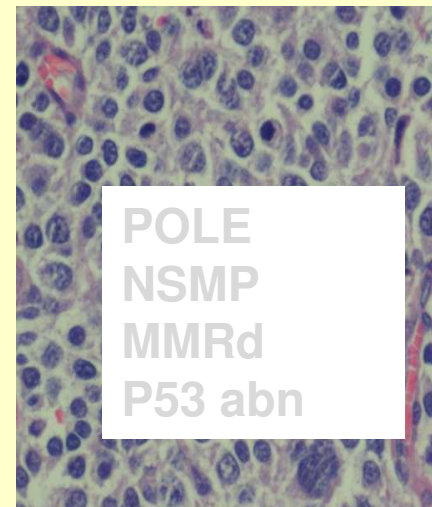
Serous



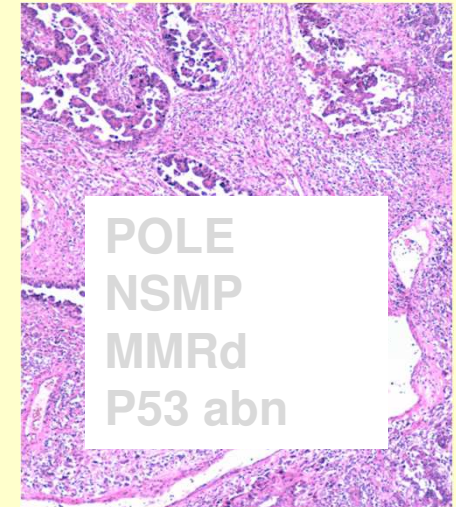
Clear Cell



Mixed



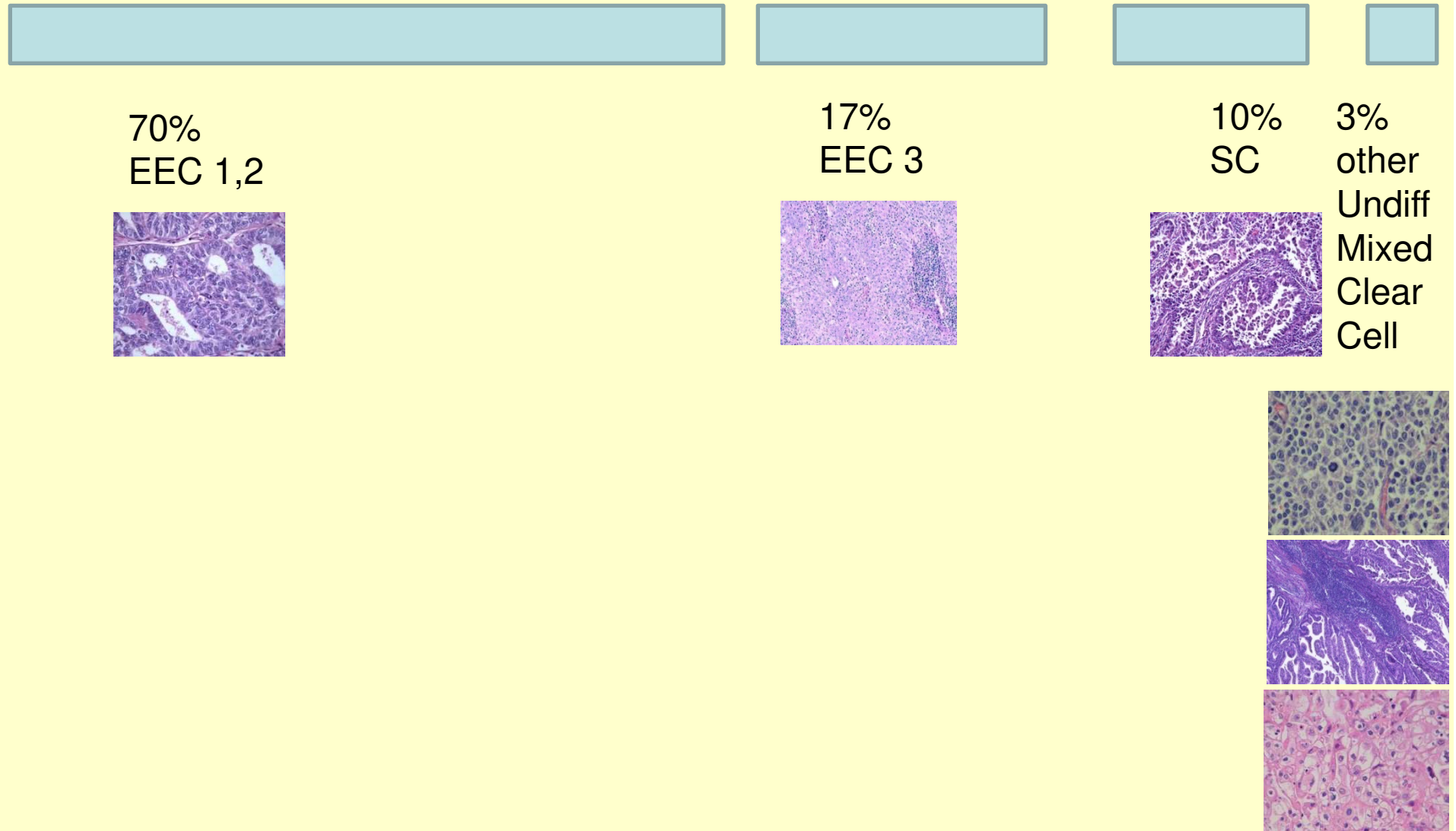
Undiff



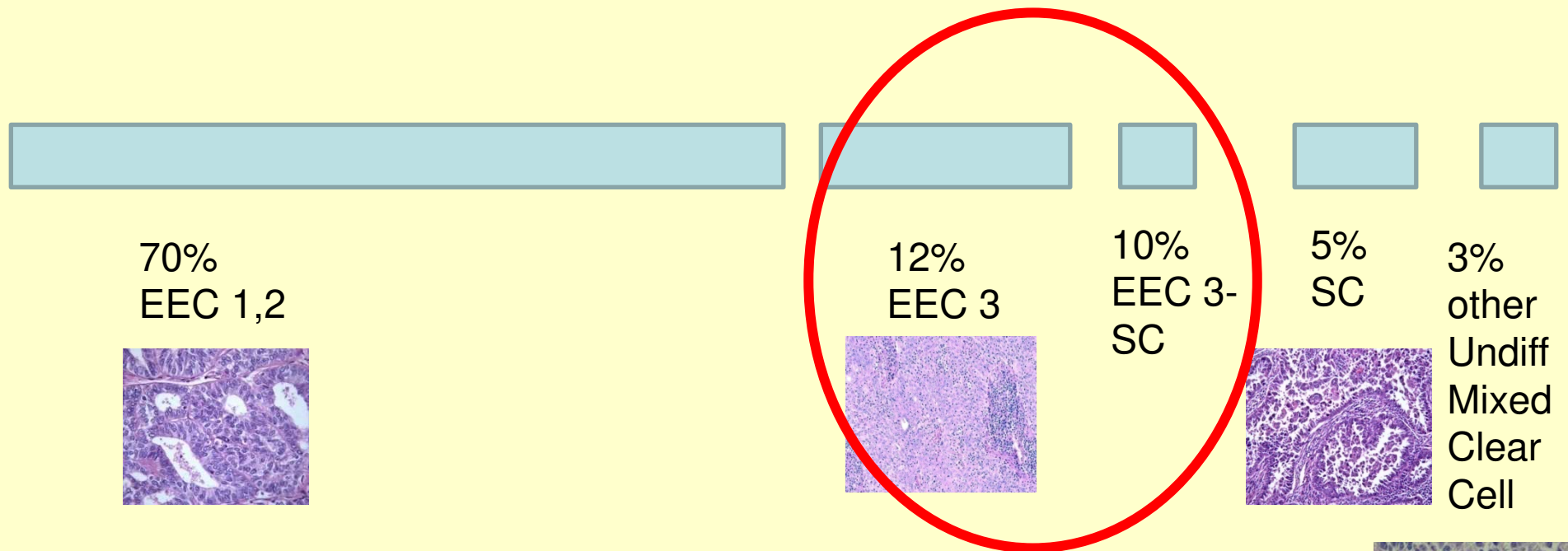
Carcinosarcoma



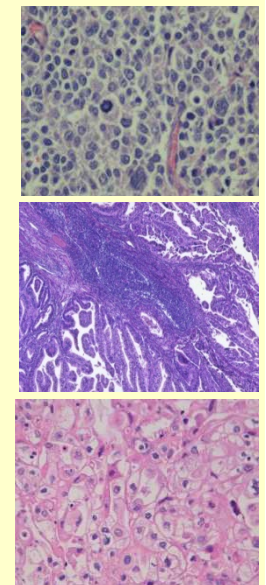
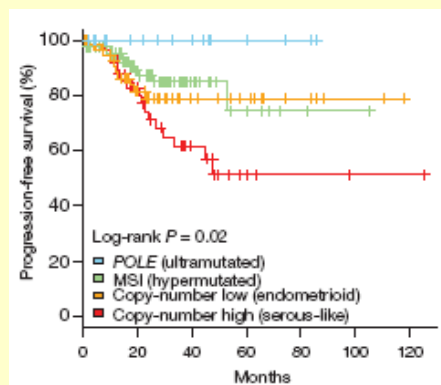
# IS MICROSCOPIC EXAMINATION USEFUL IN THE TIMES OF MOLECULAR CLASSIFICATION OF ENDOMETRIAL CARCINOMA?



# IS MICROSCOPIC EXAMINATION USEFUL IN THE TIMES OF MOLECULAR CLASSIFICATION OF ENDOMETRIAL CARCINOMA?

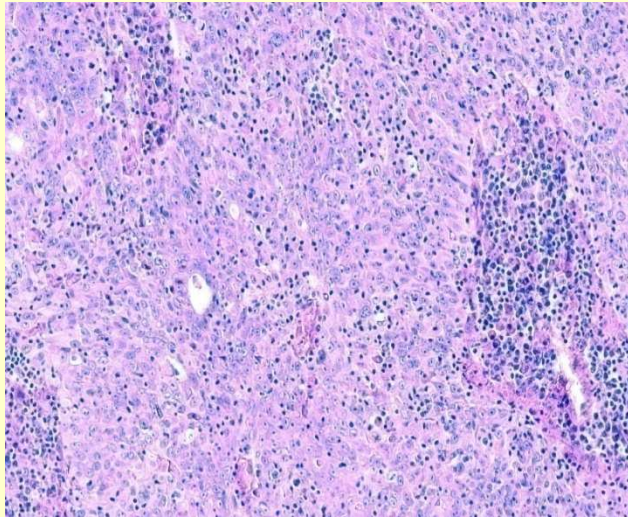


IN THIS GROUP OF TUMORS, MOLECULAR CLASSIFICATION IS MOST HELPFUL

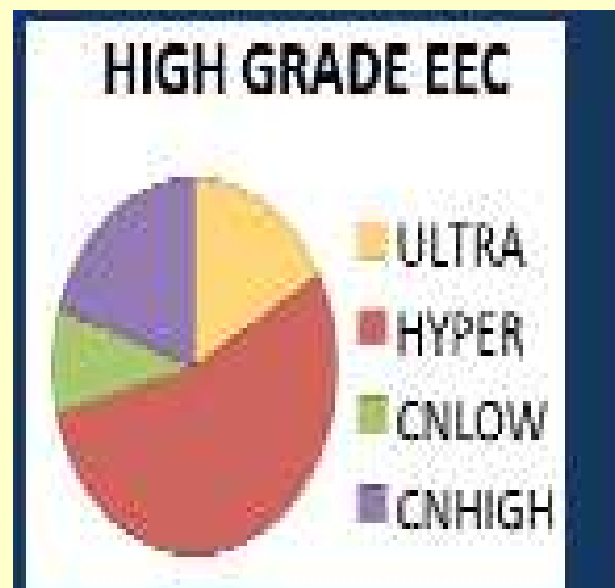




# TCGA-BASED MOLECULAR CLASSIFICATION IS APPLICABLE TO ALL HISTOLOGIC SUBTYPES OF ENDOMETRIAL CARCINOMA

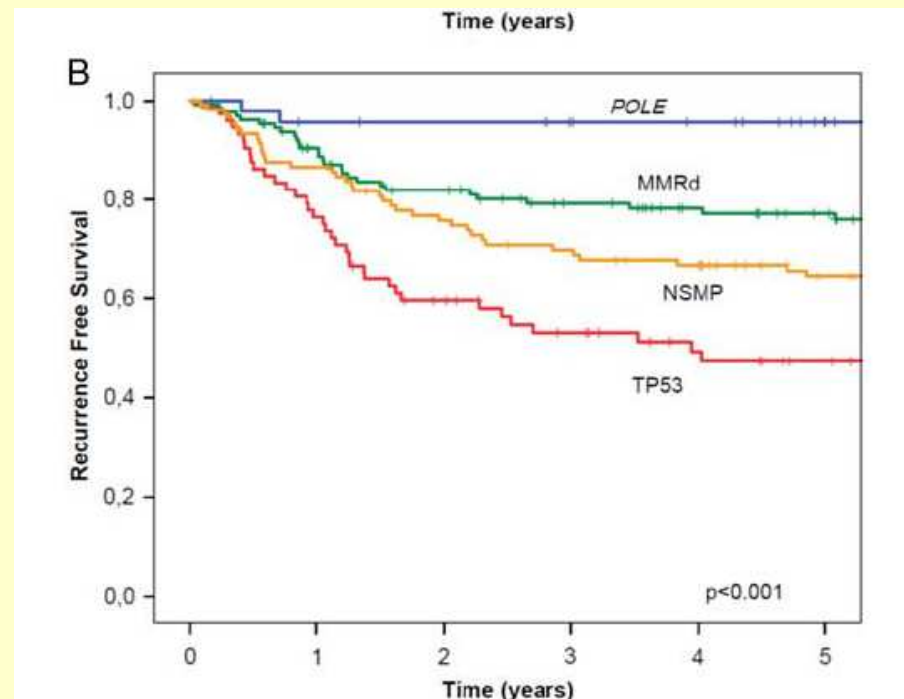


EEC 3

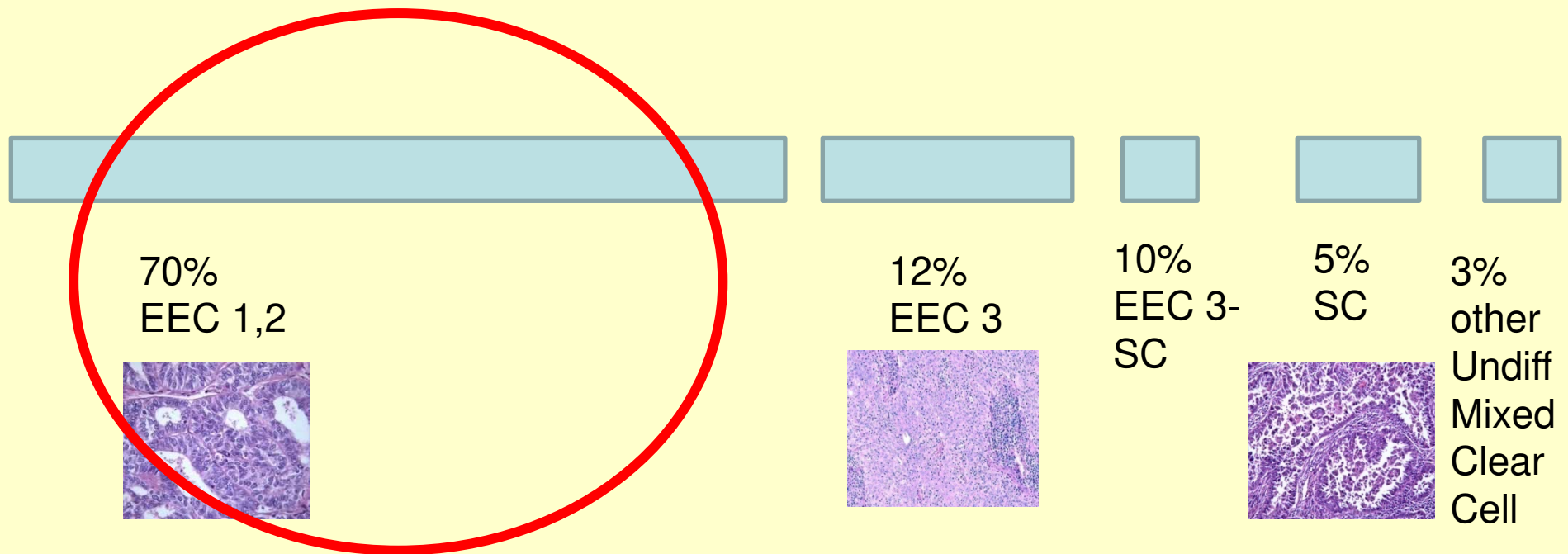


## Molecular Classification of Grade 3 Endometrioid Endometrial Cancers Identifies Distinct Prognostic Subgroups

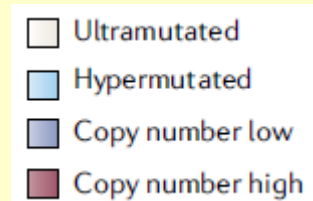
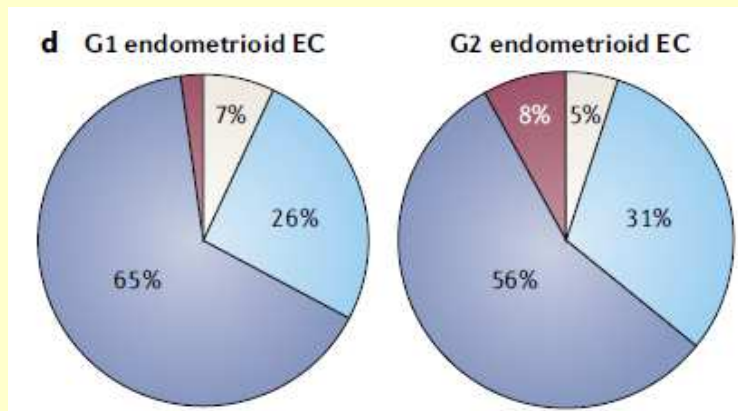
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# IS MICROSCOPIC EXAMINATION USEFUL IN THE TIMES OF MOLECULAR CLASSIFICATION OF ENDOMETRIAL CARCINOMA?



## IS MOLECULAR CLASSIFICATION HELPFUL IN THE BIG GROUP OF EEC1,2 ?



Mutated  
*POLE*

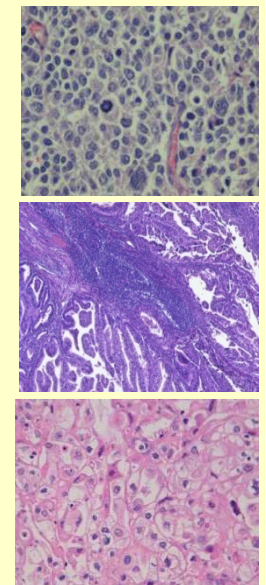
• G1/G2: 11

Mutated  
*TP53*

• G1/G2: 6–10

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# **PATHOLOGY OF ENDOMETRIAL CANCER**

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