

MOLECULAR PATHOLOGY AND BIOMARKER TESTING IN DIFERENT TYPES OF ENDOMETRIAL CARCINOMA

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Summary

- Pathologic Classification
- Molecular Classification
- Tumor Progression

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Endometrial carcinoma (Histological Classification)

1- Endometrioid carcinoma, usual type
2- Endometrioid carcinoma variants
3- Mucinous adenocarcinoma
4- Serous carcinoma
5- Clear cell adenocarcinoma
6- Neuroendocrine carcinoma
7- Mixed carcinoma
8- Undifferentiated carcinoma

Carcinosarcoma

WHO 2014

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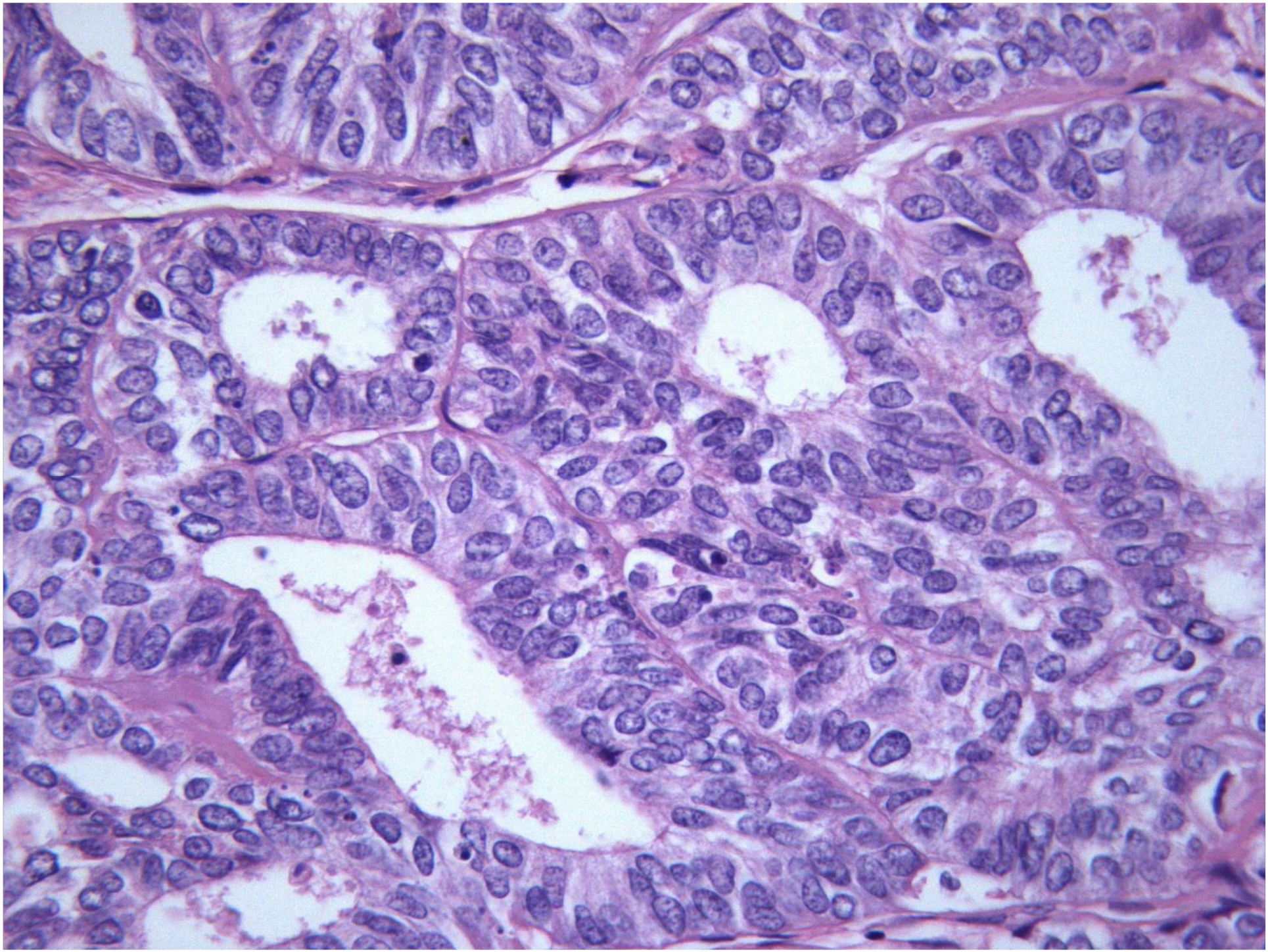
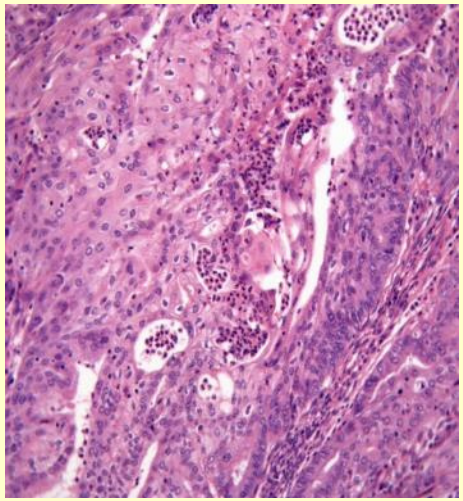
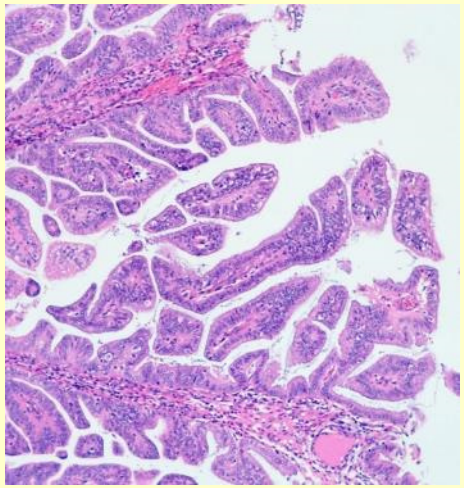
Carcinosarcoma

WHO 2014

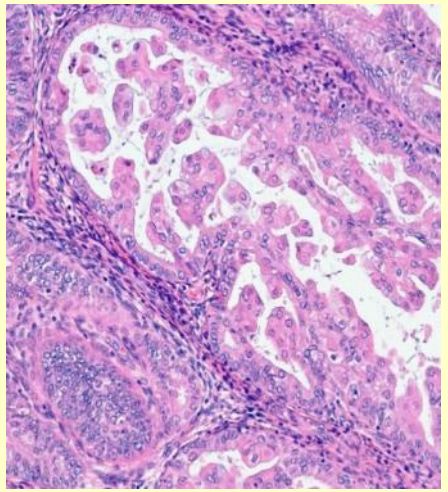




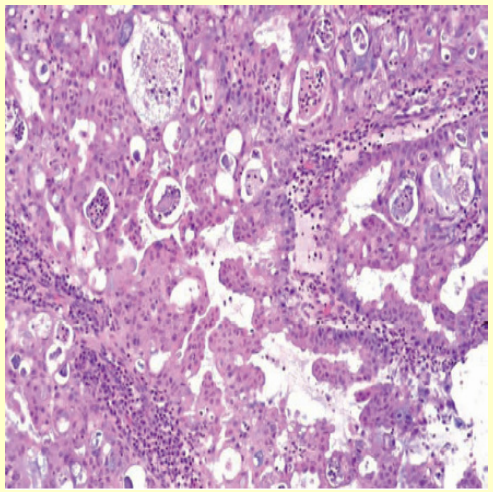
squamous differentiation



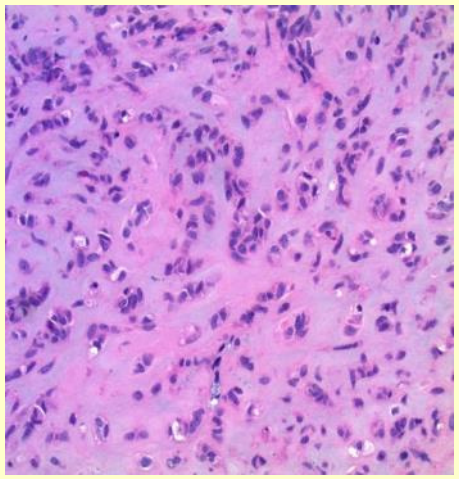
villoglandular



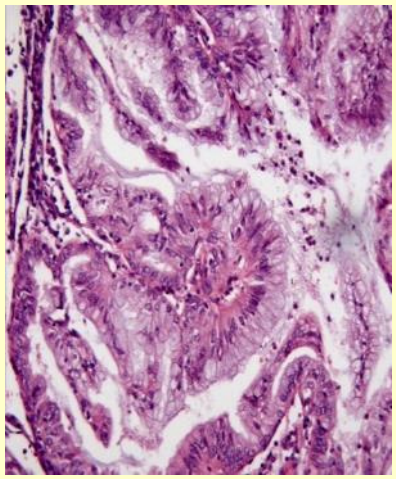
with small nonvillous



microglandular

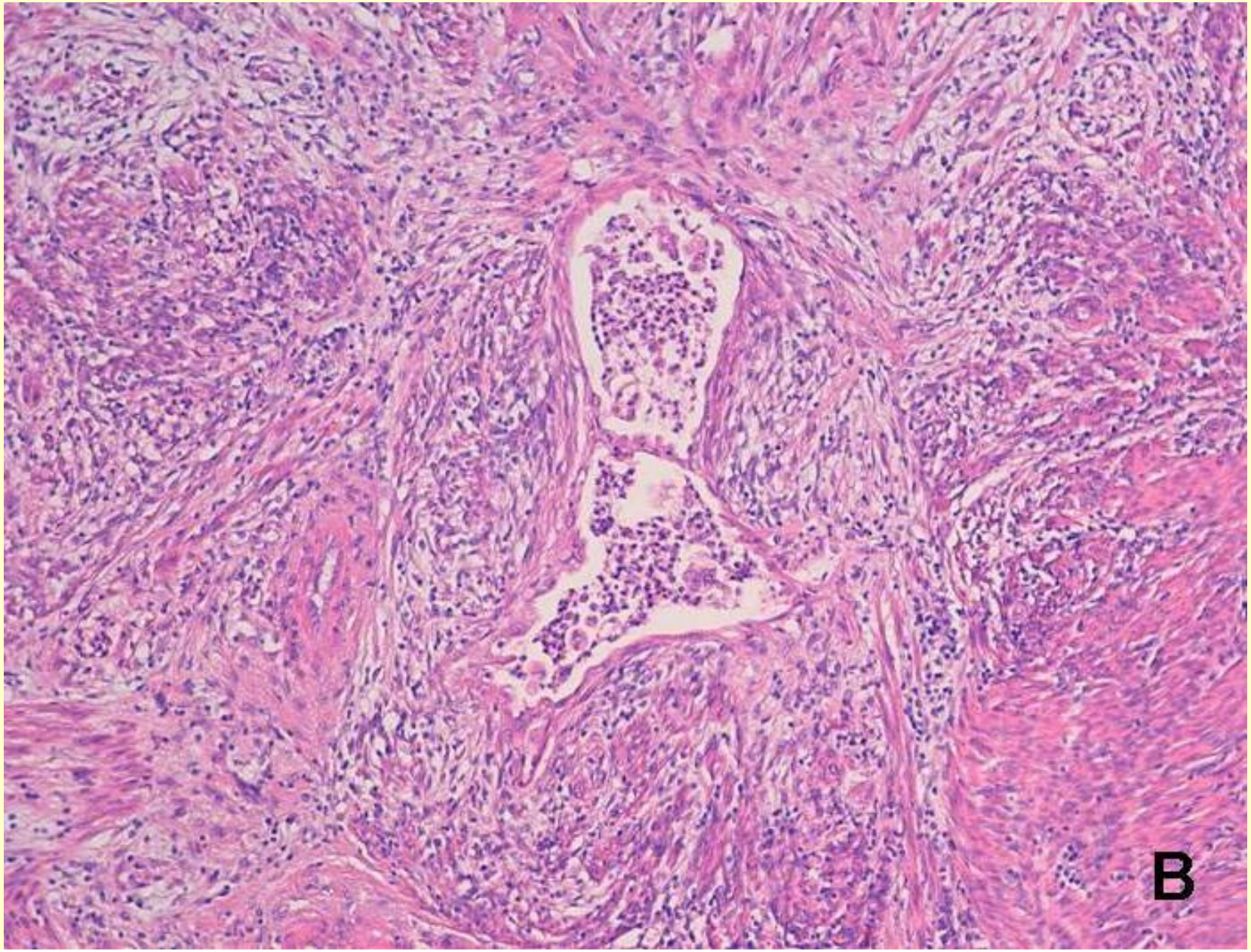


sex cord-like formations hyalinization

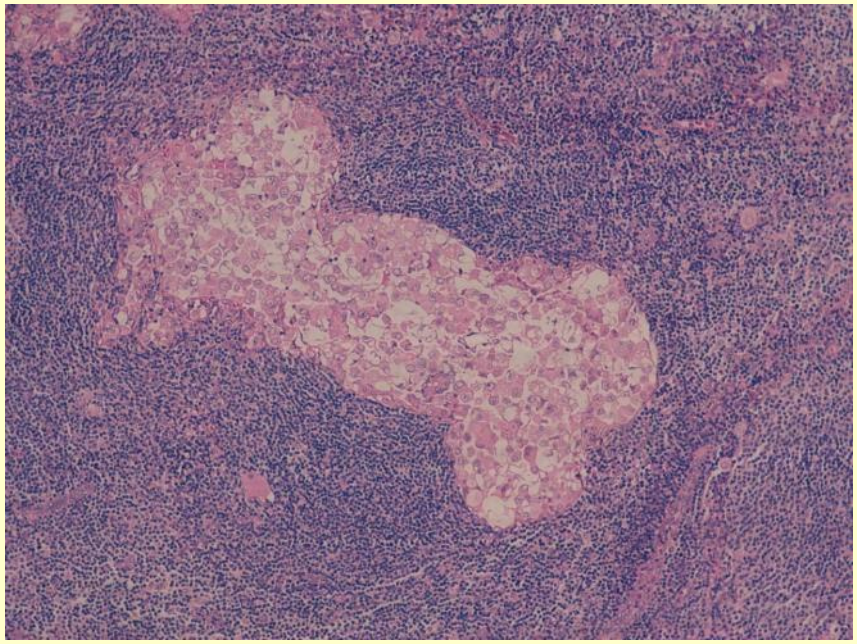


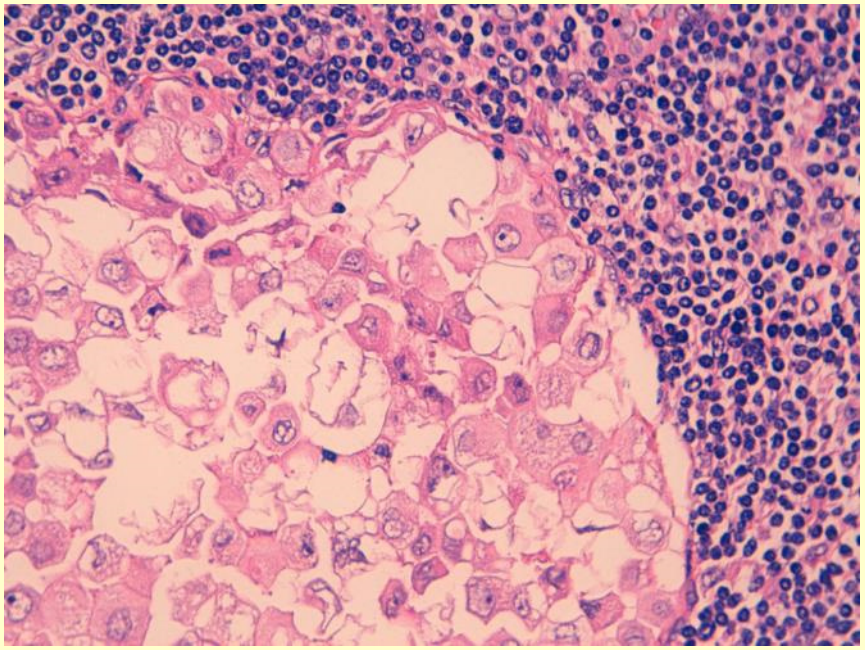
mucinous

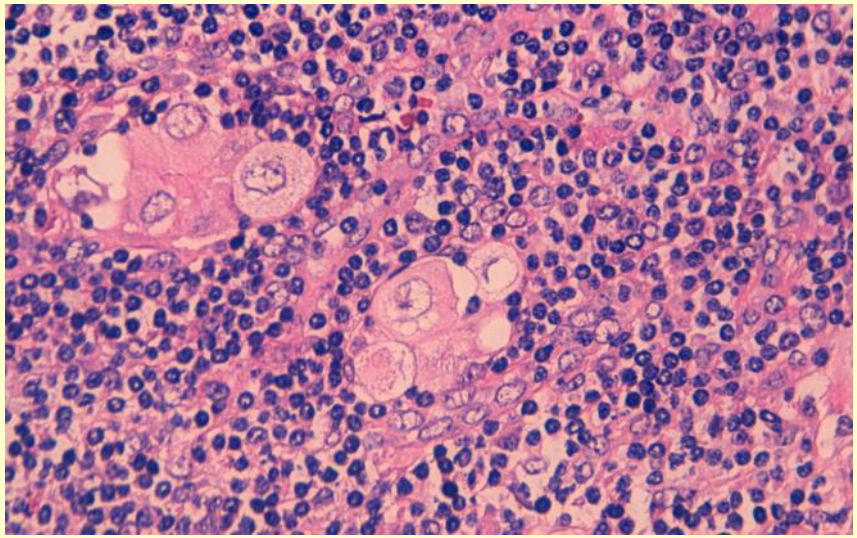
MELF pattern

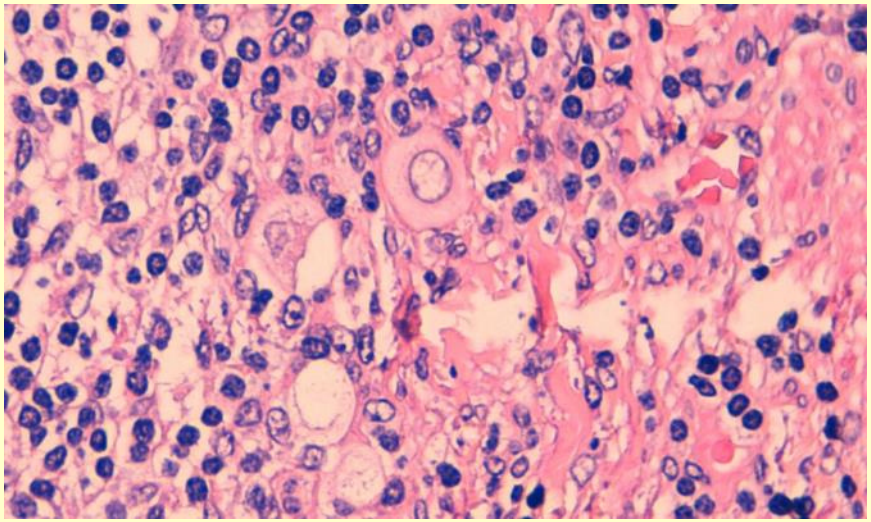


Histiocyte-like nodal metastasis in low grade EEC with MELF









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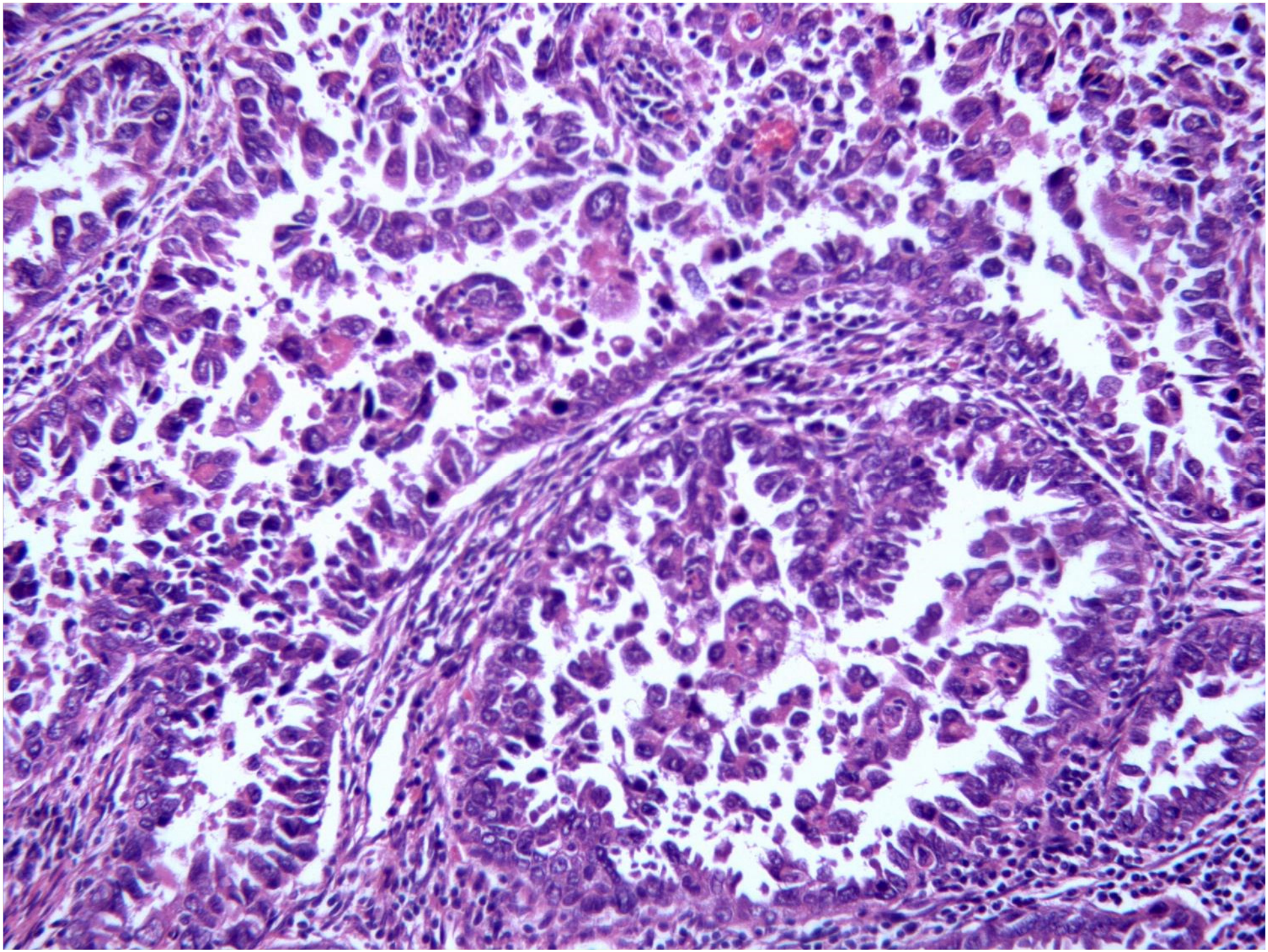
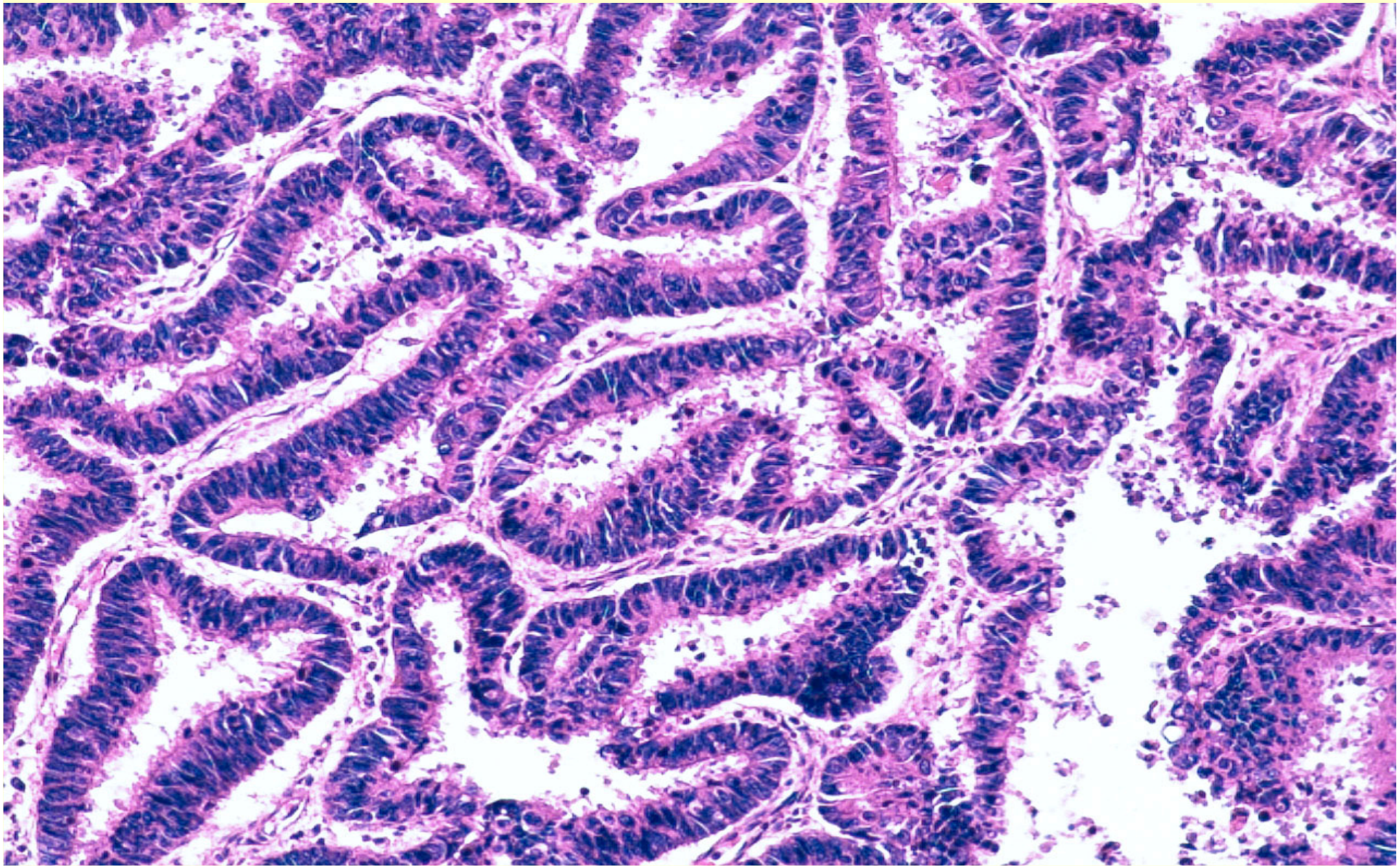


Serous carcinoma with glandular pattern
Discordant architecture/cytology



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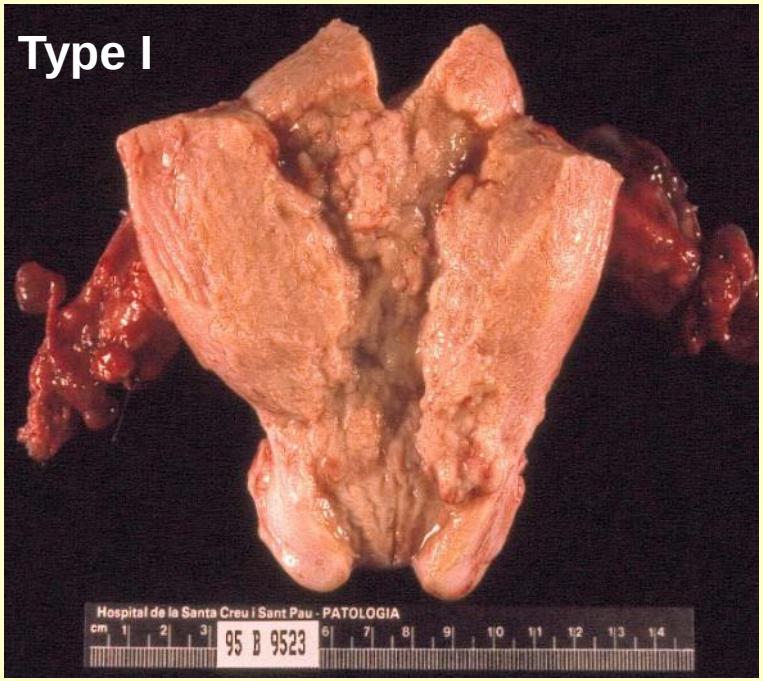
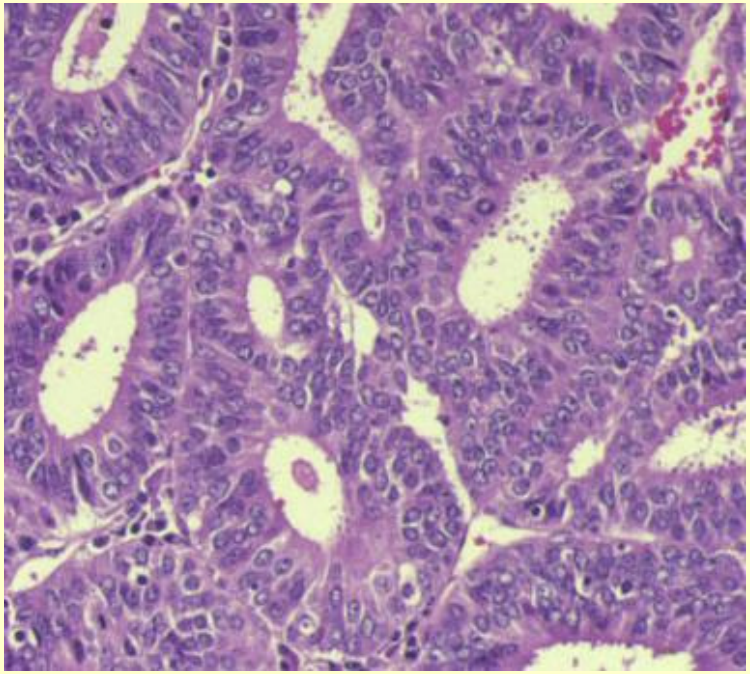
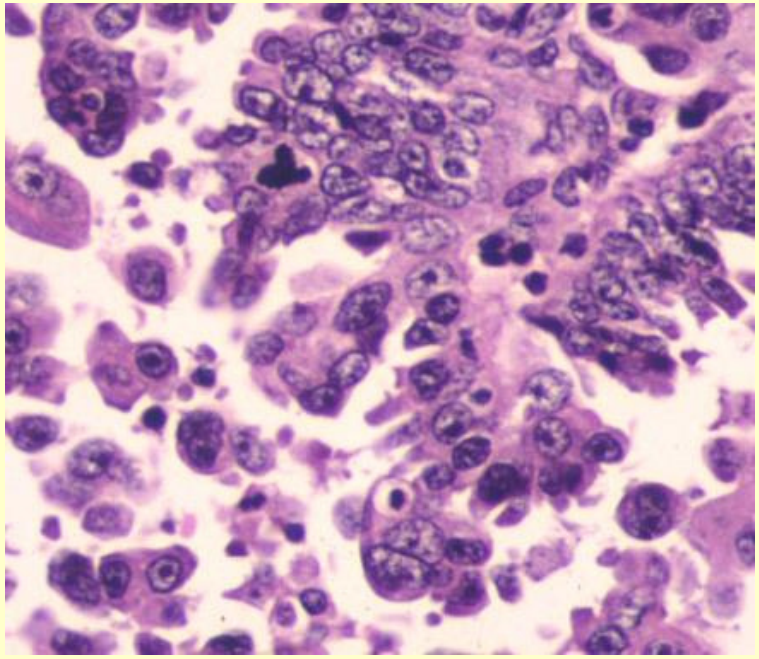
Type I



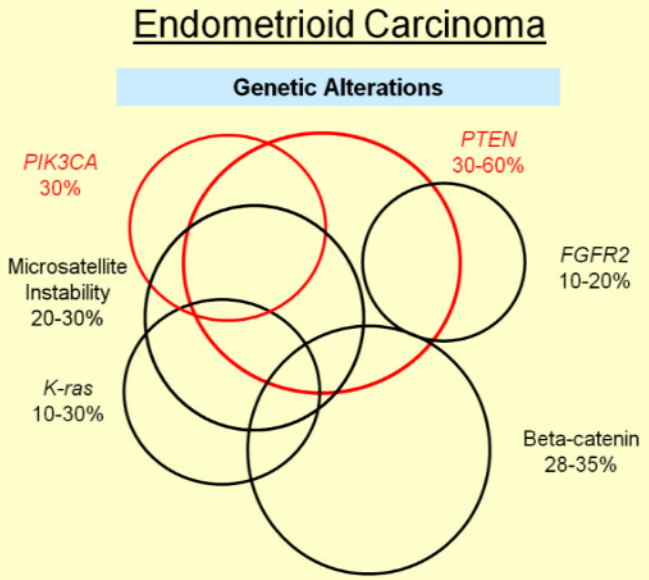


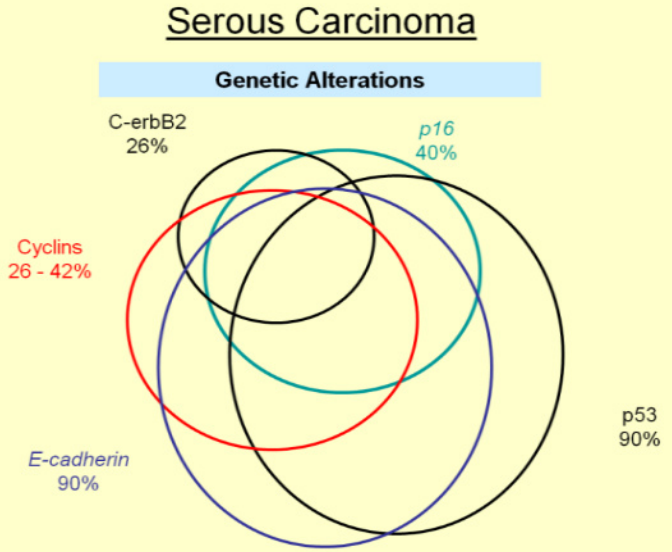
Type II

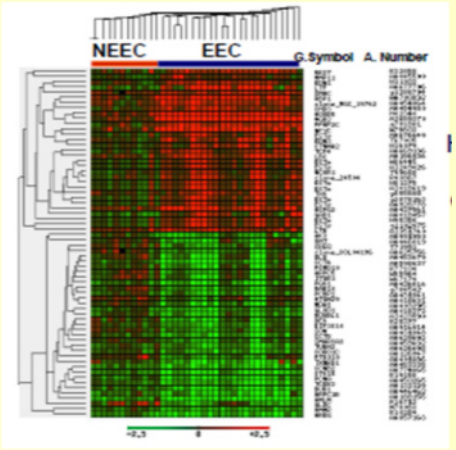


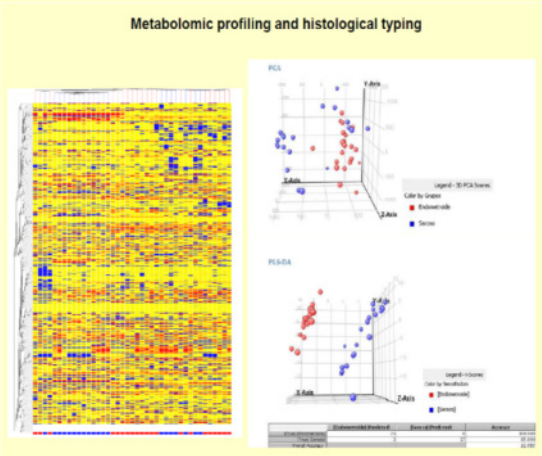


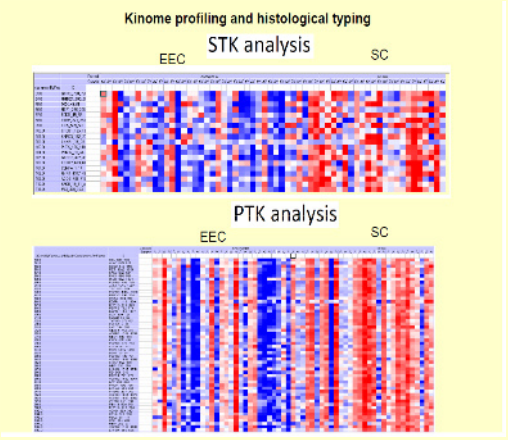
Endometrioid and serous carcinomas have different abnormalities











Gene mutations in endometrioid endometrial carcinoma

GENE	FREQUENCY	GENE	FREQUENCY
PTEN *	77.7%	*MLL4*	9.1%
PIK3CA	53.1%	*BCOR*	8.0%
PIK3R1	37.1%	*ATR*	6.9%
CTNNB1	36.6%	*CCND1*	5.7%
ARID1A	35.4%	*SPOP*	5.7%
KRAS	24.6%	*SIN3A*	5.7%
CTCF	20.6%	*MKI67*	5.7%
RPL22	12.6%	*FBXW7*	5.1%
TP53	11.4%	*FOXA2*	5.1%
FGFR2	10.9%	*NRAS*	2.9%
ARID5B	10.9%		

***62/136 (45.5%) tumors with PTEN mutations has ≥ 2 mutations**

TCGA; Nature 2013

Gene mutations in serous endometrial carcinoma

GENE	FREQUENCY	GENE	FREQUENCY
TP53	90.7%	*PRPF18*	7%
PIK3CA	41.9%	*SPOP*	7%
FBXW7	30.2%	*CDH19*	7%
PPP2R1A	36.6%	*FGFR2*	7%
CHD4	16.3%	*ARID1A*	7%
CSMD3	11.6%	*FOXA2*	4.6%
COLA11	11.6%	*USP36*	4.6%

TCGA; Nature 2013

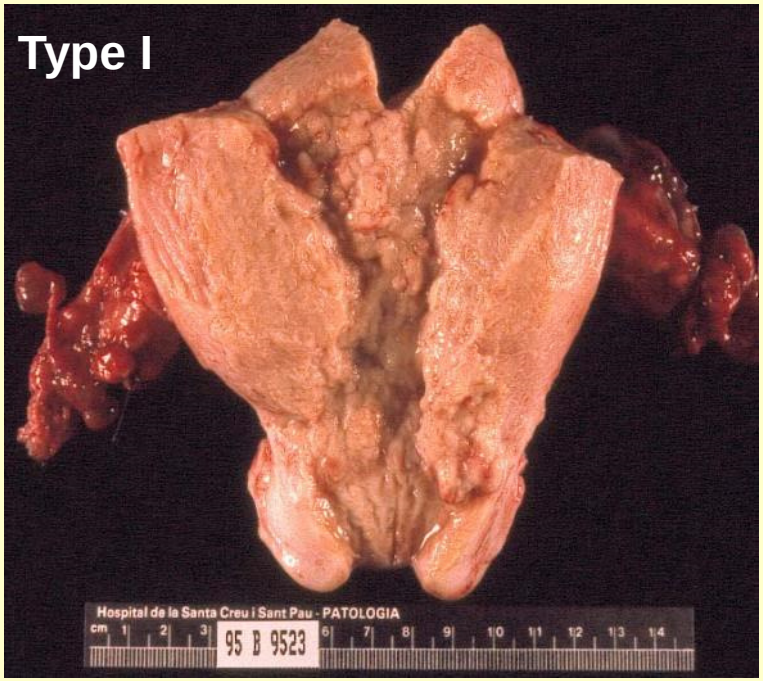
TAF1 (30%), *EP300* (8%), *TSPYL2* (6%), *MAP3K4* (6%) and *ABCC9* (6%).

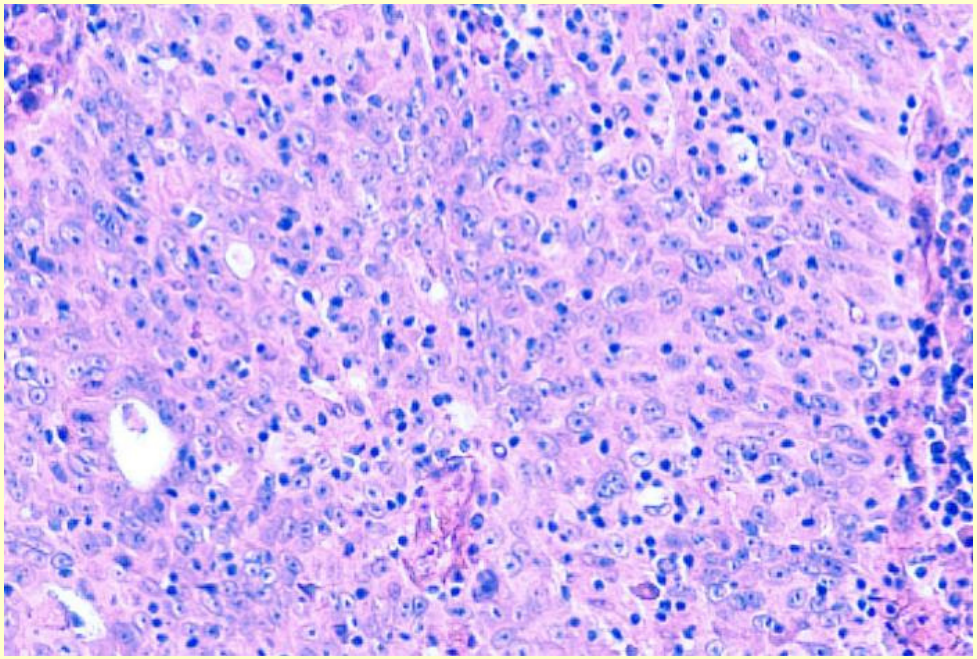
Khun et al; J Nati Cancer Inst 2012.
Le Gallo et al; Nat Genet 2012;
Zhao et al; PNAS 2013.

The 2 types of Endometrial Carcinoma

	Type I	Type II
Microsat Instability	20-40%	0–5%
PTEN	35-50%	10%
KRAS	15-30%	0-5%
beta-catenin (CTNNB1)	25-40%	0-5%
p53	10-20%	90%
P16	10%	40%
E-cadherin	10-20%	80-90%
c-erb B2	2.5%	26%
Cyclins D1 and E	2-5%	26-42%
STK15		

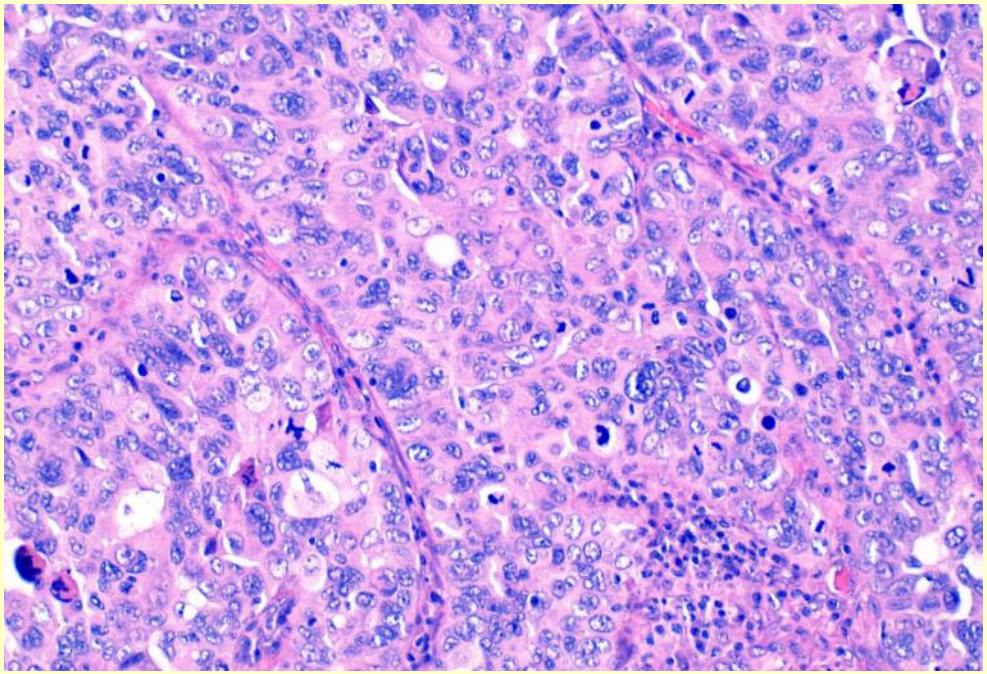
Type I





Type II





Poor Inter-observer Agreement in the Diagnosis of High-Grade Endometrial CA

Gilks B, Oliva E, Soslow RS, Am J Surg Pathol 2013

- **56 cases diagnosed as high-grade endometrial carcinoma**
- **Full agreement of all 3 reviewers regarding subtype diagnosis of exclusive (if pure) or predominant (if mixed) high-grade component reached in 35 of 56 (62.5%) cases**
- **Diagnostic consensus among 3 reviewers barely changed after adding immunohistochemistry (p16, p53, ER, PR, PTEN)**

Clinicopathologic Analysis of 187 High-grade Endometrial Carcinomas of Different Histologic Subtypes: Similar Outcomes Belie Distinctive Biologic Differences

Robert A. Soslow, MD, John P. Bissonnette, MD,† Andrew Wilton, MD,‡ Sarah E. Ferguson, MD,§ Kaled M. Alektiar, MD,‖ Linda R. Duska, MD,¶ and Esther Oliva, MD†*

Age/type	Endometrioid n = 89	Serous n = 61
≤65	55%	34%
> 65	45%	66%

Hyperplasia/type	Endometrioid n = 66	Serous n = 42
No	83%	98%
Yes	17%	2%

Peritoneal Mets/Type	Endometrioid n = 70	Serous n = 53	*P*
No	90%	60%	0.0001
Yes	10%	40%	

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

Targeted sequencing as a tool for improving histological typing



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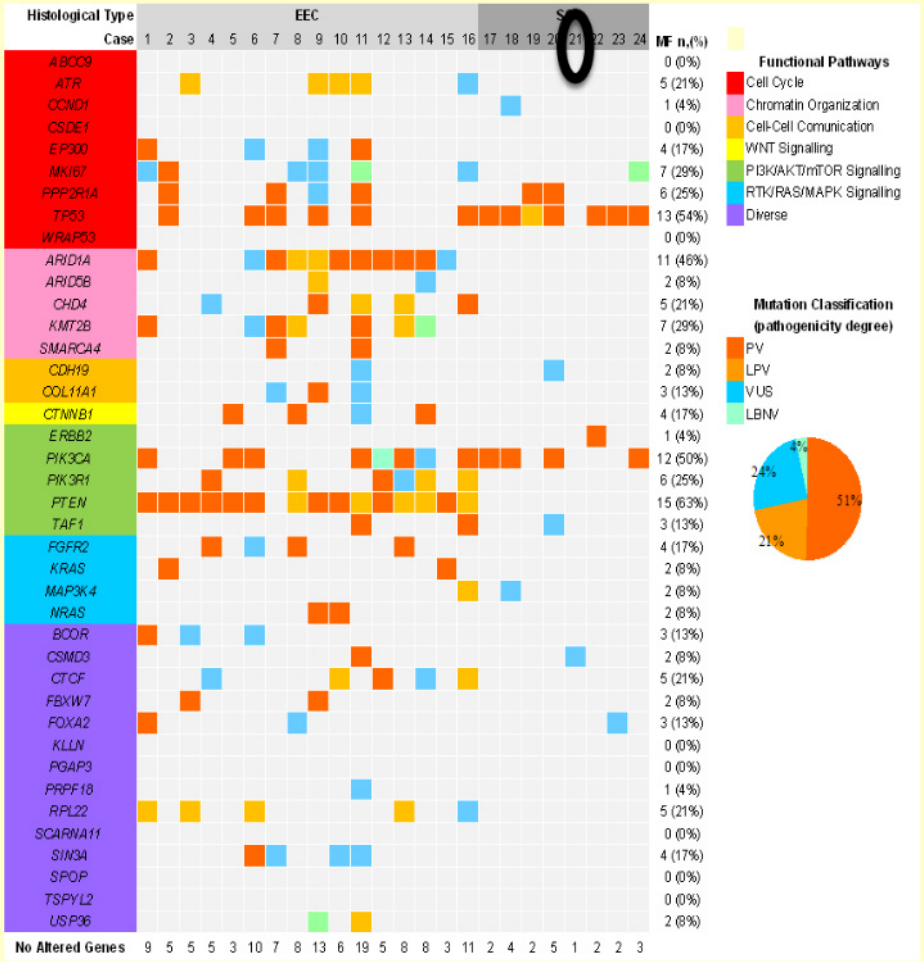
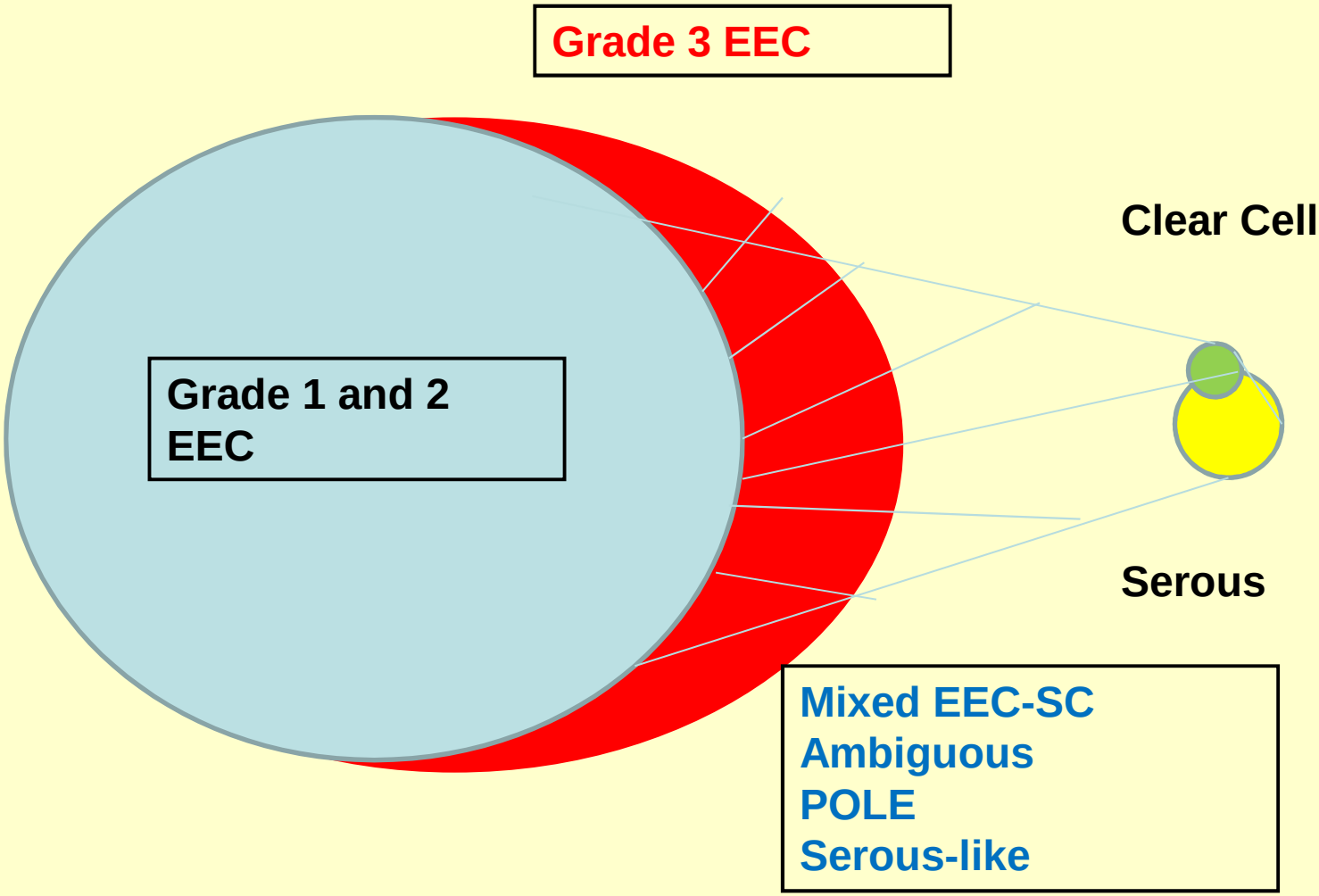


Cuevas D, Virchows Arch 2019

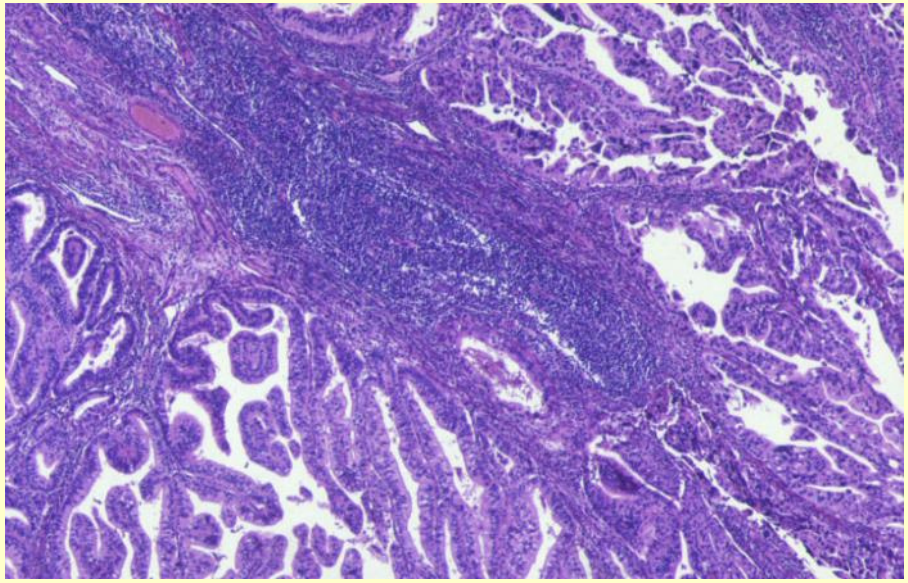
High-grade endometrioid carcinoma versus Serous

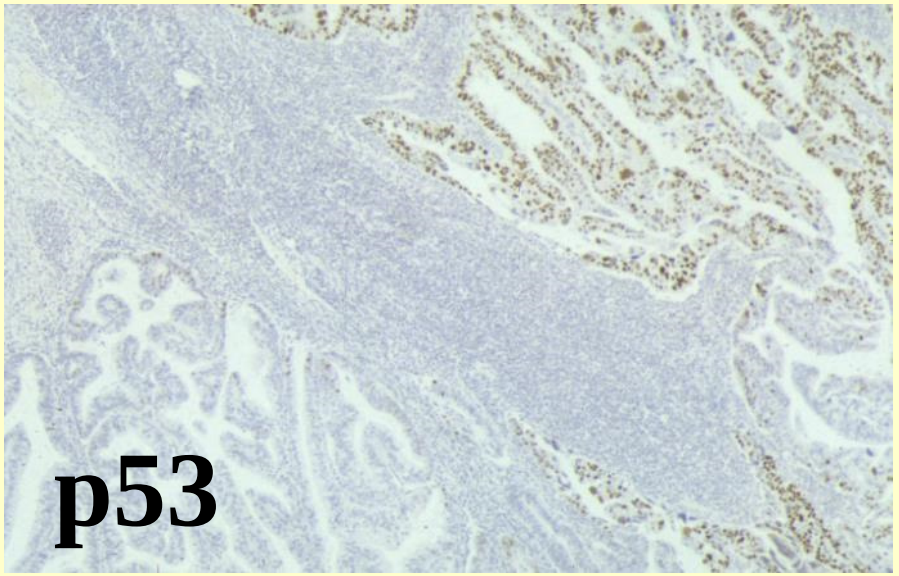
- **Presence of obvious endometrioid or serous features (sampling is important)**
- **Immunohistochemistry (p53, p16, mismatch repair, PTEN, ARID 1A)**
- **Molecular pathology in occasional cases.**



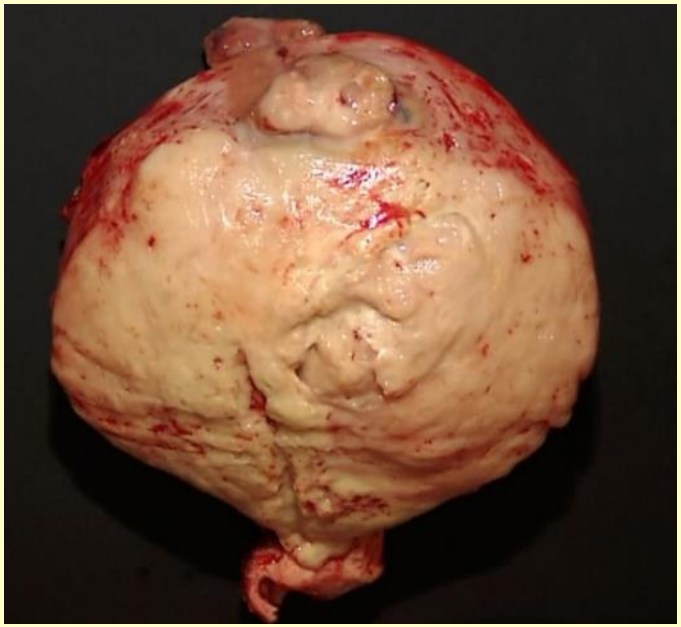
Endometrioid **Non-Endometrioid**

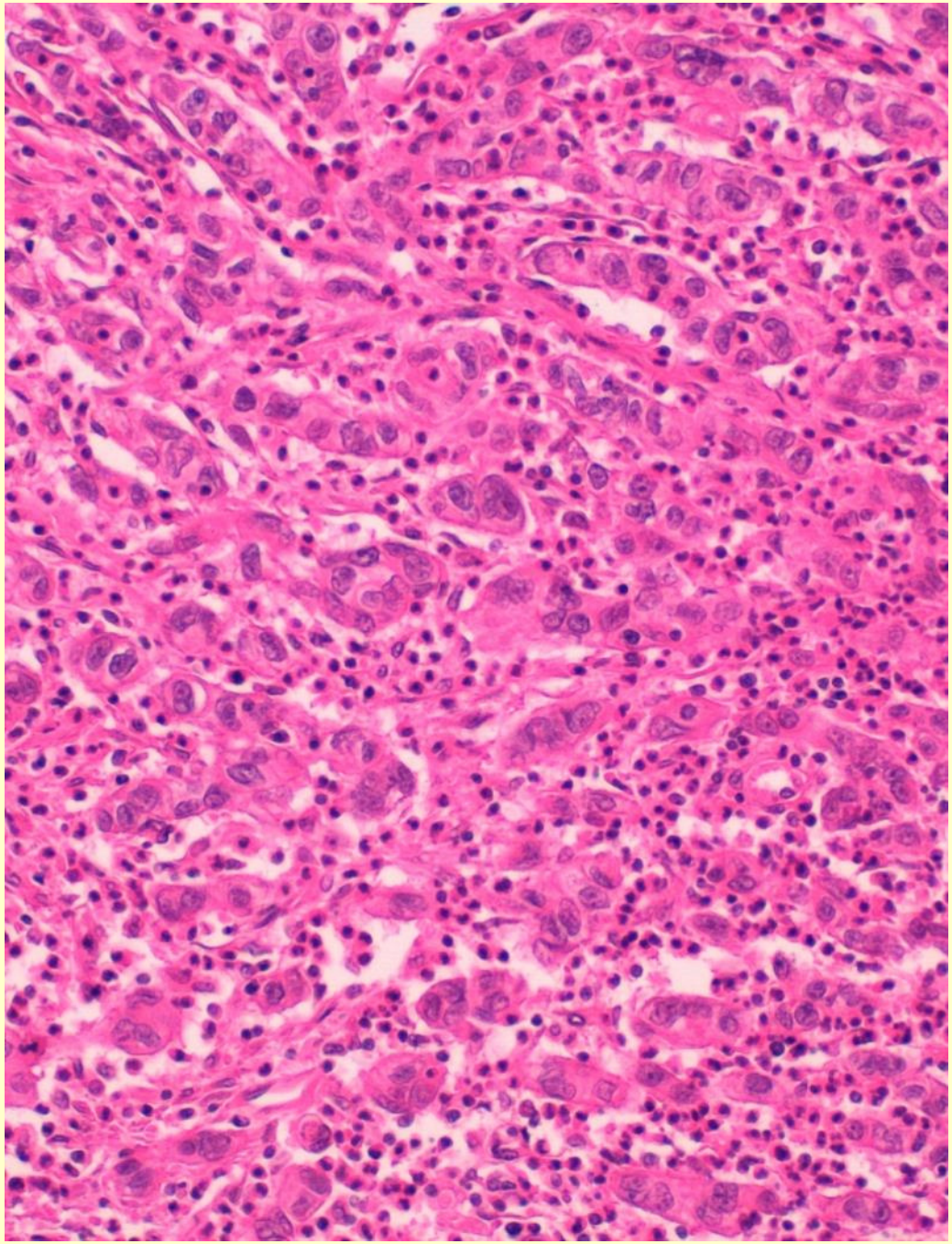
Mixed Endometrioid-Serous carcinomas





Ambiguous Endometrial Carcinoma





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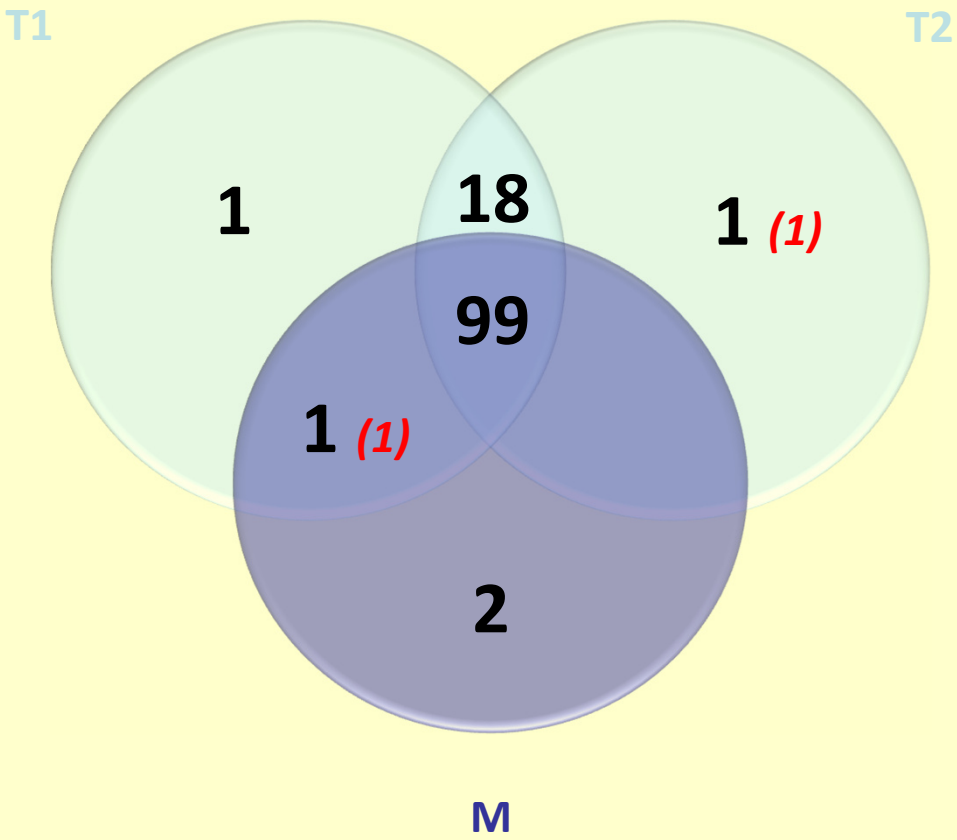

None of the 20 most frequent mutations in EEC and none of the 20 most frequent mutations in SC

Gene	Sample
ATP13A2	ALL
GPATCH3	ALL
A3GALT2	ALL
GNAT2	ALL
CD84	ALL
RYR2	ALL
VIM	ALL
ZNF239	ALL
HNRNPH3	ALL
AL162407.1	ALL
MUC2	ALL
OR51V1	ALL
OR52E4	ALL
ARFIP2	ALL
GPR152	ALL
CWF19L2	ALL
ATM	**ALL**
KDELC2	ALL
NAV3	ALL
TMEM132B	ALL
GOLGA3	ALL
MEIS2	ALL
ADAL	ALL
EIF3J	ALL
PATL2	ALL
SEMA6D	ALL
CELF6	ALL
CYP1A2	ALL
FANCI	ALL
TICRR	ALL
GSPT1	ALL
CHRNB1	ALL
MAP2K4	ALL
RNF112	ALL
IFT20	ALL
ATAD5	ALL
AC003101.1	ALL
RHBDL3	ALL
CCDC103	ALL
PLEKHM1	ALL
DDX5	ALL
TGIF1	ALL
TTC39C	ALL
TTC39C	ALL
ZNF556	ALL
CLEC4G	ALL
MYO9B	ALL
DHX34	ALL
ARMCX4	ALL

Gene	Sample
SHANK1	ALL
C2orf44	ALL
EFR3B	ALL
GAREML	ALL
CCDC121	ALL
BIRC6	ALL
CEBPZ-AS1	ALL
DYSF	ALL
CNGA3	ALL
LIPT1	ALL
C2orf49	ALL
NCKAP5	ALL
ZEB2	**ALL**
DNAH7	ALL
SPHKAP	ALL
DNER	ALL
ZNF343	ALL
FASTKD5	ALL
TTC28	ALL
EP300	ALL
TRNT1	ALL
CSRNP1	ALL
MAATS1	ALL
COPB2	ALL
TAPT1	ALL
FAM114A1	ALL
RPS3A	ALL
MSH3	ALL
ERAP2	ALL
CTD-2215E18.1	ALL
PCDHB1	ALL
ADTRP	ALL
CD109	ALL
ELFN1	ALL
MACC1	ALL
ABCA13	ALL
DYNC1I1	ALL
RELN	ALL
PUS7	ALL
KMT2C	**ALL**
MSRA	ALL
RP1	ALL
PEX2	ALL
CPNE3	ALL
NR4A3	ALL
MSANTD3	ALL
TXNDC8	ALL
MAMDC4	ALL
MAGEE1	ALL
ATRX	ALL

Gene	Sample
TBX15	M
NAF1	M
SLC22A2	T1
CRIPAK	T1+M?
PDCD11	T1+T2
ITGAL	T1+T2
DHRS11	T1+T2
SETBP1	T1+T2
DSEL	T1+T2
SSC5D	T1+T2
EHBP1	T1+T2
STK35	T1+T2
RBM38	T1+T2
STOX2	T1+T2
RHOBTB3	T1+T2
HIST1H4D	T1+T2
PHF3	T1+T2
ESR1	T1+T2
ST7	T1+T2
TMEM164	T1+T2
FAM122C	T1+T2
MAGEC3	T1+T2
TDRD9	T2?

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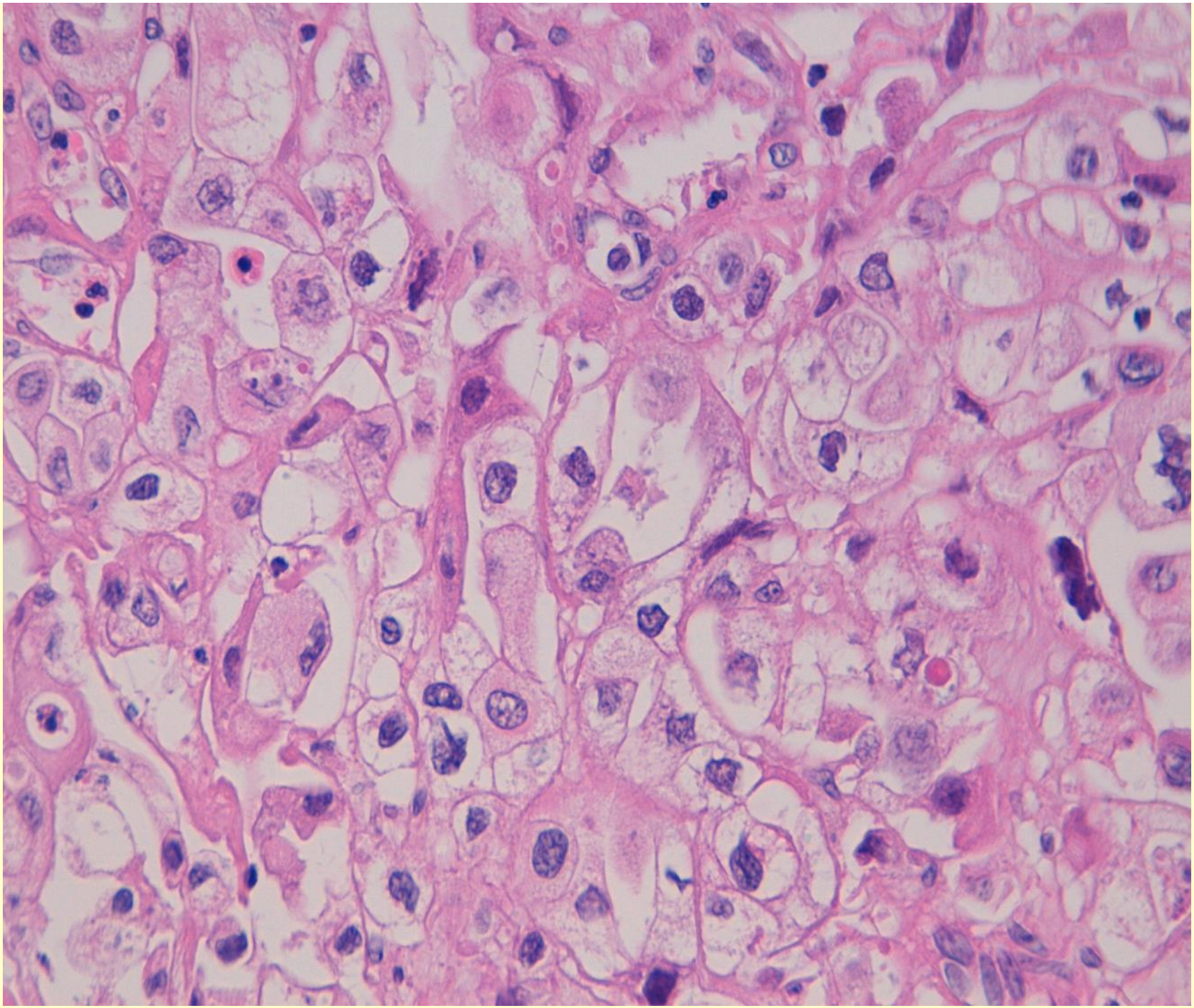
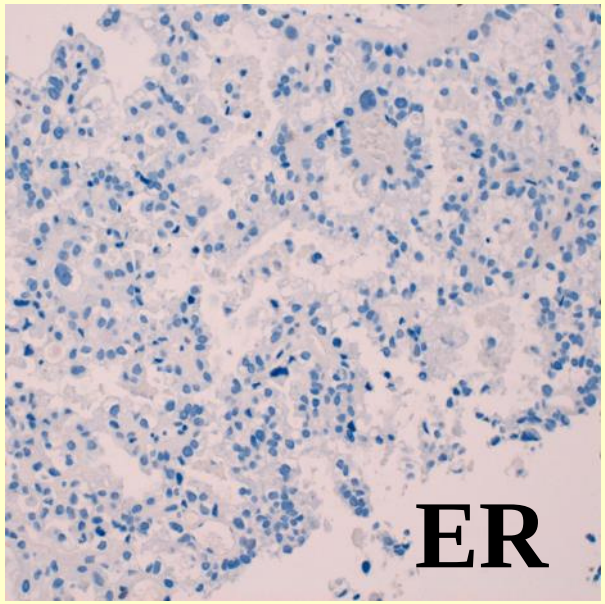
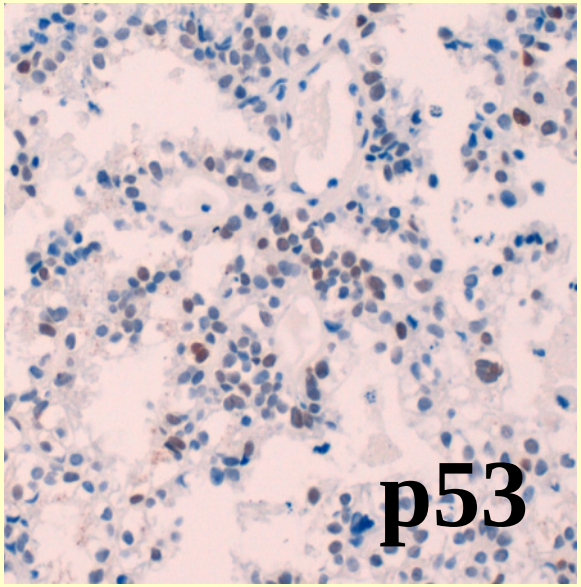


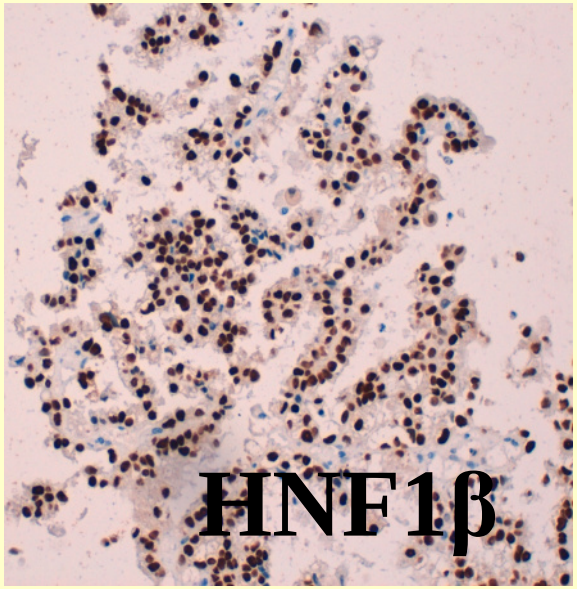
Clear Cell carcinoma of the endometrium

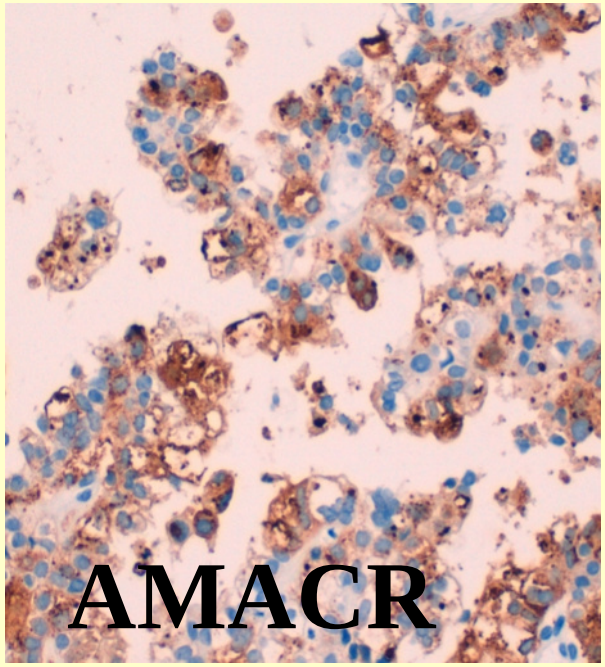
- Admixture of patterns (glandular, papillary, solid, cystic)
- Clear cells and eosinophilic cells
- Low mitotic index
- Cell stratification unusual
- Hyaline bodies, hyaline papillae, hobnail cells

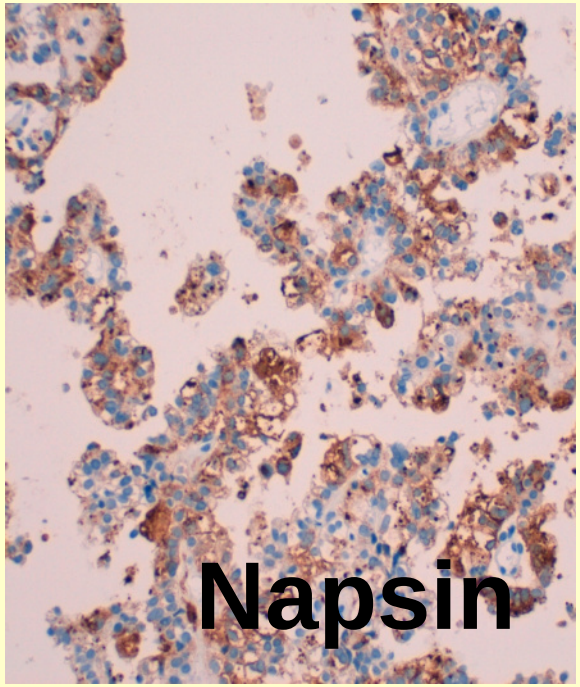
Fadare O, Am J Cancer Res 2013

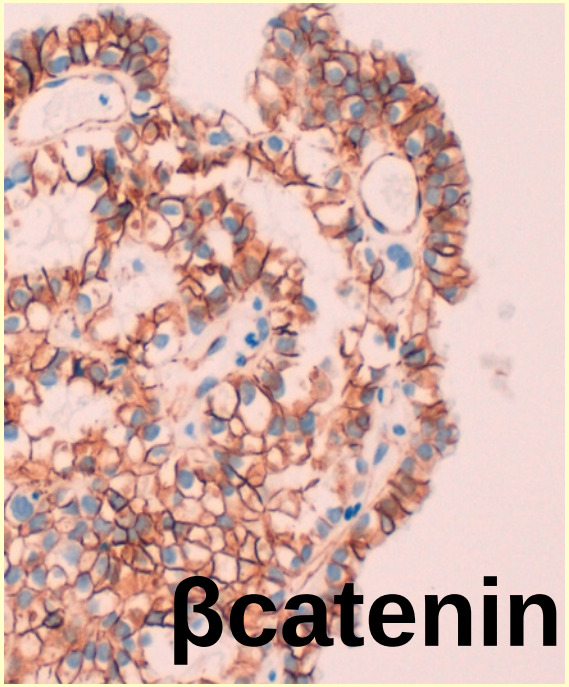

ER


p53


HNF1β


AMACR

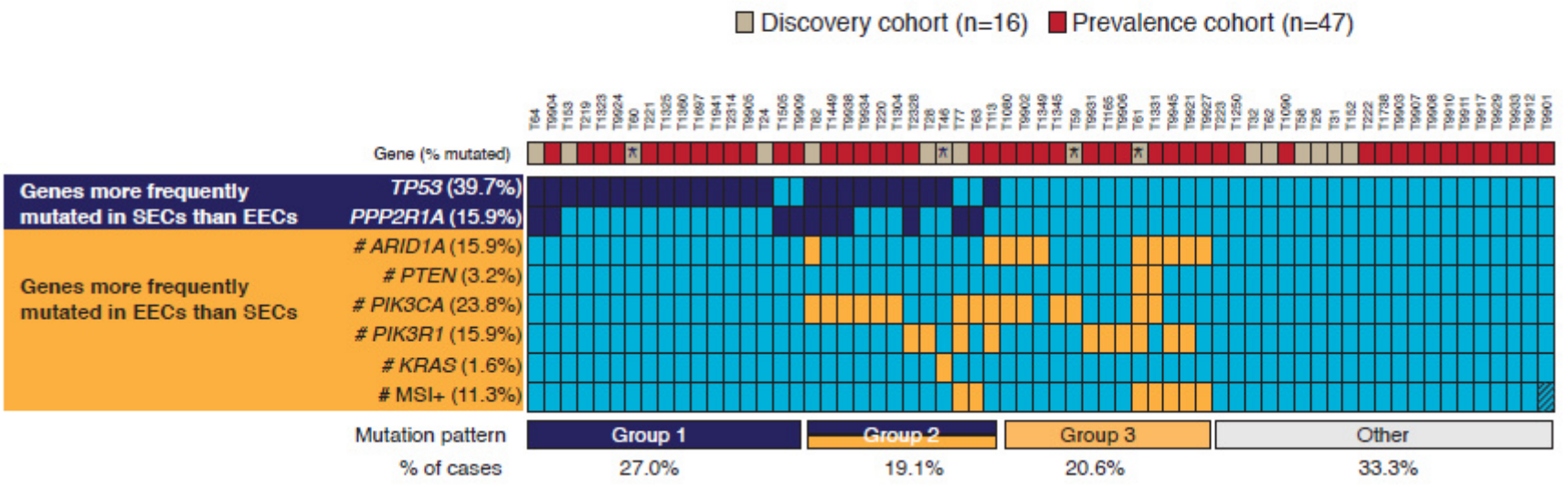

Napsin


βcatenin

Original Article

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

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



Endometrial carcinoma (Histological Classification)

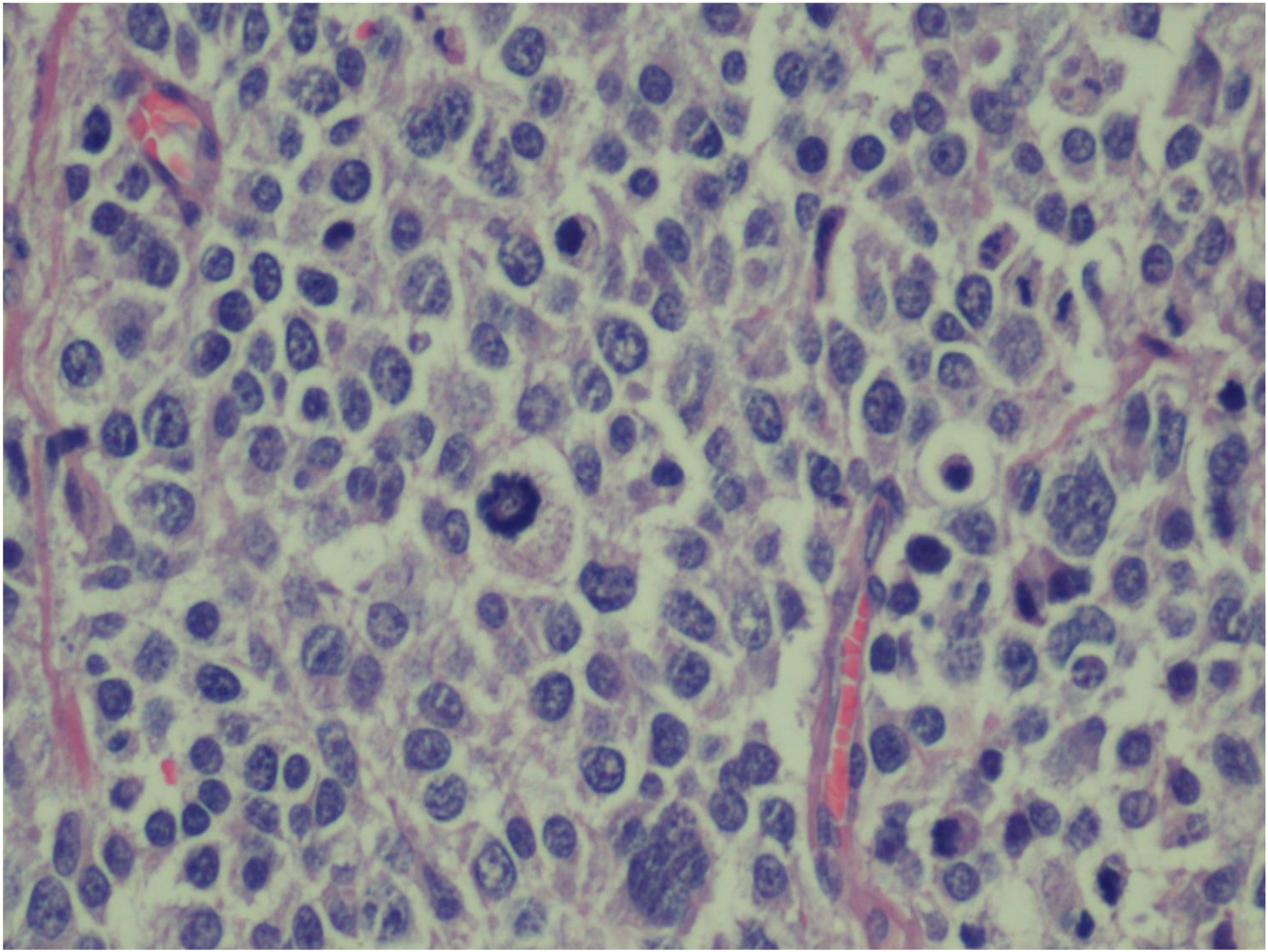
1- Endometrioid carcinoma, usual type
2- Endometrioid carcinoma variants
3- Mucinous adenocarcinoma
4- Serous carcinoma
5- Clear cell adenocarcinoma
6- Neuroendocrine carcinoma
7- Mixed carcinoma
8- Undifferentiated carcinoma

Carcinosarcoma

WHO 2014

Undifferentiated Carcinoma of the Endometrium

- 1 – 10% of endometrial carcinomas
- 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
- Focal neuroendocrine differentiation allowed.
- Frequent mismatch repair deficiency



Modern Pathology (2016), 1–9
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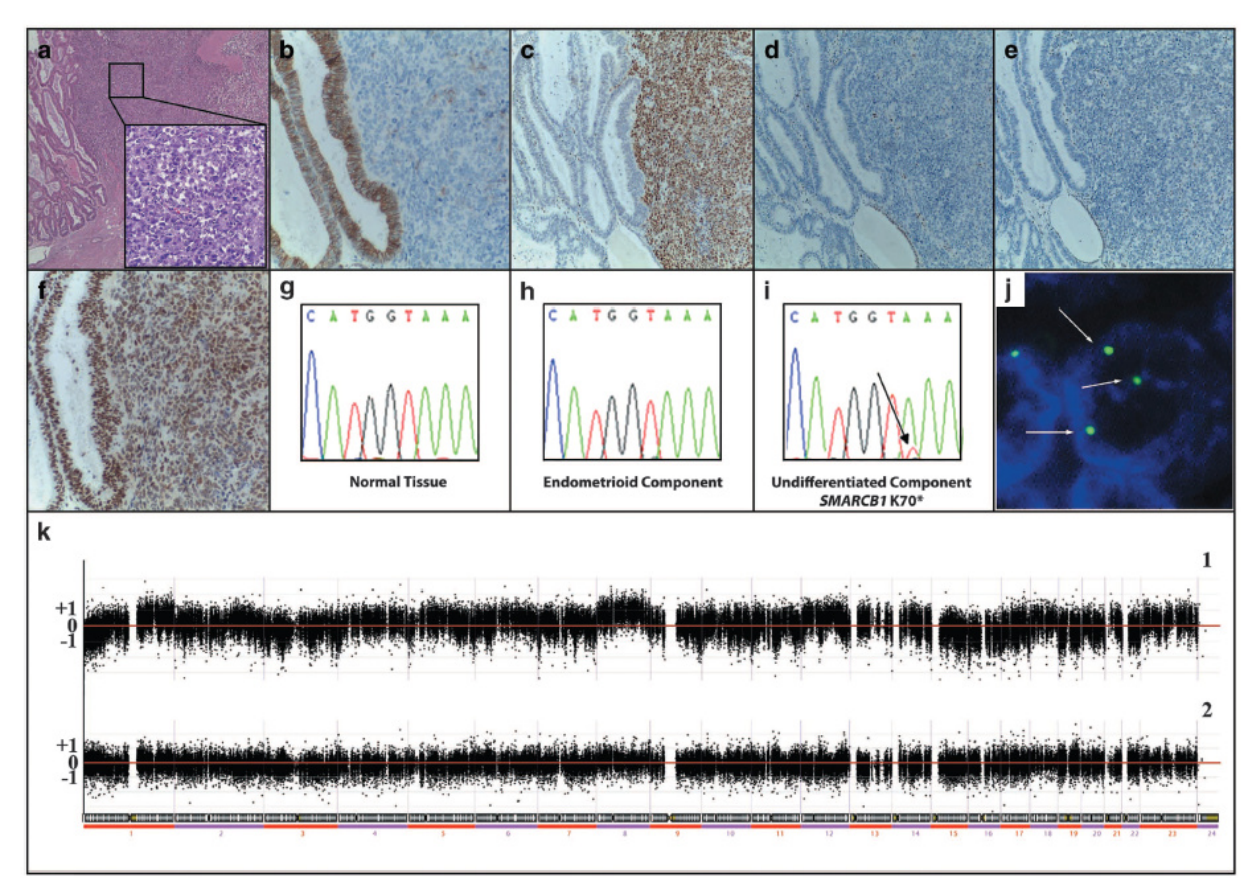
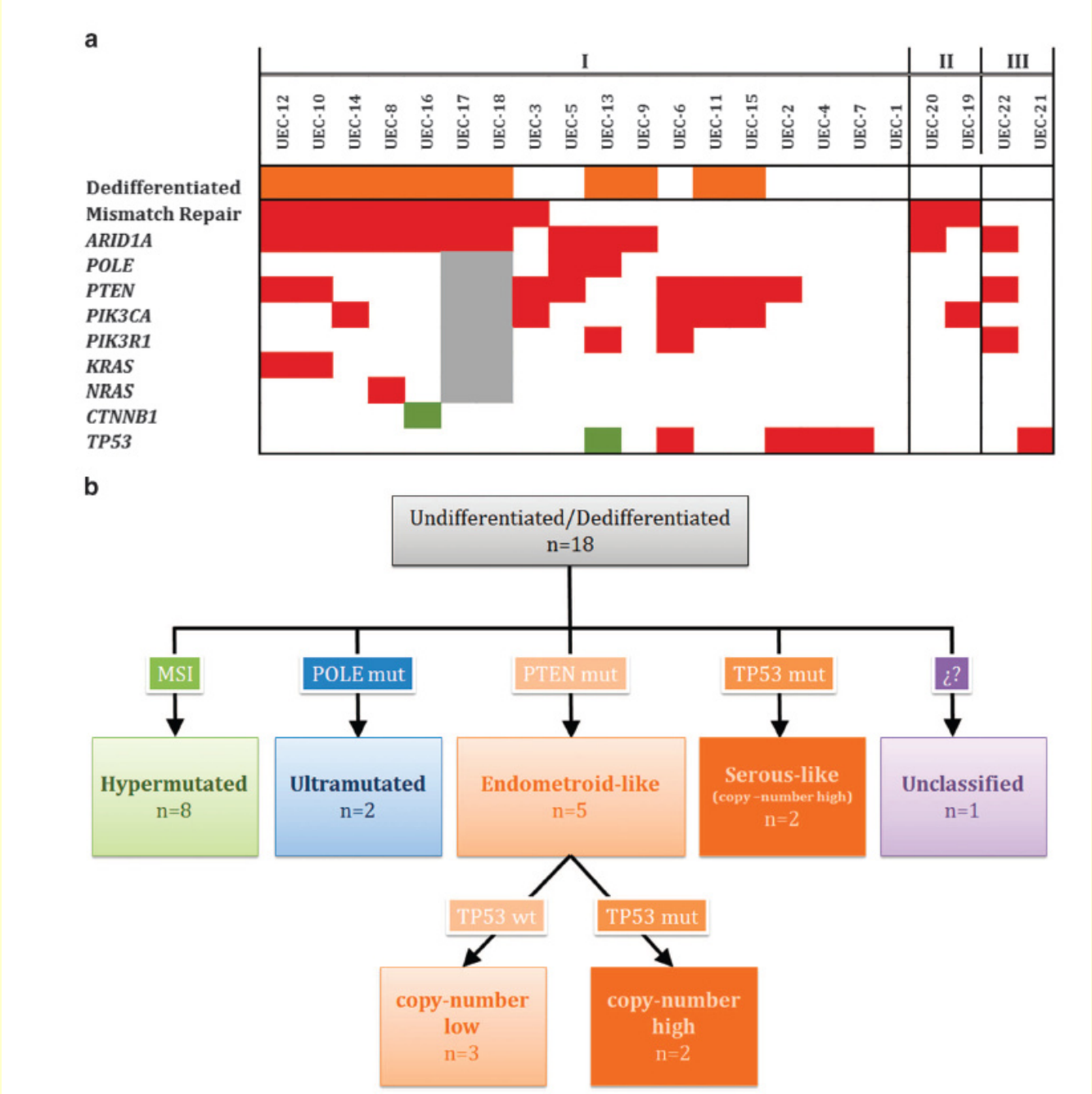
Molecular genetic heterogeneity in undifferentiated endometrial carcinomas

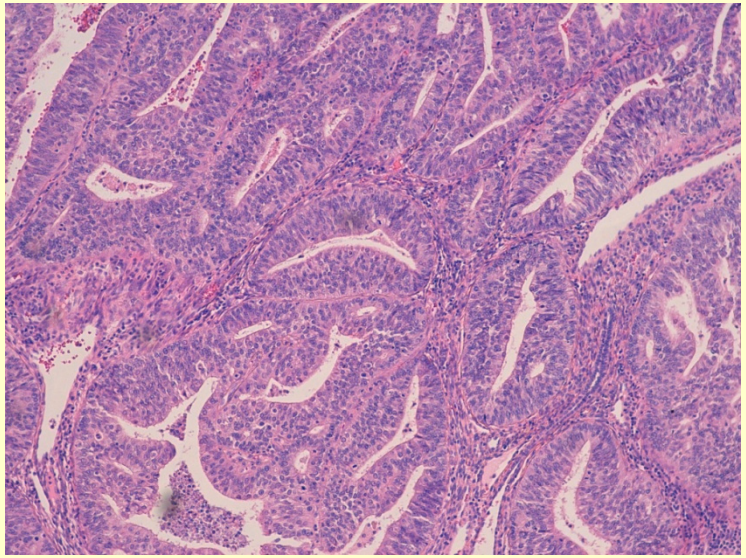
Juan M Rosa-Rosa[1], Susanna Leskelä[1], Eva Cristóbal-Lana[1], Almudena Santón[1], Ma Ángeles López-García[2], Gloria Muñoz[3], Belen Pérez-Mies[1], Michele Biscuola[2], Jaime Prat[4], Oliva E Esther[5], Robert A Soslow[6], Xavier Matias-Guiu[7,8] and Jose Palacios[1]

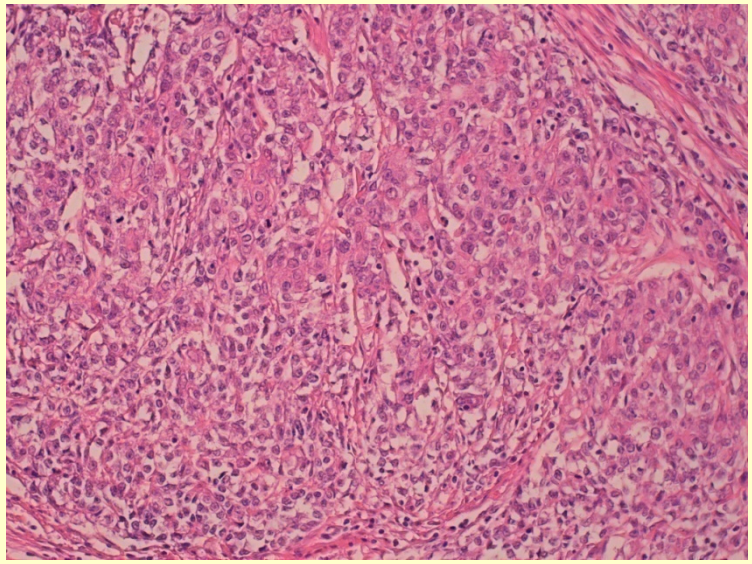



a
I
II
III
UEC-12
UEC-10
UEC-14
UEC-8
UEC-16
UEC-17
UEC-18
UEC-3
UEC-5
UEC-13
UEC-9
UEC-6
UEC-11
UEC-15
UEC-2
UEC-4
UEC-7
UEC-1
UEC-20
UEC-19
UEC-22
UEC-21
Dedifferentiated
Mismatch Repair
ARID1A
POLE
PTEN
PIK3CA
PIK3R1
KRAS
NRAS
CTNNB1
TP53
b
Undifferentiated/Dedifferentiated
n=18
MSI
POLE mut
PTEN mut
TP53 mut
¿?
Hypermutated
n=8
Ultramutated
n=2
Endometroid-like
n=5
Serous-like
(copy -number high)
n=2
Unclassified
n=1
TP53 wt
TP53 mut
copy-number
low
n=3
copy-number
high
n=2

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







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

Histological typing is good predictor of outcome but not perfect

	Frequency	Deaths
1.- Endometrioid carcinoma, low grade	72 %	26%
2.- Endometrioid carcinoma high grade	15 %	27%
3.- Mucinous adenocarcinoma		
4.- Serous carcinoma	10%	39%
5- Clear cell adenocarcinoma	3%	8%
6.- Neuroendocrine carcinoma		
7.- Mixed carcinoma		
8.- Undifferentiated carcinoma		

WHO 2014

Unresolved issues

- **Some hystotypes are composed of tumors with different prognosis (EEC3)**
- **Poor interobserver agreement in high grade tumors (EEC3 vs SC)**
- **Some hystotypes (Undiff ca and neuroendocrine ca) are similar tumors**
- **Difficulties in classifying some mixed-ambiguous tumors**
- **Imperfect predictor of prognosis**

Summary

- Pathologic Classification
- Molecular Classification
- Tumor Progression

Endometrial carcinoma
TCGA, 2013

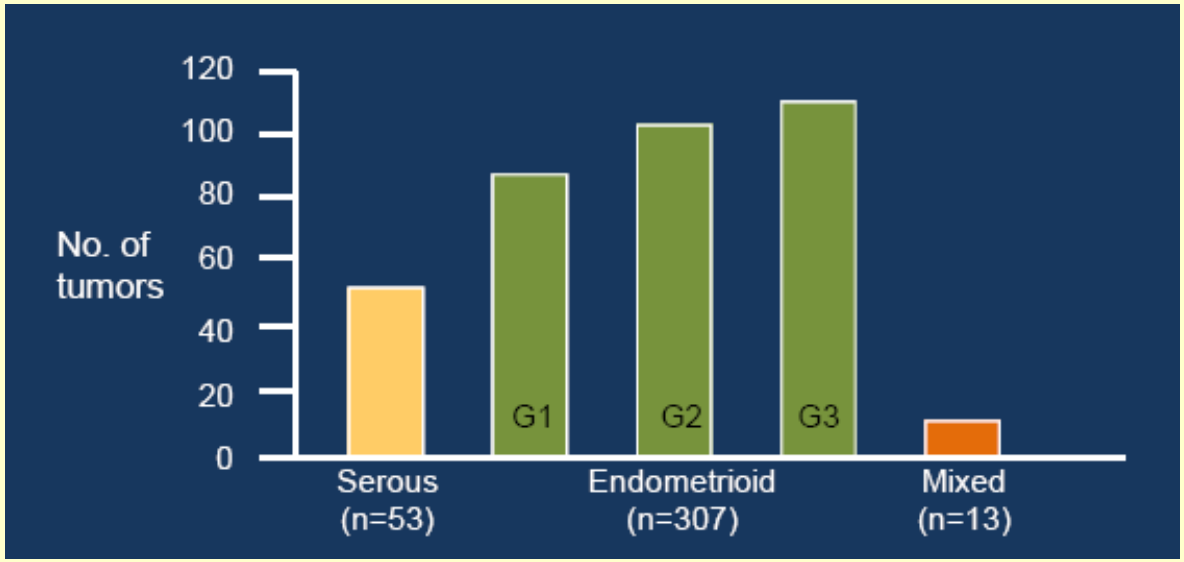
ARTICLE

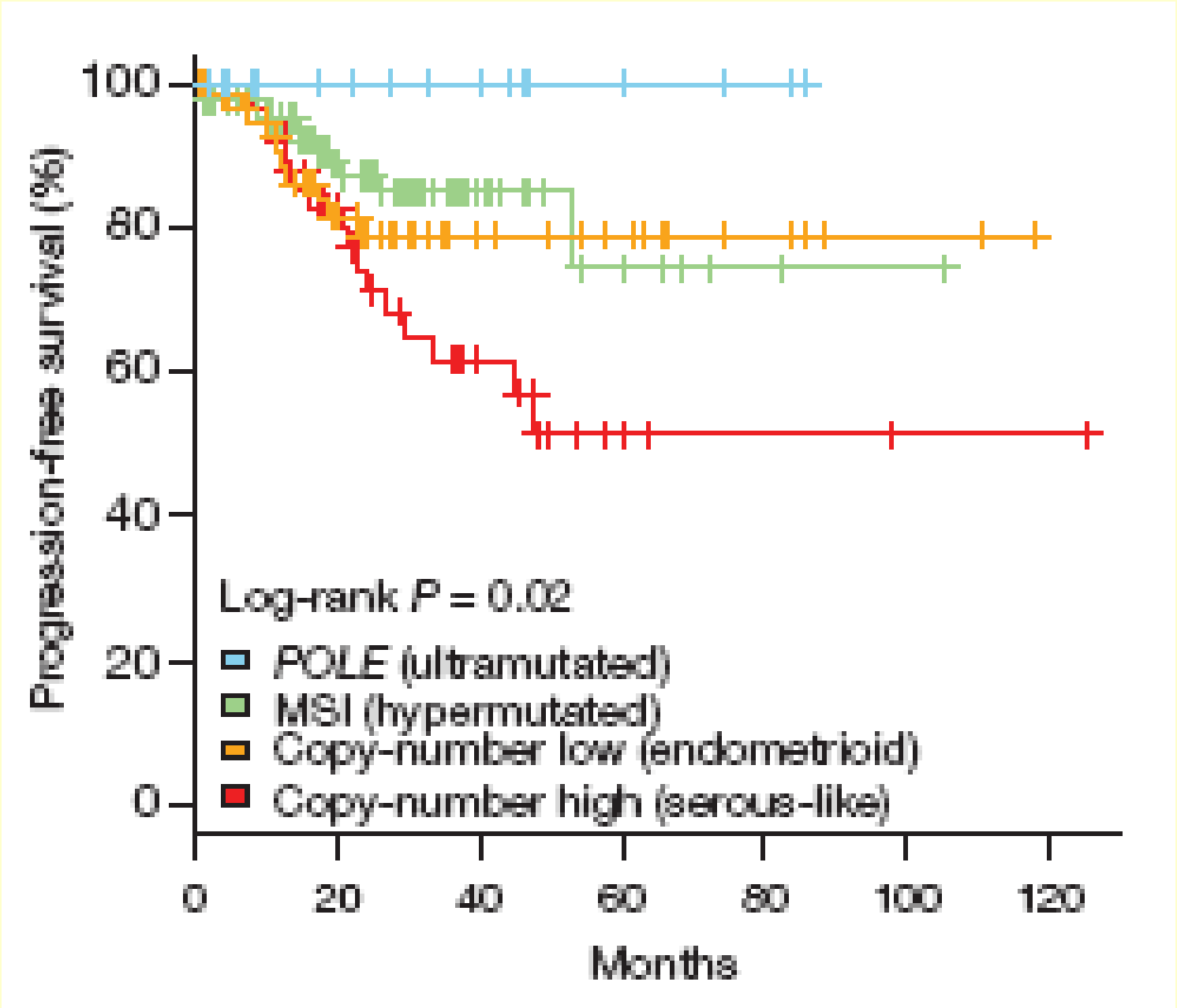
OPEN

doi:10.1038/nature12113

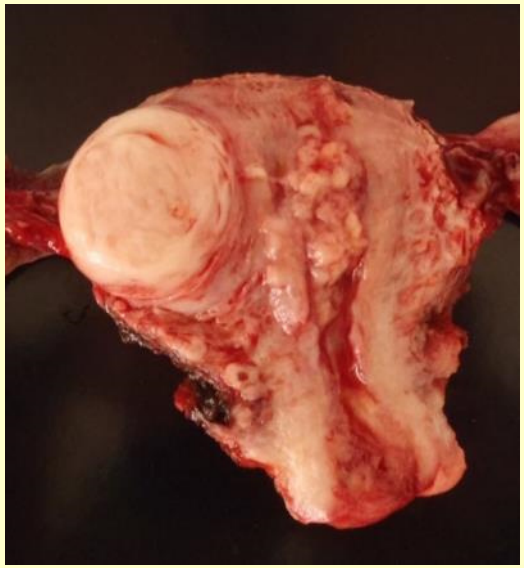
Integrated genomic characterization of endometrial carcinoma

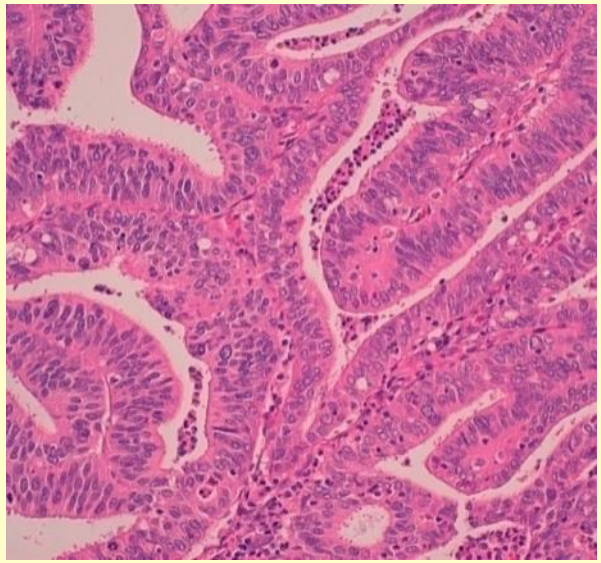
The Cancer Genome Atlas Research Network*

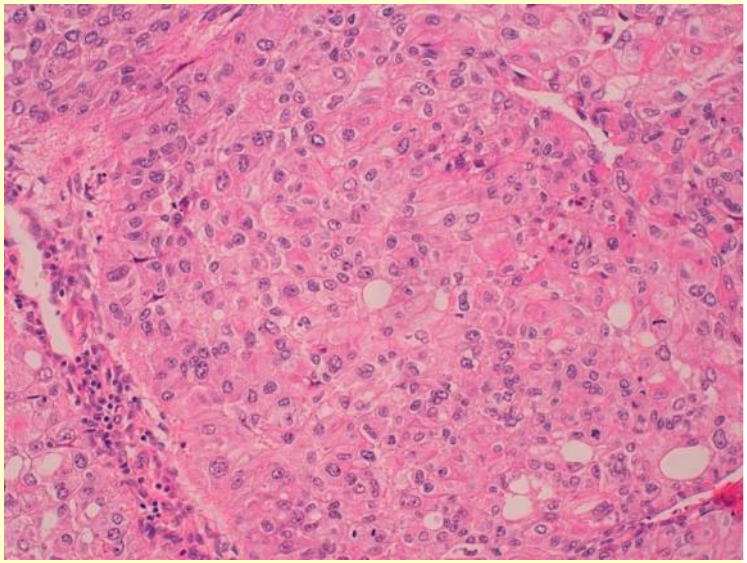


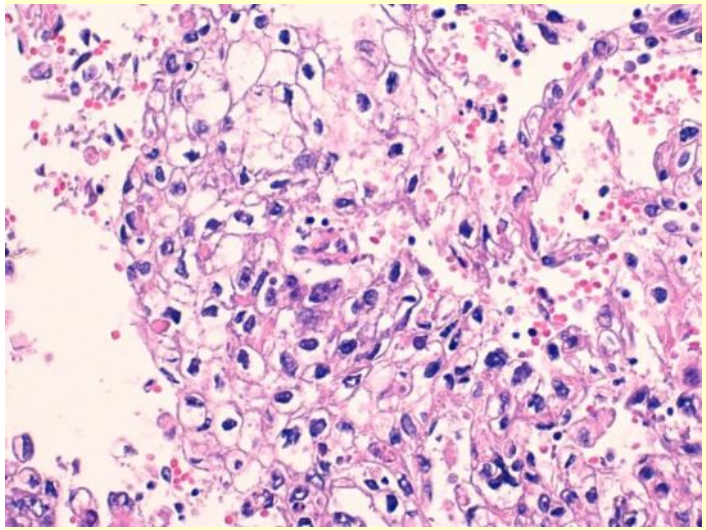

Progression-free survival (%)
100
80
60
40
20
0
Log-rank P = 0.02
POLE (ultramutated)
MSI (hypermutated)
Copy-number low (endometrioid)
Copy-number high (serous-like)
0
20
40
60
80
100
120
Months

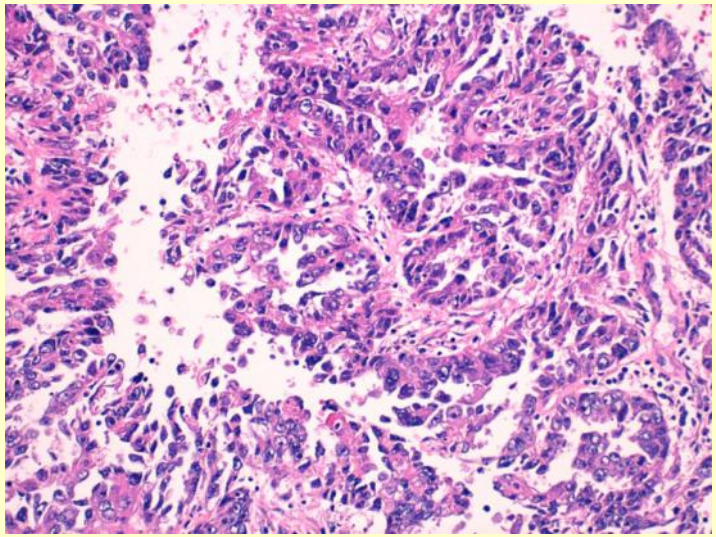
High grade endometrioid carcinoma with clear cell and serous-like features, and a POLE somatic mutation

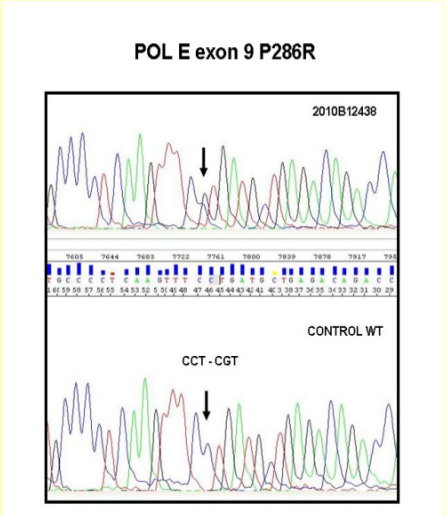












POLE exonuclease domain mutation predicts long progression-free survival in grade 3 endometrioid carcinoma of the endometrium

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

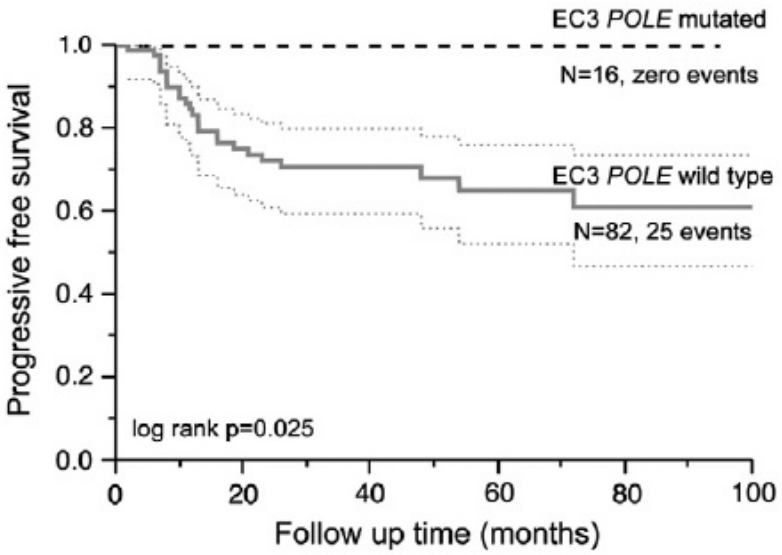


Fig. 1. Progression-free survival analysis in grade 3 endometrial endometrioid-type carcinoma stratified based on *POLE* exonuclease domain mutation status in combined HGEC and TCGA [5] cohorts. EC3, grade 3 endometrioid carcinoma. Dotted lines, 95% confidence intervals.

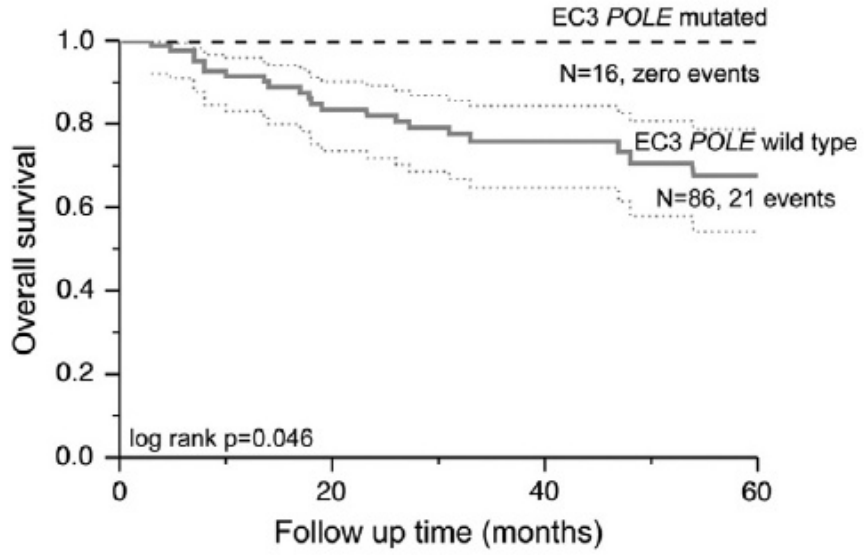
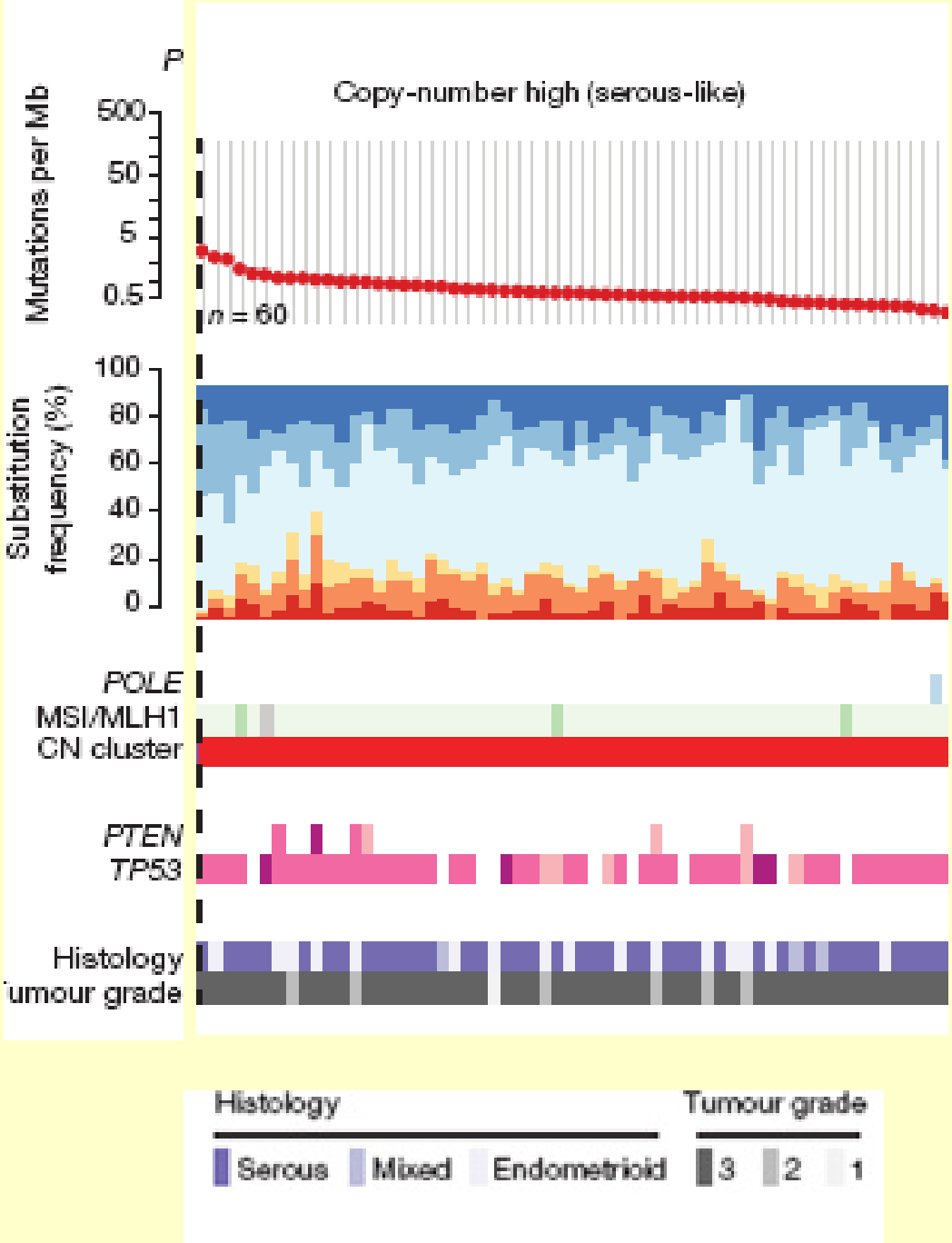


Fig. 3. Overall survival analysis in grade 3 endometrial endometrioid carcinoma stratified based on *POLE* exonuclease domain mutation status in combined HGEC and TCGA [5] cohorts. EC3, grade 3 endometrioid carcinoma. Dotted lines, 95% confidence intervals.

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)



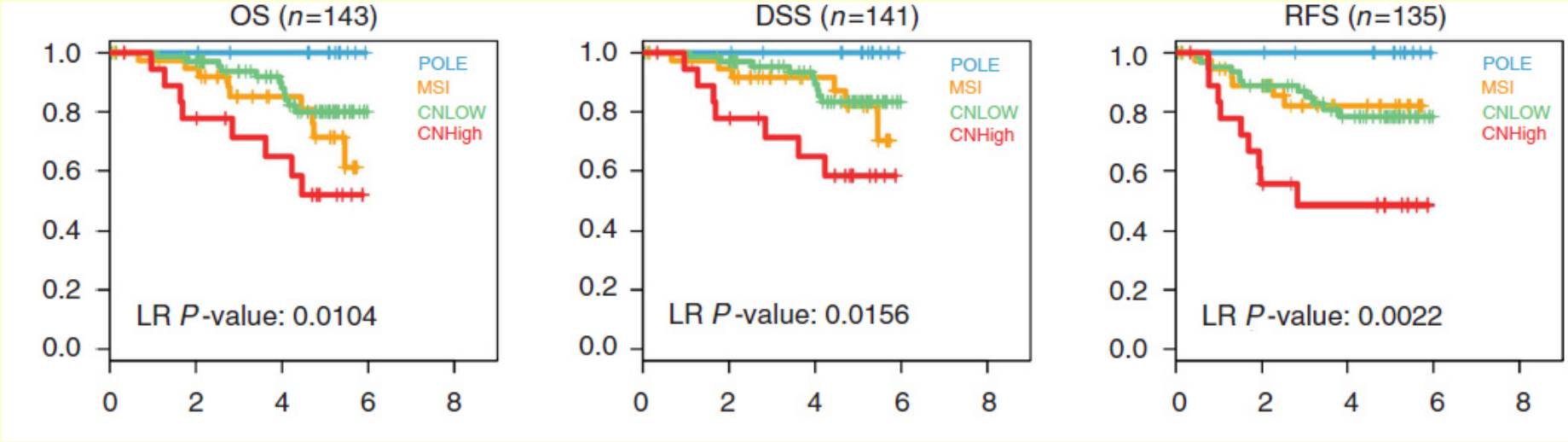
Bringing TCGA subtyping into pathology in high-grade endometrial carcinomas

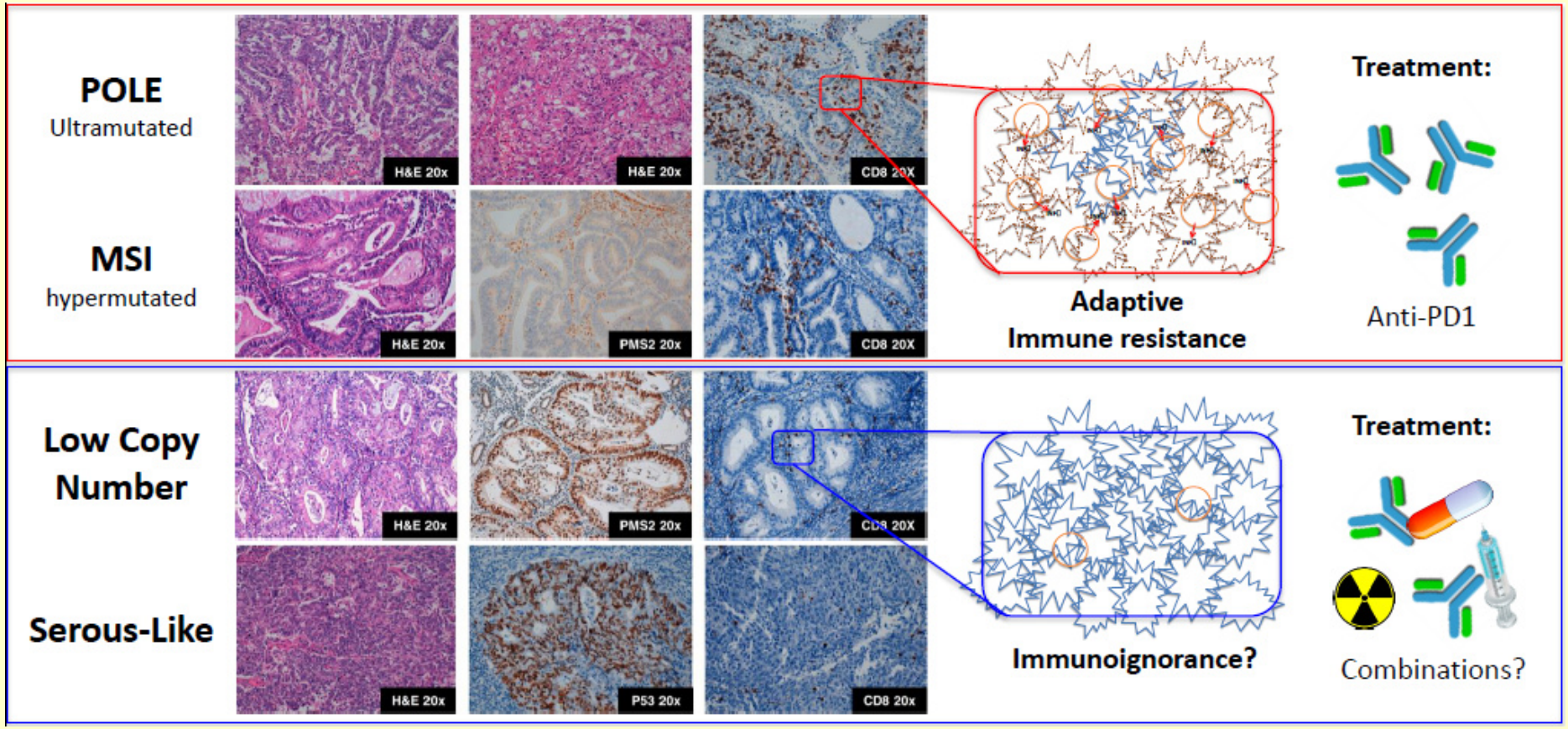
POLE mutation (hypermutated)	**POLE mutated EC**
POLE wild-type, p53 abnormal expression:	**Serous-like EC**
POLE wild-type, p53 wild-type pattern, abnormal mismatch repair:	**EEC with microsatellite instability**
POLE wild-type, p53 wild-type pattern, normal mismatch repair	**EEC with low copy number alterations**

A clinically applicable molecular-based classification for endometrial cancers

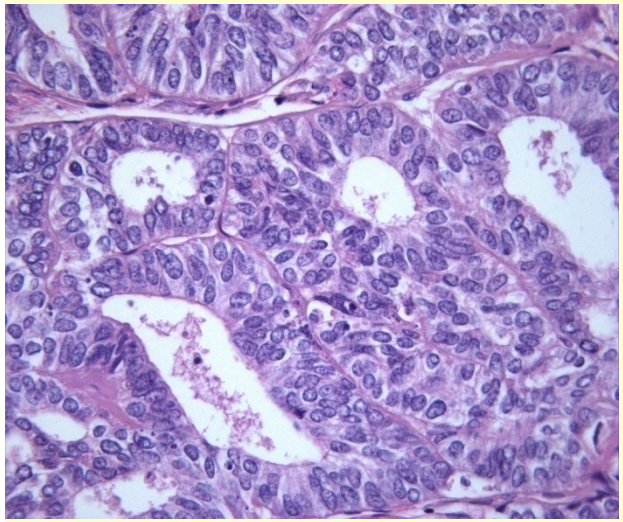
A Talhouk[1], M K McConechy[1], S Leung[2], H H Li-Chang[1,3], J S Kwon[4], N Melnyk[1], W Yang[1], J Senz[1], N Boyd[1], A N Karnezis[1], D G Huntsman[1], C B Gilks[1] and J N McAlpine[*,4]

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

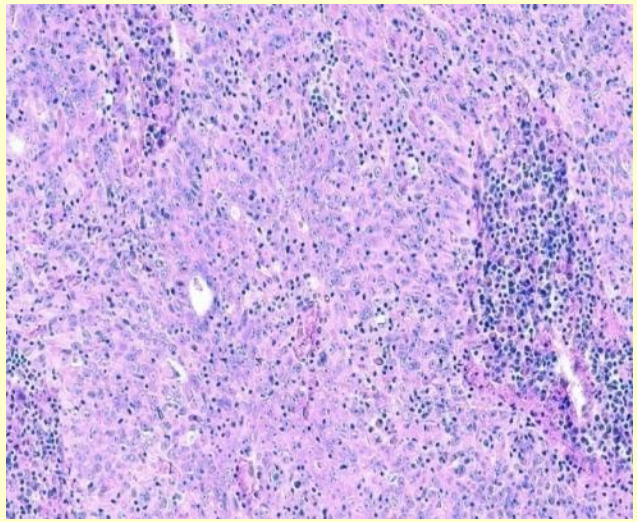



POLE
Ultramutated
MSI
hypermutated
H&E 20x
H&E 20x
CD8 20X
H&E 20x
PMS2 20x
CD8 20X
Adaptive
Immune resistance
Treatment:
Anti-PD1
Low Copy
Number
Serous-Like
H&E 20x
PMS2 20x
H&E 20x
P53 20x
CD8 20x
Immunoignorance?
Treatment:
Combinations?

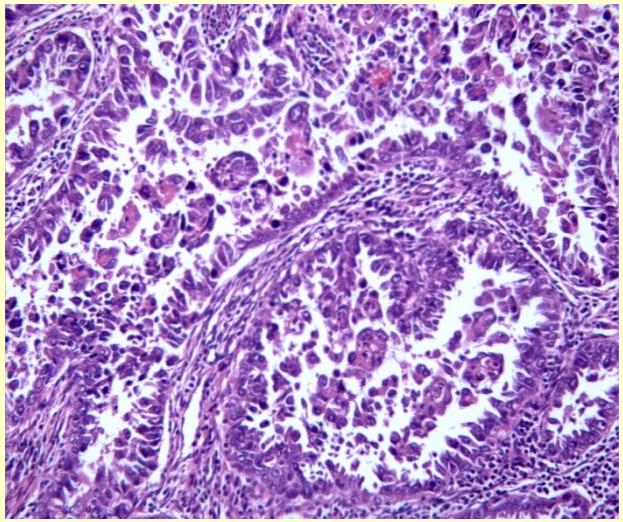
TCGA-BASED MOLECULAR CLASSIFICATION IS APPLICABLE TO ALL HISTOLOGIC SUBTYPES OF ENDOMETRIAL CARCINOMA



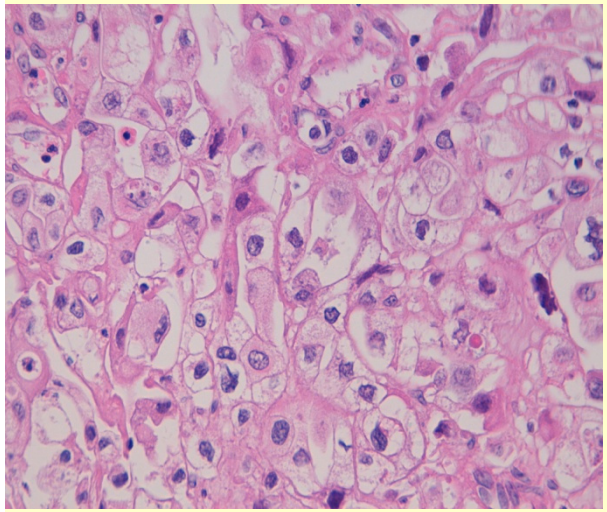
EEC 1,2



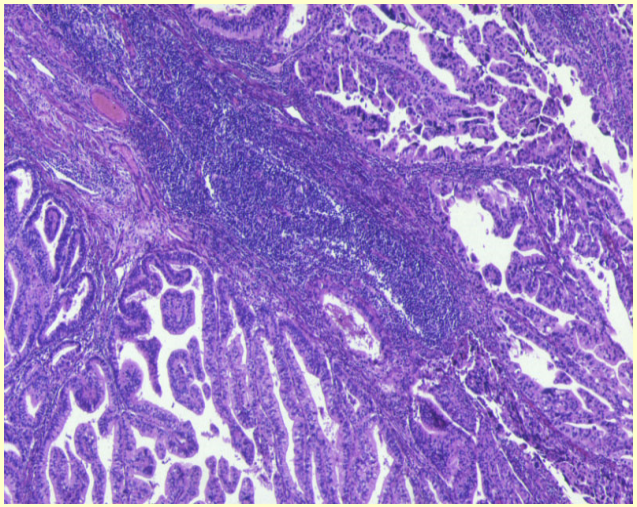
EEC 3



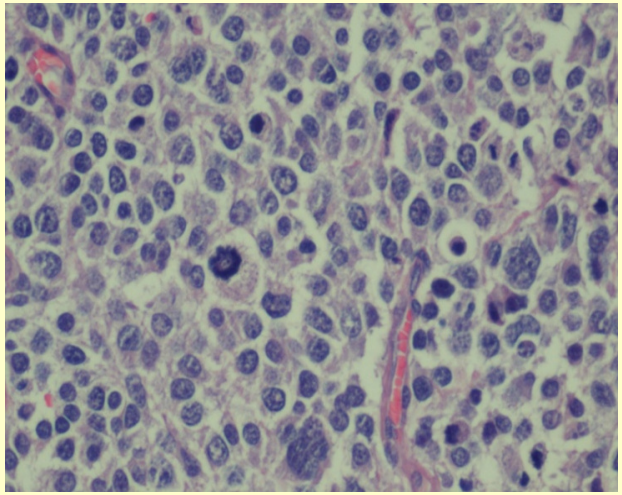
Serous



Clear Cell

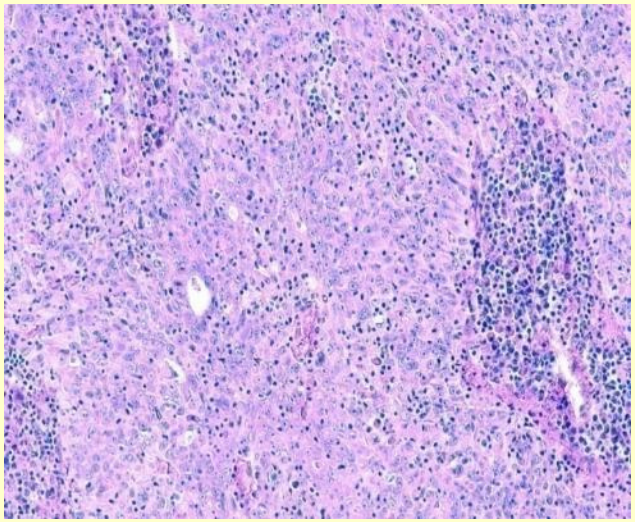


Mixed

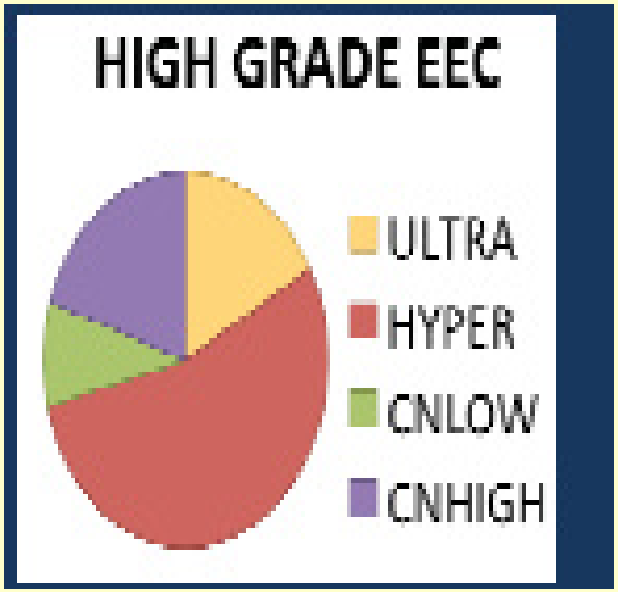


Undiff

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

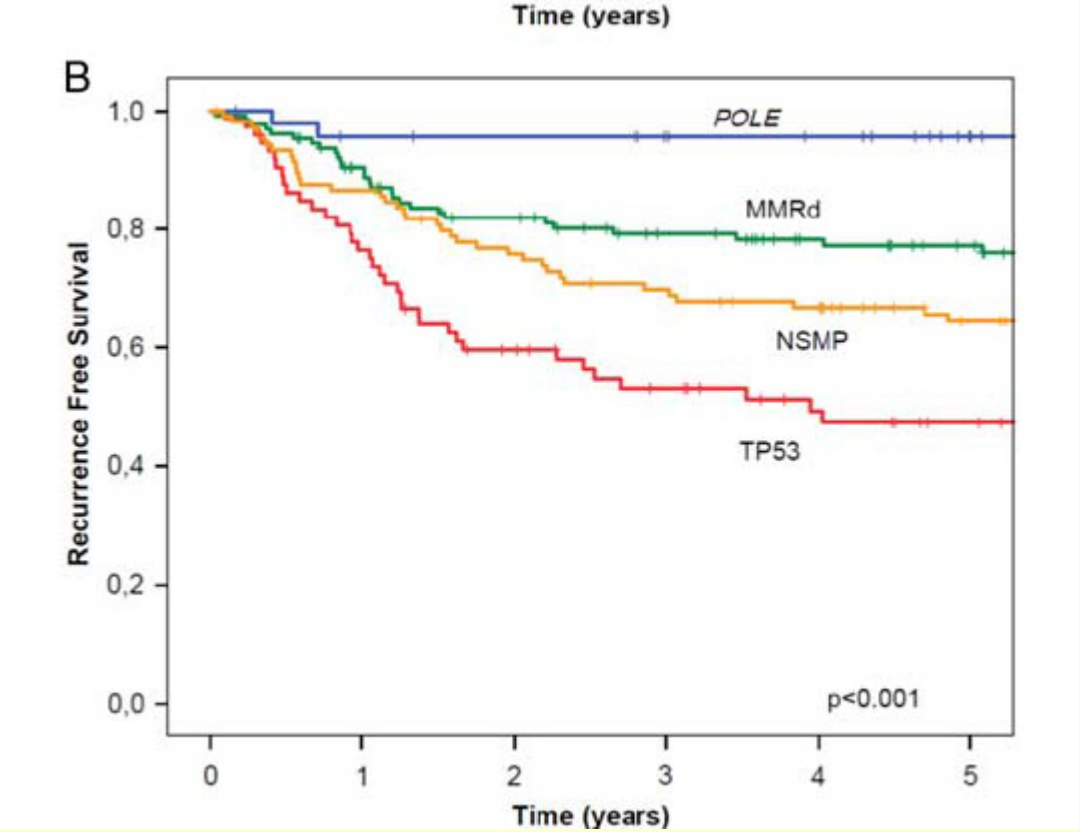


EEC 3



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

Tjalling Bosse, MD, Remi A. Nout, MD,* Jessica N. McAlpine, MD,† Melissa K. McConechy, MD,‡ Heidi Britton, MD,‡ Yaser R. Hussein, MD,§ Carlene Gonzalez, BA,§ Raji Ganesan, MD,‖ Jane C. Steele, MD,‖ Beth T. Harrison, MD,¶ Esther Oliva, MD,¶ August Vidal, MD,# Xavier Matias-Guiu, MD,# Nadeem R. Abu-Rustum, MD,** Douglas A. Levine, MD,** C. Blake Gilks, MD,‡ and Robert A. Soslow, MD§*

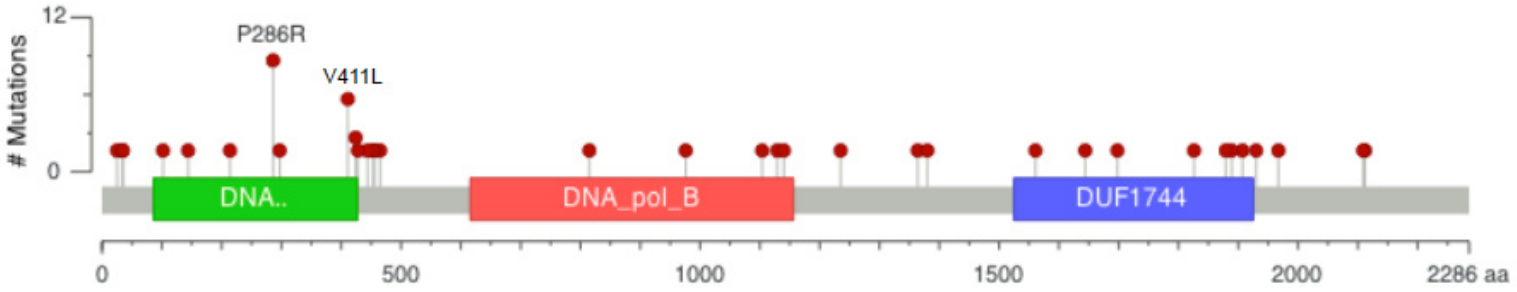


TCGA-based surrogate limitations

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

No standardized methodology (Sanger exons 9, 13 and 14 versus NGS)

Endometrial



Eve Shinbrot, HGSC; cBIO Portal

The Cancer Genome Atlas

Occurance of POLE mutations in EEC

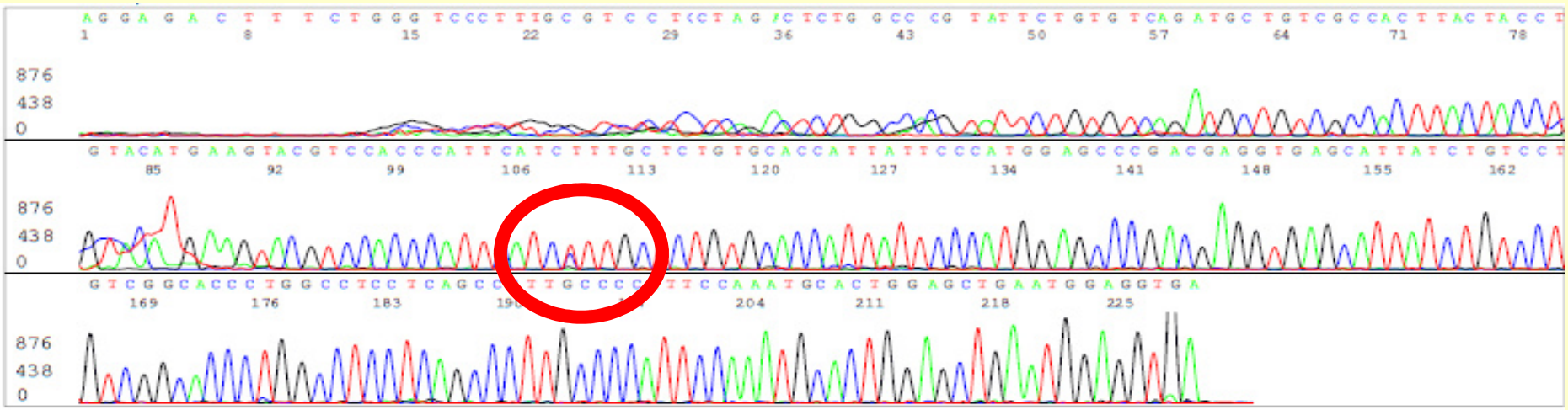
Subtype	Patients	All Sites (1-2286)	Exonuclease Domain (223-471)	Recurrent Sites (P286,V411)
MSS Low	166	6 (4%)	2 (1%)	0
MSI Hypermutated	65	9 (14%)	1 (2%)	0
MSS Ultramutated	17	45 (265%)	17 (100%)	13 (76%)

P286R and V411L account for more than 90% of POLE mutations

The Cancer Genome Atlas



POLE , F479L, exon 14



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)

Does a p53 "Wild-type" Immunophenotype Exclude a Diagnosis of Endometrial Serous Carcinoma?

Oluwole Fadare, MD, Andres A. Roma, MD,* Vinita Parkash, MD,† Wenxin Zheng, MD,‡ and Vighnesh Walavalkar, MD**

TABLE 1. A Sampling of Studies Reporting on p53 Alterations in ESC*

References	No. Cases	Frequency of p53 Abnormality [n (%)]	Testing Method	Histotype and Criteria†
Kuhn et al[28]	76	62 (82)	Seq	ESC
Zhao et al[62]	52	31 (60)	Seq	ESC
Schultheis et al[51]	42	37 (88)	Seq	ESC
Le Gallo et al[63]	52	39 (75)	Seq	ESC
McConechy et al[116]	37	25 (67.6)	Seq	ESC
Jia et al[19]	25	18 (72)	Seq	EIC
Jia et al[19]	22	21 (96)	Seq	ESC
Lax et al[44]	27	25 (92.6)	Seq	ESC
Han et al[61]	16	15 (94)	IHC	ESC
Kommoss et al[24]	28	28 (100)	IHC	ESC; positive: 80% strong positive and null; excludes cases of probable independent (tubal/endometrial) primaries or tubal primaries
Togami et al[25]	29	20 (69)	IHC	ESC; positive: >50% of cells positive was the highest level of staining category
Sho et al[26]	33	33 (100)	IHC	ESC
Zhang et al[27]	33	21 (64)	IHC	ESC
Haley et al[29]	10	10 (100)	IHC	ESC
Xue et al[30]	61	61 (100)	IHC	ESC
Mhawech-Fauceglia et al[31]	31	26 (84)	IHC	ESC; positive: >75% of cells
Yan and Hui[32]	13	13 (100)	IHC	Minimal ESC; EIC: positive: diffuse overexpression or null
Hirschowitz et al[33]	34	33 (97)	IHC	ESC: positive: 50%–74% of cells positive
Nofech-Mozes et al[34]	34	28 (84)	IHC	ESC: positive: > 50% of the tumor
Li et al[36]	45	35 (78)	IHC	ESC: positive: > 50% of the tumor
Chiesa-Vottero et al[37]	11	10 (91)	IHC	ESC and mixed carcinomas with ESC component; positive: ≥70% of the tumor or null
Zheng et al[38]	12	12 (100)	IHC	EIC; positive: cases with scores of 7-9 on a 0-9 scale
Idrees et al[39]	14	11 (79)	IHC	ESC; positive: "diffuse and strong nuclear staining, ranging from 70% to 100%"
Busmanis et al[40]	21	19 (90)	IHC	ESC: inclusive of cases classified as "completely negative (score 0 on 0-9 scale) and cases classified as positive with scores 6-9 on same scale)"
Vasil'eva and Belianin[41]	138	120 (86.7)	IHC	ESC
Ragni et al[42]	11	8 (72.7)	IHC	ESC; positive: inclusive of cases with score 3 only (0-3 scale)
Darvishian et al[43]	16	14 (87.5)	IHC	ESC: cases of ESC in control group only
Hui et al[35]	37	25 (68)	IHC	Minimal serous carcinoma; positive: score ≥7 on 0-9 scale
Lax et al[44]	44	42 (95.45)	IHC	ESC; positive: score 0 and ≥8 on 0-12 scale
Kounelis et al[45]	21	16 (76.2)	IHC	ESC: positive: score ≥3 on 0-6 scale
Halperin et al[46]	22	18 (81.8)	IHC	ESC
Schmitz et al[47]	21	13 (62)	IHC	ESC
Taskin et al[48]	18	18 (100)	IHC	ESC: positive: > 70% or null.
Kihara et al[49]	7	4 (57)	IHC	ESC
Sorbe[50]	94	90 (94.7)	IHC	ESC
Nafisi et al[52]	29	26 (90)	IHC	EIC
Hoang et al[53]	15	15 (100)	IHC	ESC; positive: ≥70% of the tumor or null
Allo et al[54]	88	68 (77)	IHC	ESC; positive: >50% of the tumor or null
Daniilidou et al[55]	12	11 (91.66)	IHC	ESC
Trahan et al[56]	10	9 (90)	IHC	ESC; positive: scores 0 or ≥7 on a 0-9 scale.
Demopoulos et al[58]	8	6 (75)	IHC	ESC
Alkushi et al[59]	13	9 (69.2)	IHC	ESC; positive: > 50% of the tumor cell nuclei stained
Chen et al[60]	52	52 (100)	IHC	ESC
Egan et al[57]	31	26 (83.9)	IHC	ESC

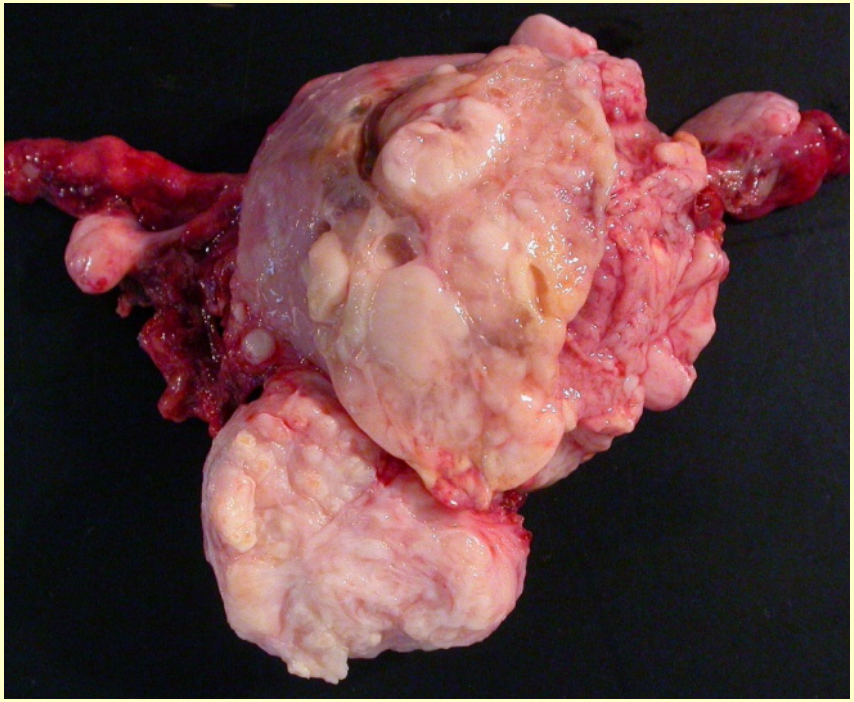
Gene mutations in serous endometrial carcinoma

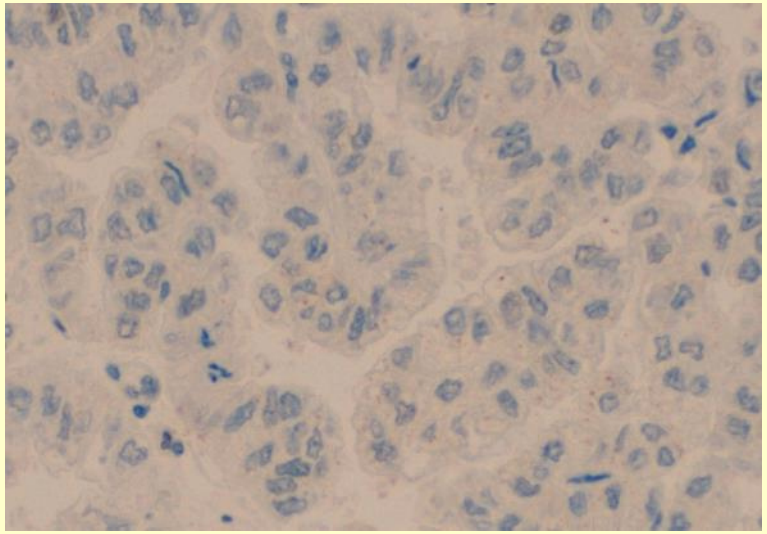
GENE	FREQUENCY	GENE	FREQUENCY
TP53	90.7%	*PRPF18*	7%
PIK3CA	41.9%	*SPOP*	7%
FBXW7	30.2%	*CDH19*	7%
PPP2R1A	36.6%	*FGFR2*	7%
CHD4	16.3%	ARID1A	7%
CSMD3	11.6%	*FOXA2*	4.6%
COLA11	11.6%	*USP36*	4.6%

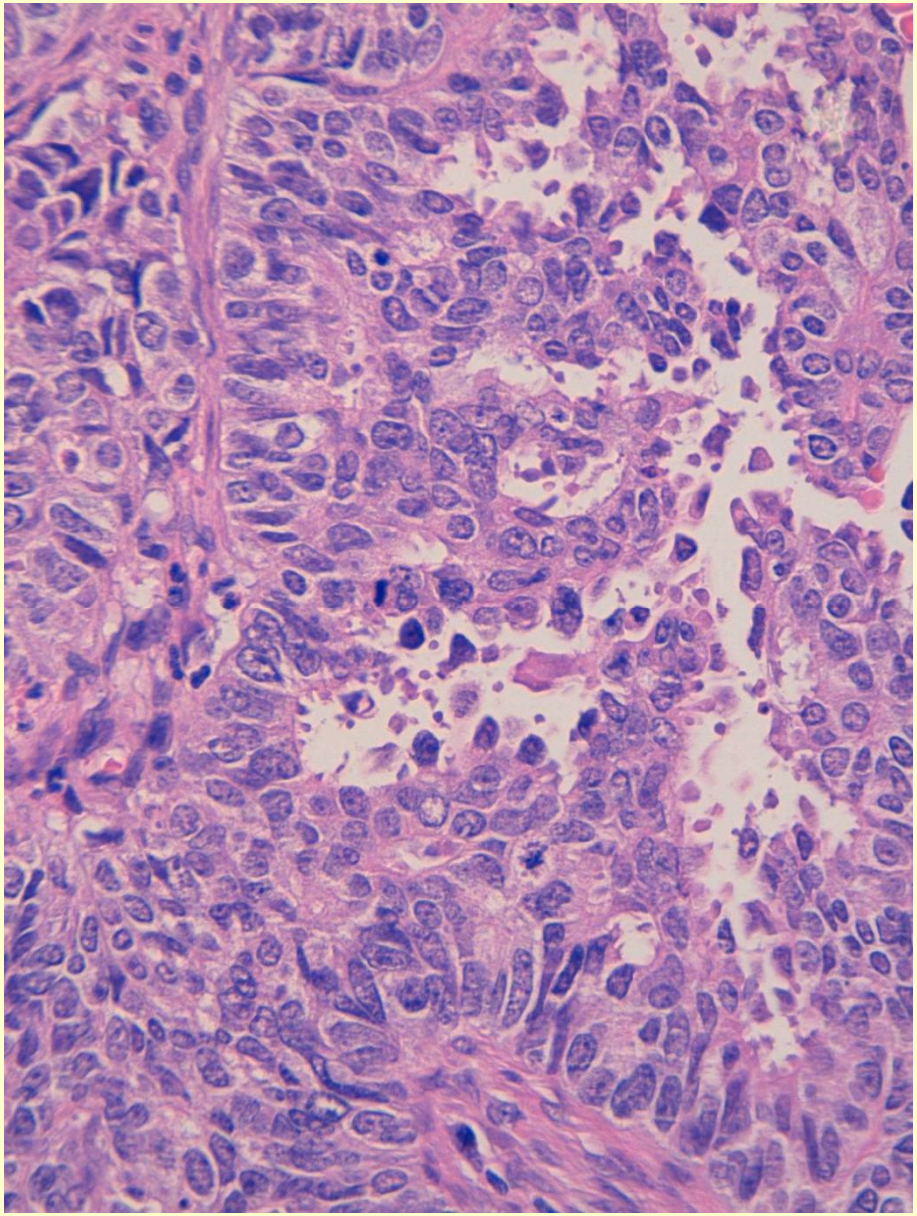
TCGA; Nature 2013

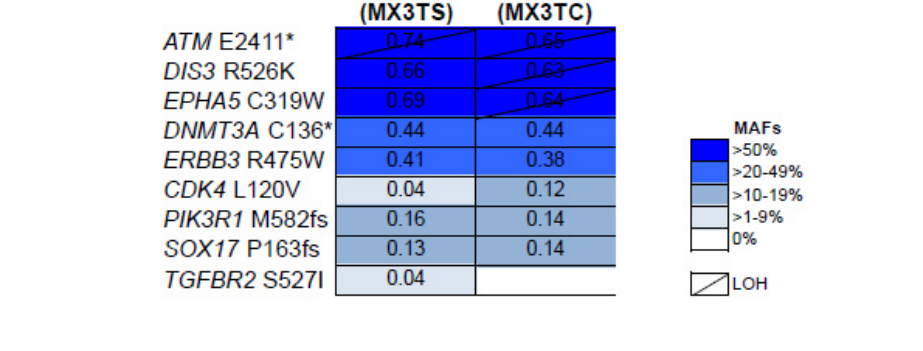
TAF1 (30%), ***EP300*** (8%), ***TSPYL2*** (6%), ***MAP3K4*** (6%) and ***ABCC9*** (6%).

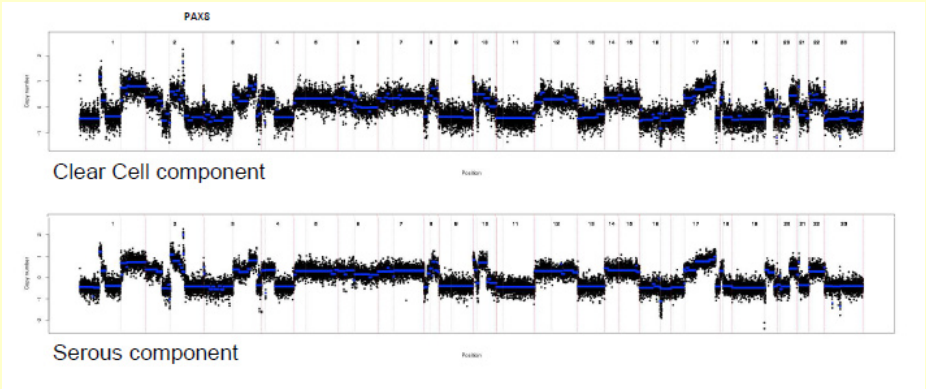
Khun et al; J Natl Cancer Inst 2012.
Le Gallo et al; Nat Genet 2012;
Zhao et al; PNAS 2013.











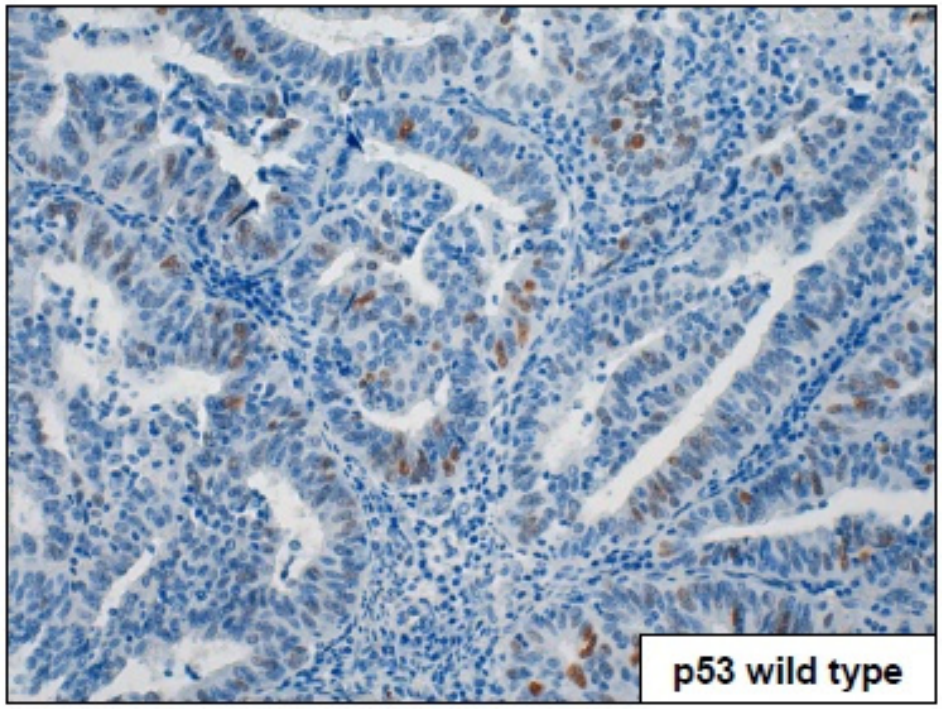
Microscopy: Serous carcinoma

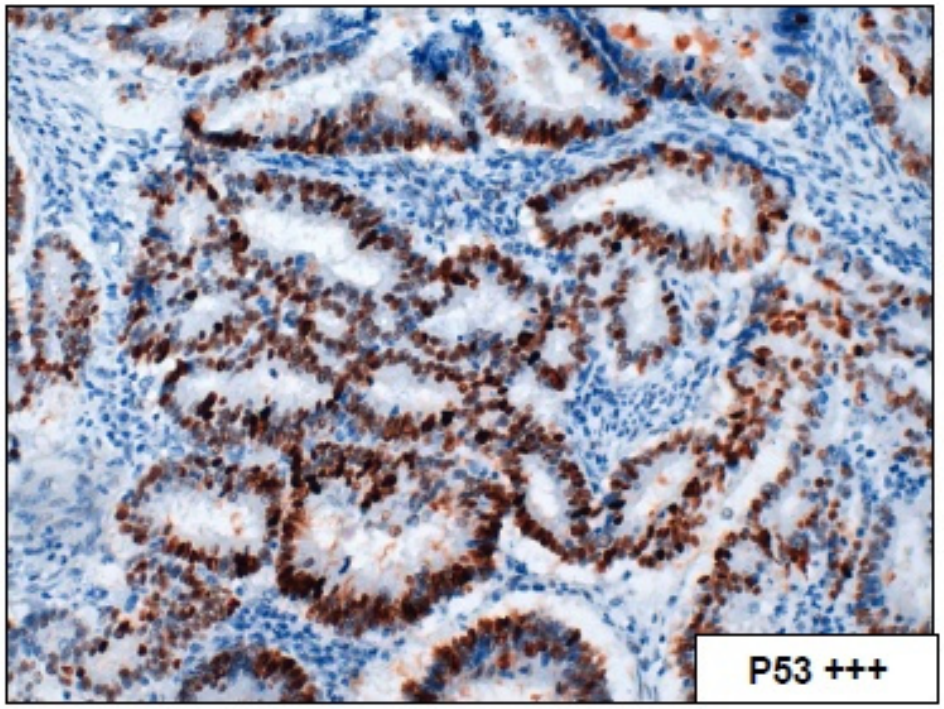
TCGA by exome sequencing: High copy number, serous-like ca

TCGA by TCGA surrogate: Low copy number EC

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

Impact of Tumor heterogeneity on TCGA classification

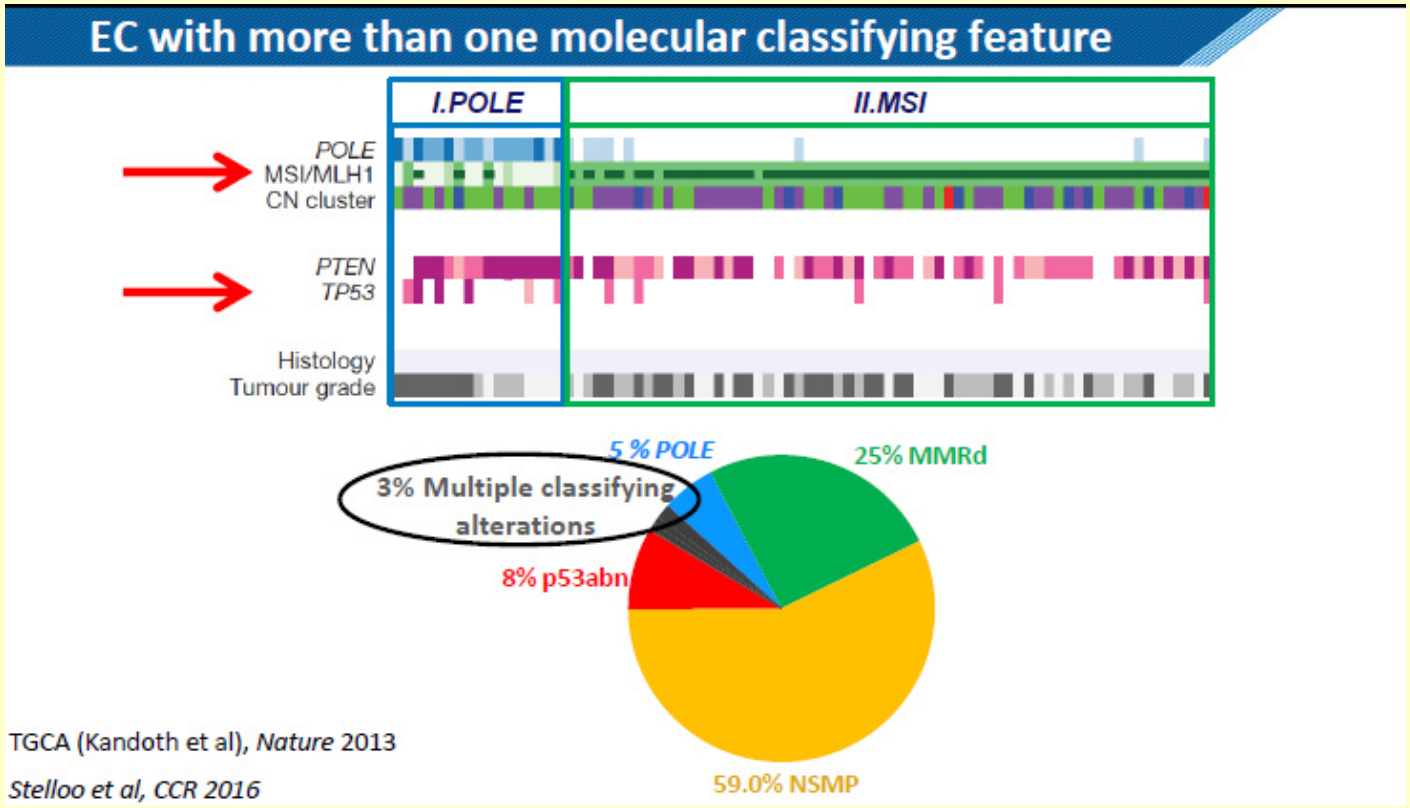




TCGA-based surrogate limitations

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

What about double classifiers ?



POLE-mutated EC with p53 mutations behave like POLE-mutated Ecs

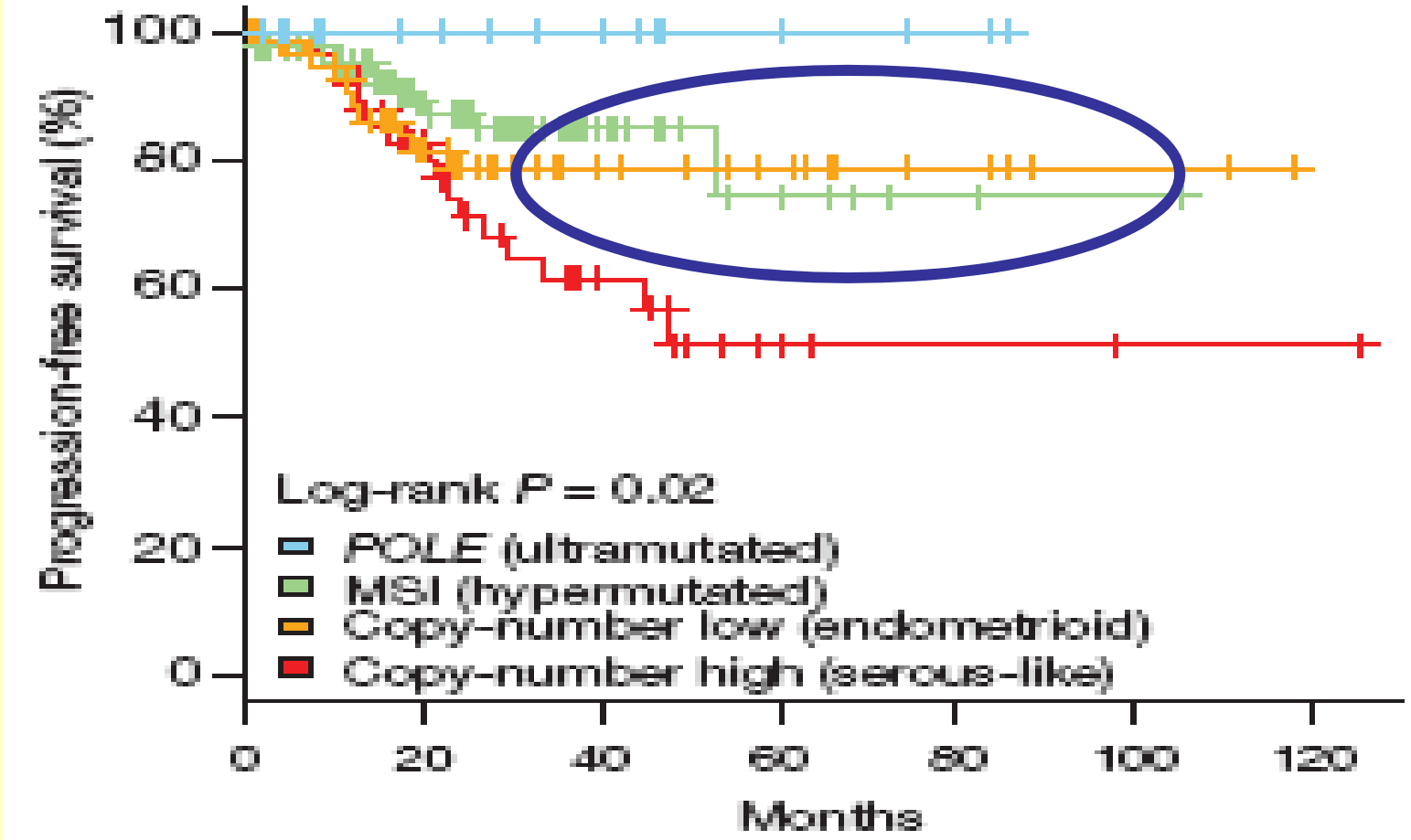
MSI EC with p53 mutations behave like MSI EC

Summary

- Pathologic Classification
- Molecular Classification
- Tumor Progression

Integrated genomic characterization of endometrial carcinoma

The Cancer Genome Atlas Research Network*



ENITEC

European Network for Individualized Treatment in Endometrial Cancer

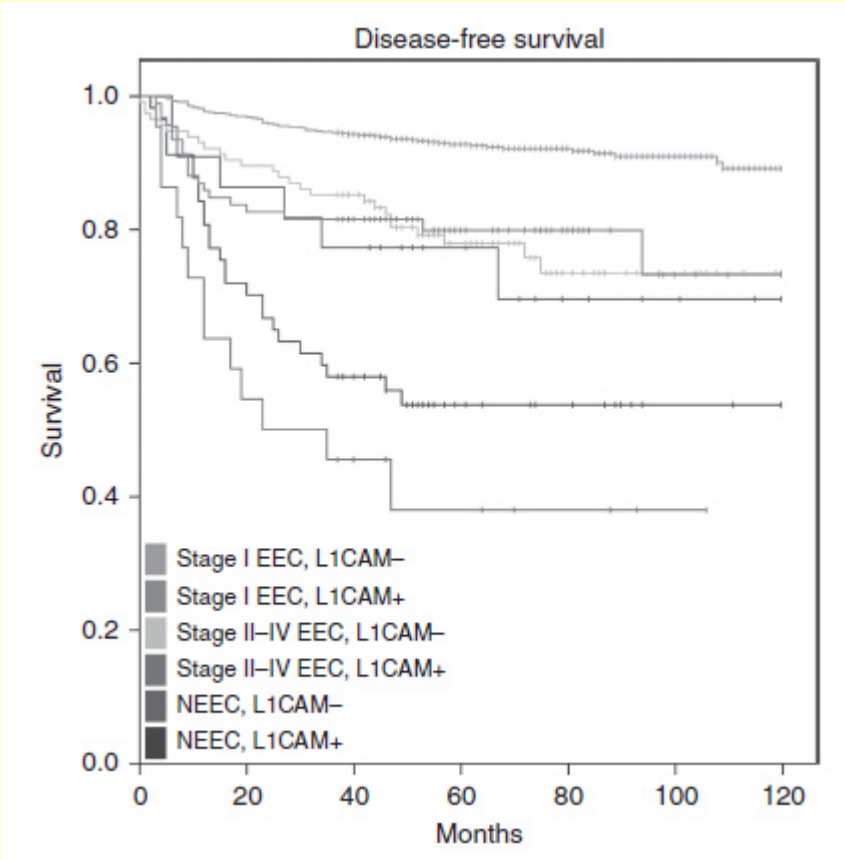


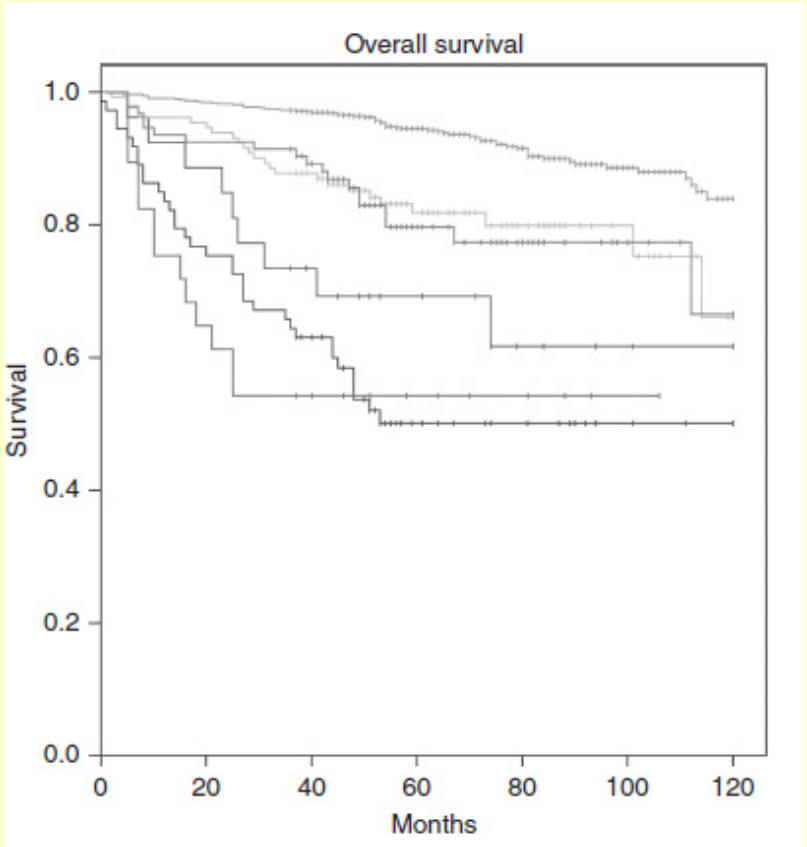
L1CAM expression in endometrial carcinomas: an ENITEC collaboration study

Louis JM van der Putten[*,1], Nicole CM Visser[2], Koen van de Vijver[3], Maria Santacana[4], Peter Bronsert[5], Johan Bulten[2], Marc Hirschfeld[6,7], Eva Colas[8], Antonio Gil-Moreno[8,9], Angel Garcia[10], Gemma Mancebo[11], Fransesc Alameda[12], Jone Trovik[13], Reidun K Kopperud[14,15], Jutta Huvila[16], Stefanie Schrauwen[17], Martin Koskas[18], Francine Walker[19], Vit Weinberger[20], Lubos Minar[20], Eva Jandakova[21], Marc PLM Snijders[22], Saskia van den Berg-van Erp[23], Xavier Matias-Guiu[4], Helga B Salvesen[13], Frederic Amant[17], Leon FAG Massuger[1] and Johanna MA Pijnenborg[24]

British Journal of Cancer (2016) 115, 716–724

933 stage I EEC



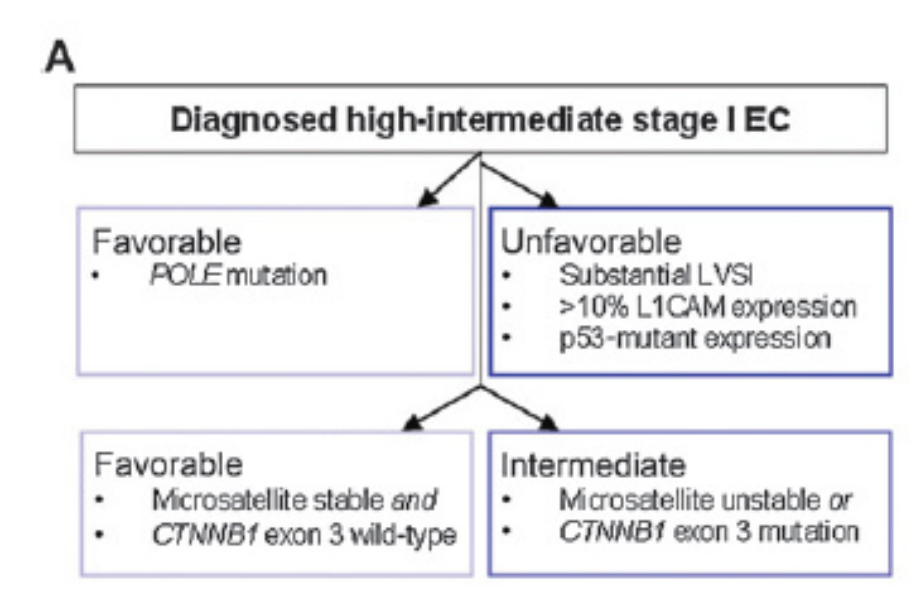


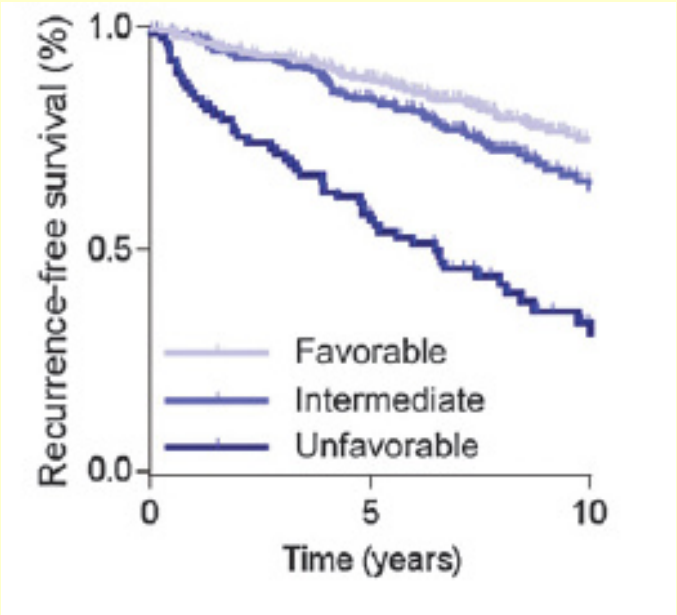
Improved Risk Assessment by Integrating Molecular and Clinicopathological Factors in Early-stage Endometrial Cancer—Combined Analysis of the PORTEC Cohorts

Clin Cancer Res; 22(16); 4215–24.

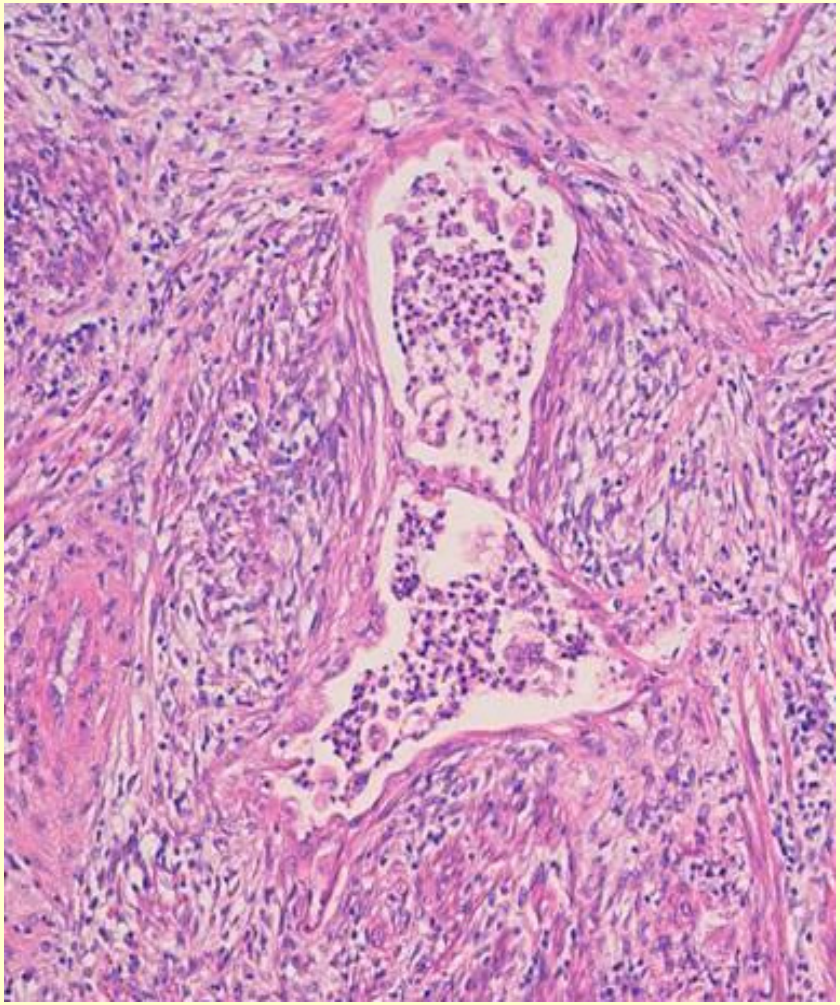
2016

Ellen Stelloo[1], Remi A. Nout[2], Elisabeth M. Osse[1], Ina J. Jürgenliemk-Schulz[3], Jan J. Jobsen[4], Ludy C. Lutgens[5], Elzbieta M. van der Steen-Banasik[6], Hans W. Nijman[7], Hein Putter[8], Tjalling Bosse[2], Carien L. Creutzberg[2], and Vincent T.H.B.M. Smit[1]

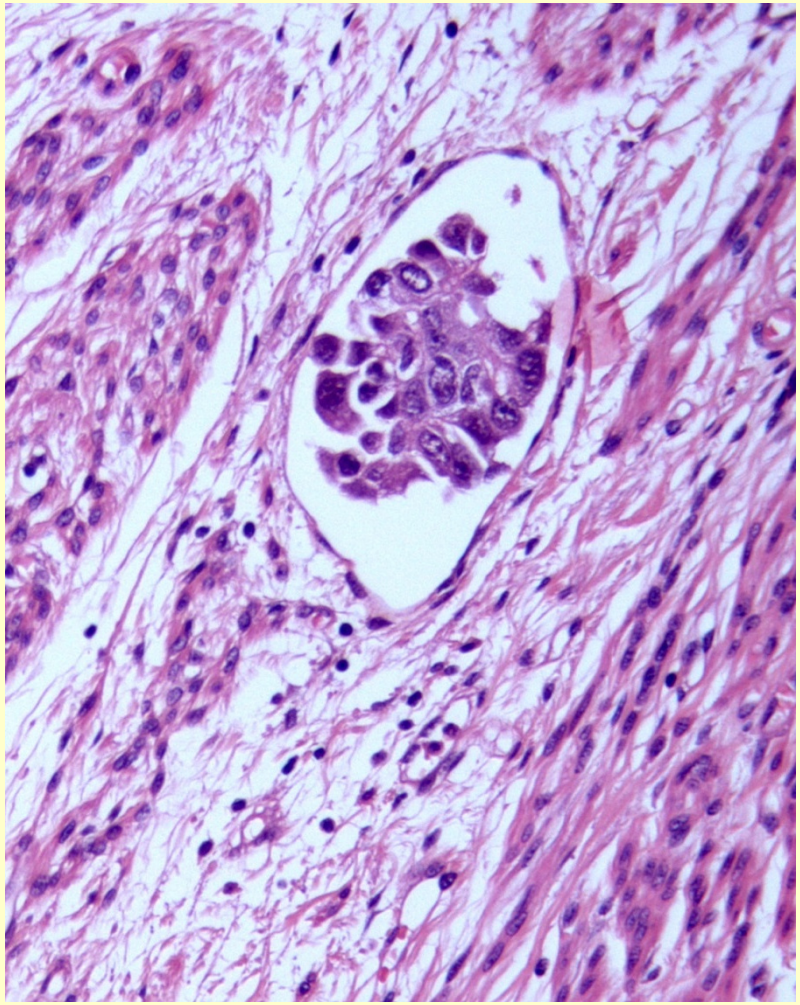




MELF pattern



LVI



Summary

- Pathologic Classification
- Molecular Classification
- Tumor Progression

Conclusions

- Pathologic Classification is prognostically important
- Molecular Classification provides additional information, but still requires refinement.
- Molecular pathology gives important information regarding Tumor Progression

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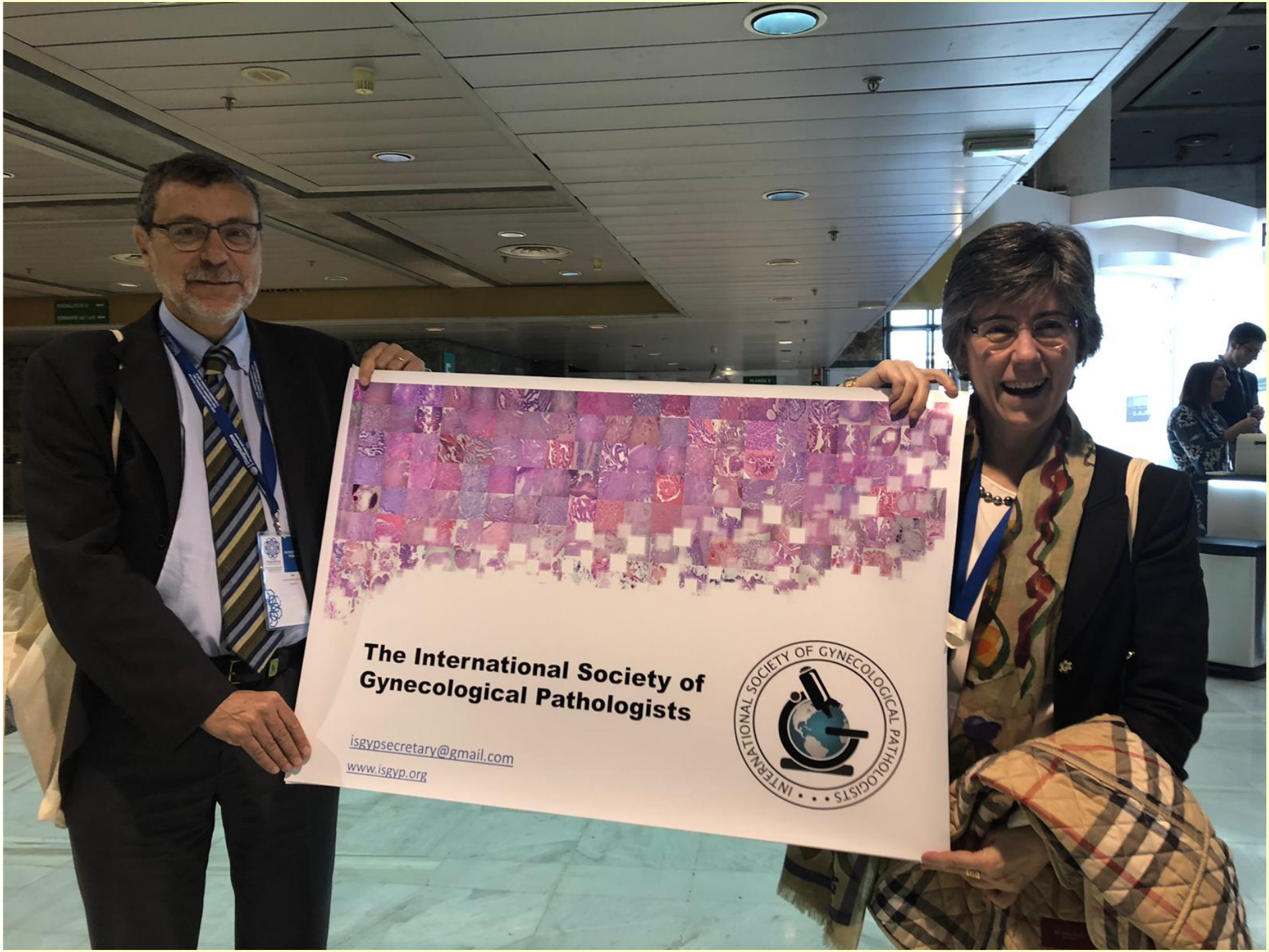
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INTERNATIONAL SOCIETY OF GYNECOLOGICAL PATHOLOGISTS



MOLECULAR PATHOLOGY AND BIOMARKER TESTING IN DIFERENT TYPES OF ENDOMETRIAL CARCINOMA

Xavier Matias-Guiu, MD, PhD, Hospital U Arnau de Vilanova, Univ Lleida. IRBLLEIDA, Hospital U de Bellvitge, IDIBELL