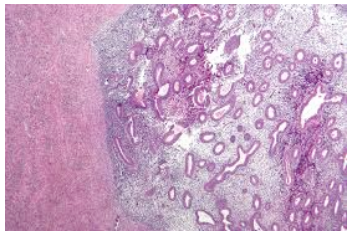
Università degli Studi di Padova
Dipartimento di Scienze Ginecologiche e della Riproduzione Umana
Scuola di Specializzazione in Ginecologia e Ostetricia
Direttore Prof. Giovanni Battista Nardelli

ENDOMETRIOSIS AND OVARIAN CANCER

Shara Borgato

ENDOMETRIOSIS

- Endometriosis is a common gynecological disorder that is carachterised by ECTOPIC GROWTH OF ENDOMETRIAL GLANDA AND STROMA

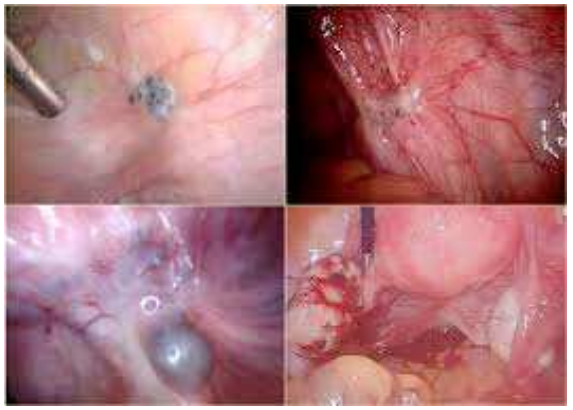


- The estimate PREVALENCE in the general population is about 4%

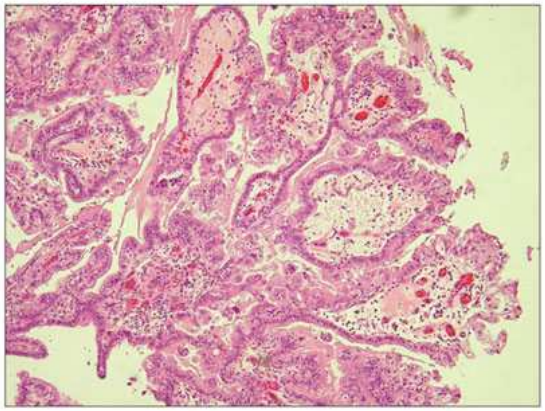
- The <u>etiology is not fully understood</u> but the predominant hypotesis are:
  1. RETROGRADE MENSTRUATION
  2. METAPLASIA: mesotelium turns into endometrial tissue
  3. LYMPHATIC SPREAD: endometrial cell may spread through linfatic and vascular channels and gain capacity for implantation in varous sites in the pelvic cavity

- Endometriosis might cause pelvic inflamation, adhesion, chronic pain and infertility.

- Epidemiological studies have consistently shown that <u>endometriosis is associated with an increased risk of ovarian cancer</u>.



SAMPSON AND SCOTT'S CRITERIA



- Already in 1925, SAMPSON proposed criteria for the diagnosis of ovarian cancer arising from endometriosis:

  1. evidence of endometriosis near the tumor,
  2. demonstration of cancer arising within ovarian endometriosis and not elsewhere
  3. presence of tissue similar to the endometrial stroma surrounding characteristic epithelial glands.

- In 1953, SCOTT added a fourth criterion:

  4. histologic demonstration of transition ofendometriosis to neoplasm

This has raised the question of whether endometriosis is a premalignant condition.

EPIDEMIOLOGY: quantification of the risk

Human Reproduction, Vol.28, No.12 pp. 3358–3369, 2013
Advanced Access publication on September 5, 2013 doi:10.1093/humrep/det340

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Increased risk for ovarian cancer and borderline ovarian tumours in subfertile women with endometriosis

C.C.M. Buis[1], F.E. van Leeuwen[2], T.M. Mooij[2], and C.W. Burger[1,*] on behalf of the OMEGA Project Group[†]

[1]Department of Obstetrics and Gynaecology, Division of Gynaecologic Oncology, Erasmus Medical Center Rotterdam, PO Box 2040, Rotterdam 3000 CA, The Netherlands [2]Department of Epidemiology, Netherlands Cancer Institute, Plesmanlaan 121, Amsterdam 1066 CX, The Netherlands

- OMEGA cohort (hormone stimulation in IVF-treated women) linked with PALMA (all citological and histological dignosis) linked with NCR (data on invasive malignat neoplasm).
- 3657 endometriosis group
- 5247 comparison group
- Follow up 15.2 years

1. **Fist analitic group**: diagnosis of CO and BOT at the same time of endometriosis
2. **Second analitic group**: diagnosis of endometriosis occurred before CO

Table II Risk of ovarian tumours associated with endometriosis.

	All cases ($n = 34$)		Ovarian cancer ($n = 19$)		BOT ($n = 15$)	
	HR	95% CI	HR	95% CI	HR	95% CI
First analytic approach						
No endometriosis ($n = 5247$)	1.0	Ref.	1.0	Ref.	1.0	Ref.
Any endometriosis ($n = 3657$)						
Crude	7.9	3.0–20.3	11.6	2.7–50.2	5.4	1.5–19.1
Age adjusted	9.7	3.7–25.1	13.4	3.1–58.4	7.3	2.0–26.3
	All cases ($n = 31$)		Ovarian cancer ($n = 18$)		BOT ($n = 13$)	
	HR	95% CI	HR	95% CI	HR	95% CI
Second analytic approach[a]						
Any endometriosis						
Crude	7.0	2.7–18.3	10.9	2.5–47.4	4.4	1.2–16.1
Age adjusted	8.2	3.1–21.6	12.4	2.8–54.2	5.5	1.5–20.2
Adjusted for all confounders[b,c]	8.4	3.2–22.1	12.7	2.9–55.5	5.5	1.5–20.4
Ovarian endometriosis[d]	11.3	4.0–31.8	15.0	3.1–72.4	8.9	2.2–35.7
Extraovarian endometriosis[d]	7.7	2.1–28.7	19.1	3.5–104.5	—[e]	—[e]
Unknown location endometriosis[d]	6.0	2.0–18.1	8.1	1.6–41.8	4.7	1.0–21.5

- **3 to 8 fold increased** risk of ovarian tumors associated with endometriosis
- when excluded the info from pathology database the risk is lower → studies using this method may have a too low risk assesment

EPIDEMIOLOGY:
specific or generic risk?

Association between endometriosis and risk of histological subtypes of ovarian cancer: a pooled analysis of case–control studies

Celeste Leigh Pearce, Claire Templeman, Mary Anne Rossing, Alice Lee, Aimee M Near, Penelope M Webb, Christina M Nagle, Jennifer A Doherty, Kara L Cushing-Haugen, Kristine G Wicklund, Jenny Chang-Claude, Rebecca Hein, Galina Lurie, Lynne R Wilkens, Michael E Carney, Marc T Goodman, Kirsten Moysich, Susanne K Kjaer, Estrid Hogdall, Allan Jensen, Ellen L Goode, Brooke L Fridley, Melissa C Larson, Joellen M Schildkraut, Rachel T Palmieri, Daniel W Cramer, Kathryn L Terry, Allison F Vitonis, Linda J Titus, Argyrios Ziogas, Wendy Brewster, Hoda Anton-Culver, Alexandra Gentry-Maharaj, Susan J Ramus, A Rebecca Anderson, Doerthe Brueggmann, Peter A Fasching, Simon A Gayther, David G Huntsman, Usha Menon, Roberta B Ness, Malcolm C Pike, Harvey Risch, Anna H Wu, Andrew Berchuck, on behalf of the Ovarian Cancer Association Consortium

- Data from 13 ovarian cancer case-control studies
- **13 226** controls (818 with endometriosis)
- **7911** women with invasive ovarian cancer (738 with endometriosis)
- **1907** women with borderline ovarian cancer

	Crude		Stratified only		Stratified and adjusted	
	OR (95% CI)	p value	OR (95% CI)*	p value	OR (95% CI)†	p value
Invasive	1·49 (1·34–1·65)	<0·0001	1·53 (1·37–1·70)	<0·0001	1·46 (1·31–1·63)	<0·0001
Clear-cell	3·73 (3·04–4·58)	<0·0001	3·44 (2·78–4·27)	<0·0001	3·05 (2·43–3·84)	<0·0001
Endometrioid	2·32 (1·94–2·78)	<0·0001	2·20 (1·82–2·66)	<0·0001	2·04 (1·67–2·48)	<0·0001
Mucinous	1·09 (0·76–1·58)	0·63	1·04 (0·71–1·51)	0·86	1·02 (0·69–1·50)	0·93
High-grade serous	1·11 (0·96–1·29)	0·16	1·16 (1·00–1·35)	0·056	1·13 (0·97–1·32)	0·13
Low-grade serous	2·02 (1·38–2·97)	<0·0001	2·22 (1·48–3·31)	<0·0001	2·11 (1·39–3·20)	<0·0001
Borderline	1·26 (1·05–1·50)	0·012	1·19 (0·99–1·43)	0·062	1·12 (0·93–1·35)	0·24
Mucinous	1·27 (0·97–1·67)	0·078	1·19 (0·90–1·57)	0·23	1·12 (0·84–1·48)	0·45
Serous	1·31 (1·05–1·63)	0·015	1·28 (1·02–1·61)	0·034	1·20 (0·95–1·52)	0·12

Self reported endometriosis was associated with a significantly increased risk of :

- **CLEAR CELL**
- **LOW-GRADE SEROUS**
- **ENDOMETRIOID**

Sensitivity analyses suggest that the risk is increased even among women whose endometriosis was diagnosed many years before ovarian cancer

	Clear-cell		Endometrioid		Low-grade serous	
	OR (95% CI)*	p value	OR (95% CI)*	p value	OR (95% CI)*	p value
Exclusions						
None	3·07 (2·44–3·86)	<0·0001	2·05 (1·68–2·49)	<0·0001	2·31 (1·50–3·55)	<0·0001
<3 years	2·78 (2·06–3·74)	<0·0001	1·70 (1·30–2·24)	<0·0001	2·01 (1·20–3·35)	0·008
<5 years	2·51 (1·84–3·42)	<0·0001	1·60 (1·21–2·13)	0·001	1·97 (1·17–3·34)	0·01
<10 years	2·38 (1·71–3·33)	<0·0001	1·49 (1·09–2·03)	0·01	1·88 (1·06–3·32)	0·03

EPIDEMIOLOGY:
specific or generic risk?

AOGS
ACTA Obstetricia et Gynecologica Scandinavica

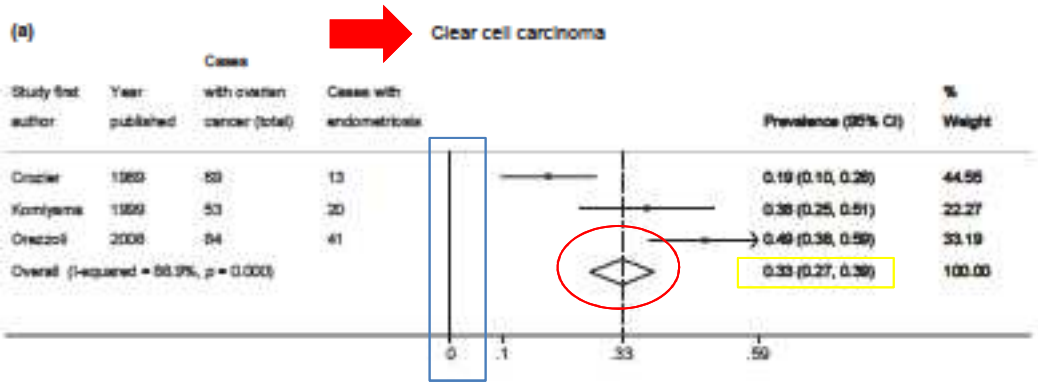
AOGS REVIEW ARTICLE

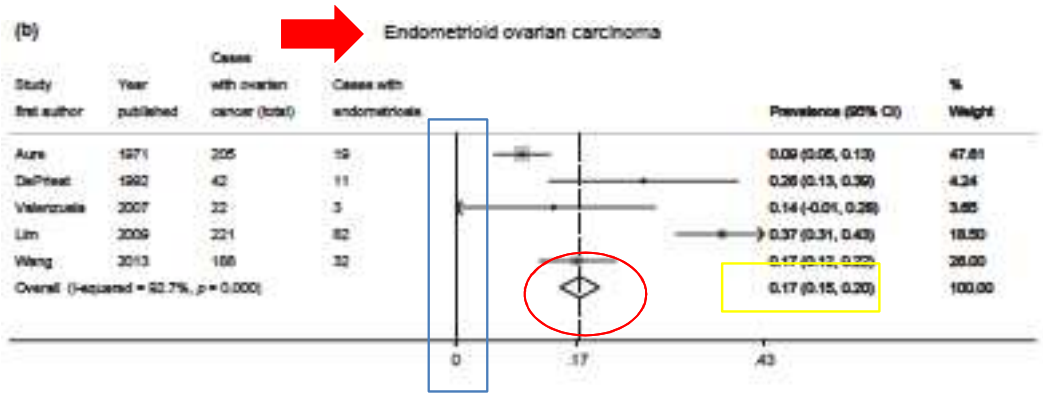
The relation between endometriosis and ovarian cancer – a review

LENE N. HEIDEMANN[1,*], DORTHE HARTWELL[2], CHRISTIAN H. HEIDEMANN[3] & KIRSTEN M. JOCHUMSEN[1]

[1]Department of Obstetrics and Gynecology, Odense University Hospital, Odense, [2]Department of Gynecology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, and [3]Faculty of Health Sciences, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark

- Eletronic database PUBMED
- Studies based on fewer than 20 cases of ovarian cancer were excluded
- 28 articles





Women with histologically verified endometriosis have an increased risk of epithelial ovarian cancer predominantly of the CLEAR-CELL and ENDOMETRIOID subtypes

PATHOGENESIS

Published in final edited form as:
Am J Surg Pathol. 2010 March ; 34(3): 433–443. doi:10.1097/PAS.0b013e3181cf3d79.

The Origin and Pathogenesis of Epithelial Ovarian Cancer- a Proposed Unifying Theory

Robert J. Kurman, M.D. and **Ie-Ming Shih, M.D., Ph.D.**
Departments of Pathology, Gynecology and Obstetrics and Oncology The Johns Hopkins University School of Medicine, Baltimore, Maryland

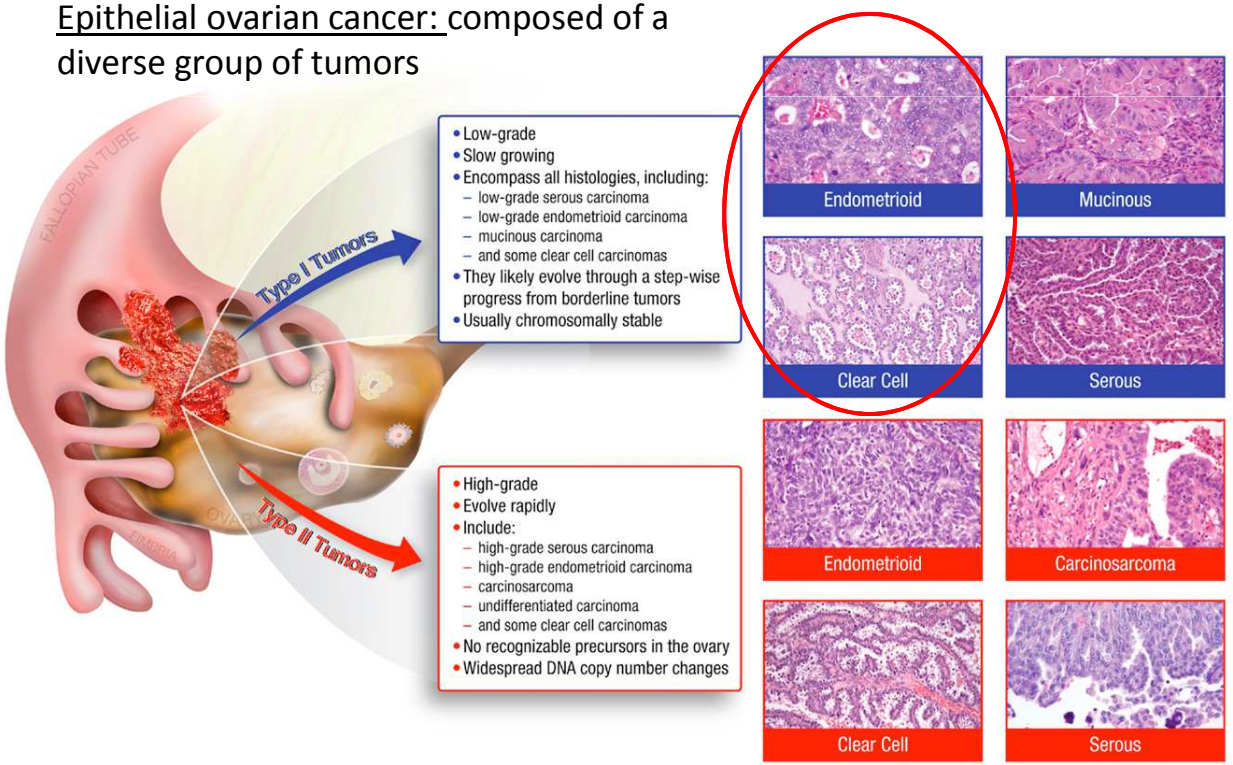
Virchows Arch (2012) 460:237–249
DOI 10.1007/s00428-012-1203-5

REVIEW AND PERSPECTIVES

Ovarian carcinomas: five distinct diseases with different origins, genetic alterations, and clinicopathological features

Jaime Prat

Epithelial ovarian cancer: composed of a diverse group of tumors



Type I (low-grade serous, endometrioid, clear cell, mucinous, Brenner)

- Genetically more stable
- Distinctive pattern of mutations in specific cell type
- TP53 mutation very rare

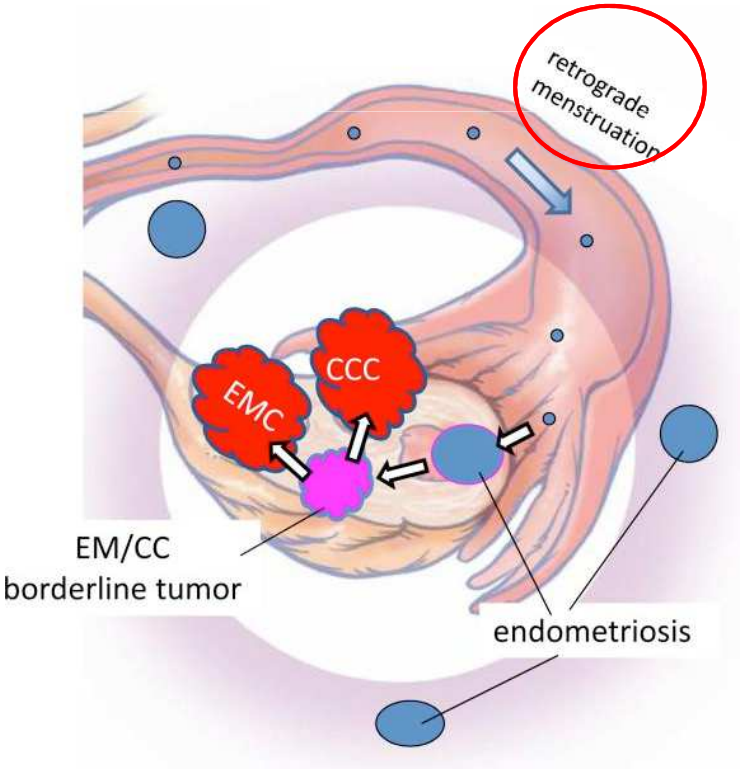
Type II (high grade serous, carcinosarcoma)

- Genetically unstable
- High frequency of TP53 mutation

Endometriosis is commonly linked to the tumorogenesis of TYPE I ovarian carcinomas and precisely to ENDOMETRIOD and CLEAR CELL subtypes

PATHOGENESIS

Endometrial tissue, by a process of RETROGRADE MENSTRUATION, implants on the ovarian surface to form an endometrioic cyst



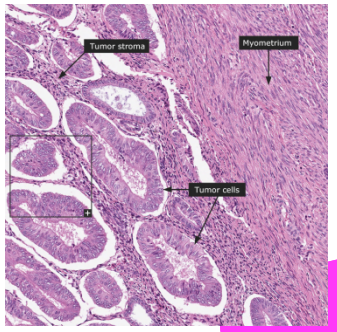
Eutopic endometrium in women with endometriosis exhibit molecular abnormalities including ACTIVATION OF ONCOGENIC PATHWAYS

Borderline tumors

LOW GRADE ENDOMETRIOID or CLEAR CELL CARCINOMA can develop

Evidence: protective effect for tubal ligation was seen only for endometrioid and clear cell carcinoma of the ovary

PATHOGENESIS: what makes the connection?



Histologic evidence

Immunologic evidence

Genetiche ed epigenetic evidence

ELSEVIER

JMIG The Journal of Minimally Invasive Gynecology

Review Article

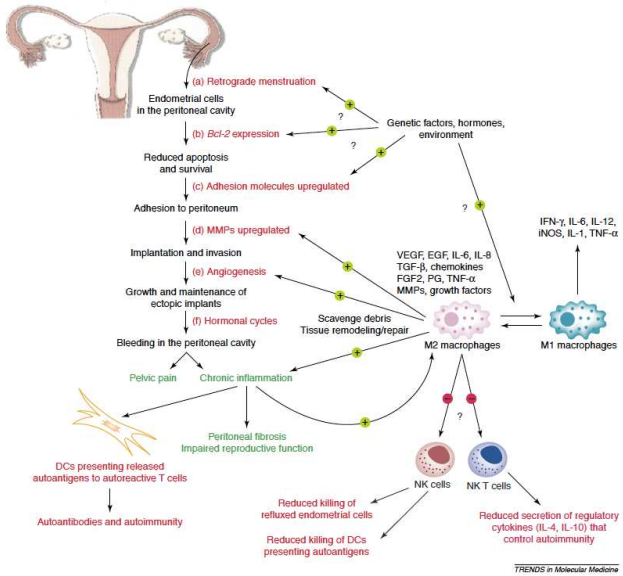
Cellular, Histologic, and Molecular Changes Associated With Endometriosis and Ovarian Cancer

João Siufi Neto, MD*, Rosanne M. Kho, MD, Daniela Freitas dos Santos Siufi, MD, Edmund Chada Baracat, MD, Karen S. Anderson, PhD, and Maurício Simões Abrão, MD

Table 1

Frequency of genetic alterations associated with endometriosis and malignant neoplasms

Source	Mutated gene	Endometriosis	Ovarian carcinoma	Endometriosis-associated ovarian carcinoma
Orezzoli et al [58]	*PTEN*	15%		75%
Gounaris et al [59]				
Cancer Genome Atlas Research Network [56]	*p53*		96% (high-grade serous)	
Xiao et al [78]			7% (clear cell carcinoma)	
Akahane et al [63]		0	30.8% (clear cell carcinoma)	
Auner et al [68]	*KRAS*		>50% (mucinous)	10%–20%
Mayr et al [69]				
Stewart et al [71]				29%
Xiao et al [78]	*ARID1A*	80.6%	42.3% (clear cell carcinoma)	
Wiegand et al [74]			46% (clear cell carcinoma)	
			30% (endometrioid carcinoma)	
			0% (high-grade serous)	
Xiao et al [78]	*HNF-1β*	33.3%	92.3% (clear cell carcinoma)	



PATHOGENESIS: what makes the connection?

Histologic evidence

"ABNORMAL ENDOMETRIUM"

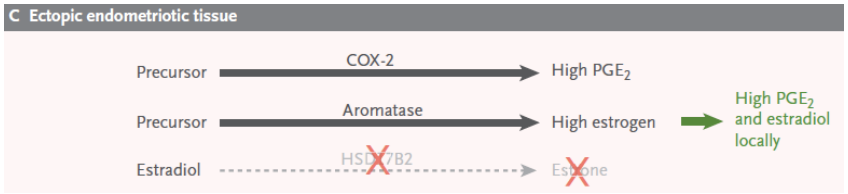
The NEW ENGLAND JOURNAL of MEDICINE

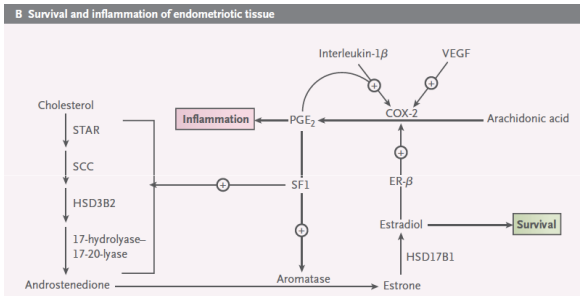
REVIEW ARTICLE

MECHANISMS OF DISEASE

Endometriosis

Serdar E. Bulun, M.D.





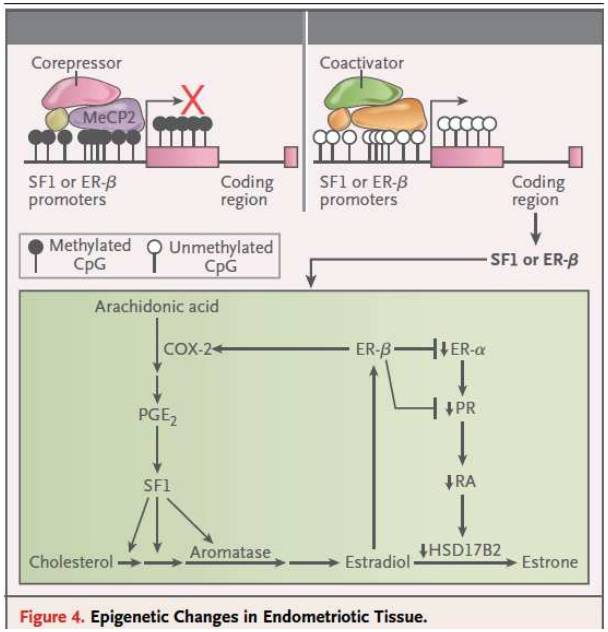
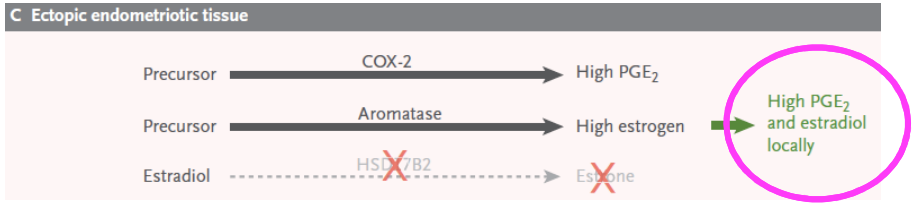


Figure 4. Epigenetic Changes in Endometriotic Tissue.

EUTOPIC ENDOMETRIUM in women with endometriosis has intrinsic molecular abnormalities including activation of oncogenic pathways. These changes presumably enable implantation, survival, and invasion of the endometrial tissue in the ovary and in the peritoneal surfaces

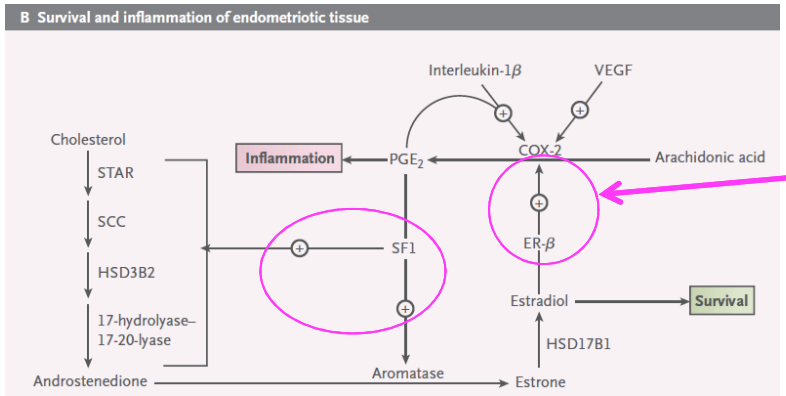
PATHOGENESIS: what makes the connection?

"ABNORMAL ENDOMETRIUM"



1. High COX2 and AROMATASE levels
   → increased PGE2 and ESTRADIOL

2. Decreased progesterones receptors levels in stroma cell
   → DISRUPTION OF THE PARACRINE PATHWAY that inactivates estradiol and PROGESTERONE RESISTANCE



Originate from **overexpression of SF1 and ESTROGEN RECEPTOR β** in endometrioic stromal cells

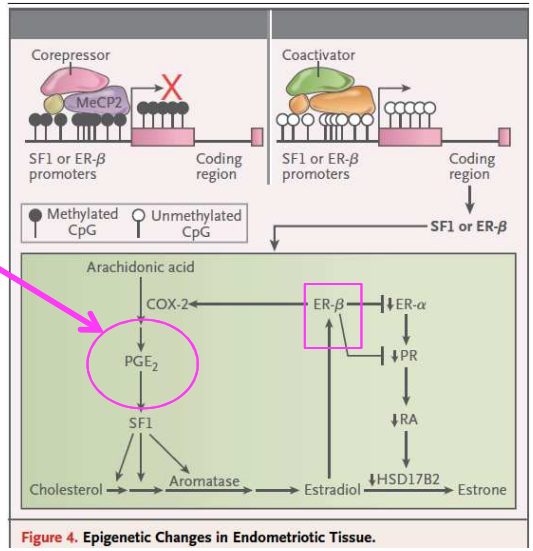


Figure 4. Epigenetic Changes in Endometriotic Tissue.

PATHOGENESIS: what makes the connection?

Immunologic evidence

- ↑ **PROINFLAMMATORY CYTOKINES**
- ↑ **PERITONEAL MACROPHAGES**
- ↓ **CITOTOXICITY OF NATURAL KILLER and T-CELL**

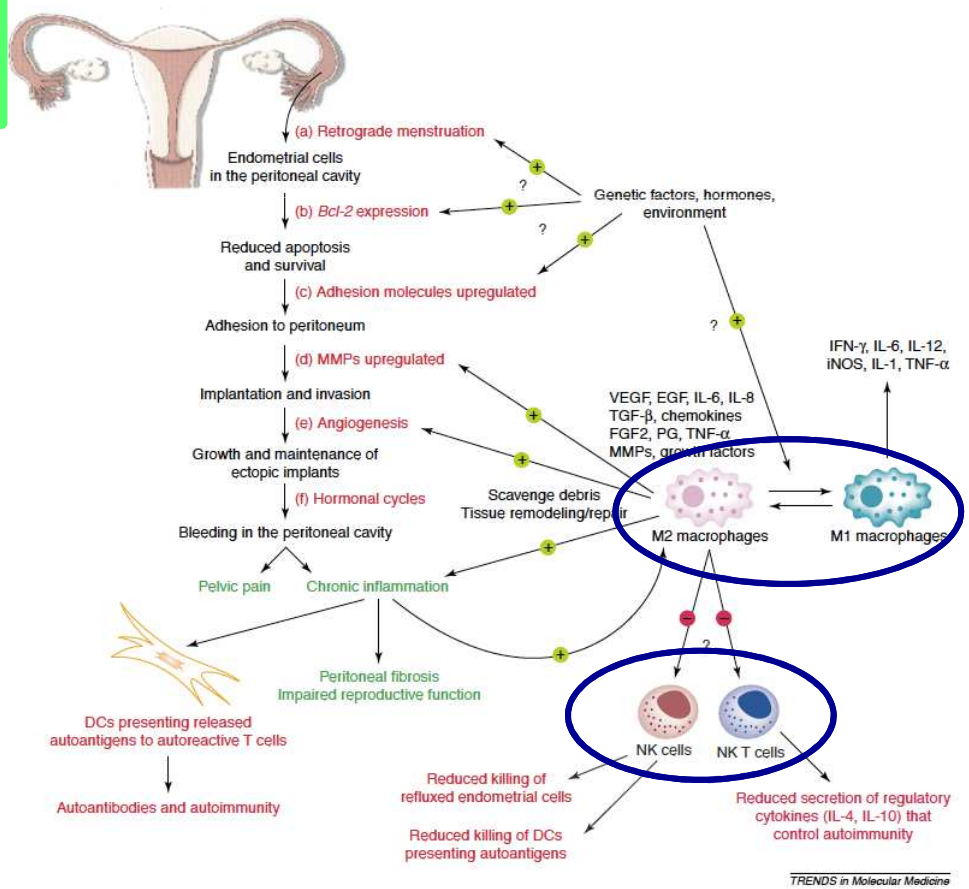
Defective system with altered NK and PM activities:

- Increased local production of factors promoting ANGIOGENESIS and IMPLANTATION OF ENDOMETRIAL CELL
- Reduced killing of ECTOPIC ENDOMETRIUM
- Rediced killing of DENDRITIC CELLS
- Reduced secretion of REGULATORY CYTOKINES that control autoimmunity

Review TRENDS in Molecular Medicine Vol.9 No.5 May 2003 223

Pathogenesis of endometriosis: natural immunity dysfunction or autoimmune disease?

Giuseppe Matarese[1], Giuseppe De Placido[2], Yorgos Nikas[3] and Carlo Alviggi[2]



PATHOGENESIS: what makes the connection?

Immunologic evidence

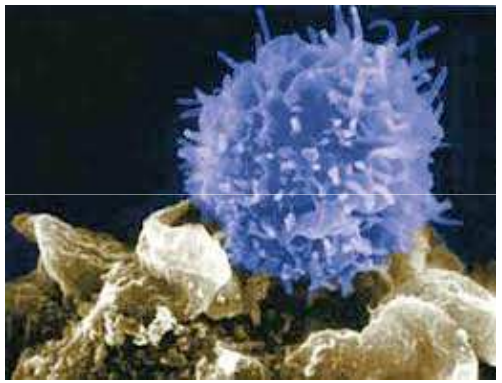
REGULATORY T LYMPHOCYTES (suppress the activation of immune system)

Hindawi Publishing Corporation
Journal of Oncology
Volume 2012, Article ID 345164, 7 pages
doi:10.1155/2012/345164

Review Article

Regulatory T Cells in Human Ovarian Cancer

Dong-Jun Peng,[1] Rebecca Liu,[2] and Weiping Zou[1,3,4]



⬆ FOXP3-POSITIVE LYMPHOCYTES has been observed in the eutopic endometrium of patients with endometriosis during the secretory phase of the menstrual cycle

⬆ FREQUENCY OF TREGS in the peritoneal fluid in women with endometriosis → compensatory anti-inflammatory mechanism and may account for abrogated local cellular immune responses

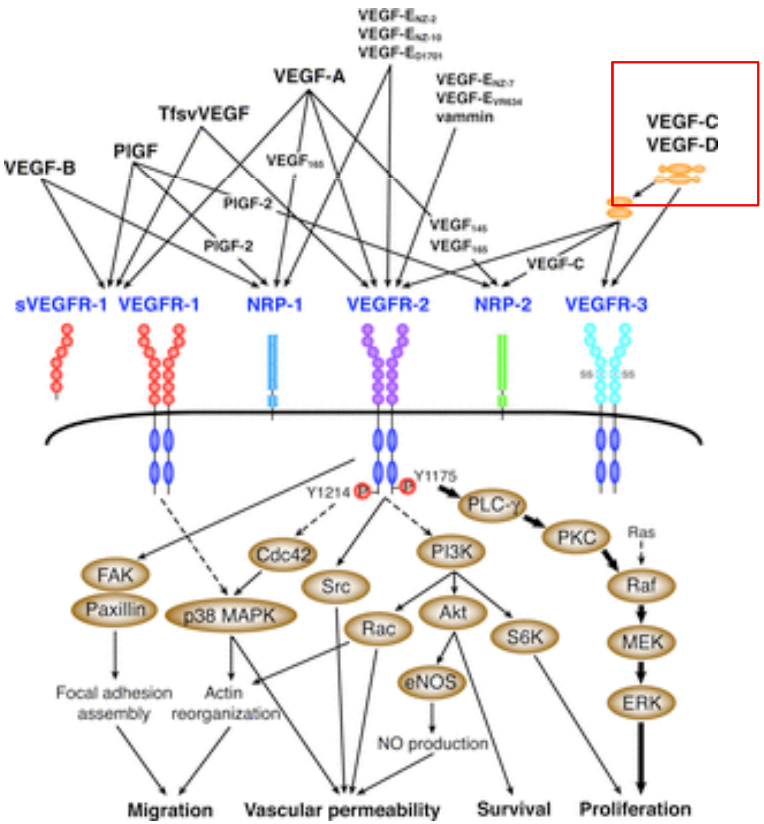
ENDOMETRIOSIS and OVARIAN CANCER share similar immune aspects such as increased levels of Foxp3 and Tregs, resulting in malfunction of the immune system and creating conditions for disease establishment.

PATHOGENESIS: what makes the connection?

Evidenze immunologiche

NEOANGIOGENESIS

LYNPHANGIOGENESIS



values of LYMPHOVASCULAR DENSITY are observed in the endometriotic tissues compared with adjacent healthy tissue

EXPRESSION of VEGF C and D, both important factors in lymphovascular growth produced by endometriotic epithelial cells, suggests the presence of lymphangiogenesis in deep endometriosis

PATHOGENESIS: what makes the connection?

Genetic and epigenetic evidence

Several studies have shown evidence of MONOCLONALITY in endometriosis, a characteristic of malignant lesions, with a positive frequency in 60% to 100% of the samples studied

MONOCLONALITY

MICROSATELLITES

LOSS OF HETEROZIGOSIS

Can contribute to development of endometriosis alone and no doubt represent important mutagenic events

detected in 12 samples of ovarian tumors associated with endometriosis and in 12 samples of ovarian endometriosis only (9p, 11q, 22q) → OVARIAN ENDOMETRIOSIS AND OVARIAN TUMORS MAY HAVE SIMILAR GENETIC ORIGIN

PATHOGENESIS: what makes the connection?

Genetiche and epigenetic evidence

GENES

Mutation genes frequently occured in endometrial and ovarian carcinomas

Table 1

Frequency of genetic alterations associated with endometriosis and malignant neoplasms

Source	Mutated gene	Endometriosis	Ovarian carcinoma	Endometriosis-associated ovarian carcinoma
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PATHOGENESIS: what makes the connection?

Genetic and epigenetic evidence

frontiers in ONCOLOGY

REVIEW ARTICLE
published: 12 June 2013
doi: 10.3389/fonc.2013.00153

The role of microRNAs in the tumorigenesis of ovarian cancer

*Gianpiero Di Leva and Carlo M. Croce**

Department of Molecular Virology, Immunology, and Medical Genetics, Comprehensive Cancer Center, The Ohio State University Columbus, OH, USA

- MicroRNA expression signature differentiates ovarian cancer tissues from normal ovary
- MiR-200 family is the most significantly overexpressed group in ENDOMETRIOID and CLEAR CELL CARCINOMAS
- miR-17-5p and miR-20 involved in angiogenesis are DOWN-REGULATED IN OVARIAN ENDOMETRIOMAS compared with eutopic endometrium
- miR-222 are significantly increased in endometriomas

In ovarian carcinogenesis MUTATION OF MICRORNA have been identified

Table 2 | miRNA profiling studies in human epithelial ovarian cancers.

Reference	Number of samples/subtypes	Method of analyses	Main findings
Iorio et al. (2007)	15 Normals/69 tumors 31 Serous/8 endometrioid/4 clear cells/9 poorly differentiated/1 mucinous	miRNA microarray	Ovarian cancer-specific miRNA signature Subtypes specific miRNA signature Epigenetic mechanism responsible for their aberrant expression
Yang et al. (2008a)	10 Tumors and 10 "normal" HOSE cell line	miRNA microarray	Ovarian cancer-specific miRNA signature miR-214 induces cell survival and cisplatin resistance through targeting PTEN
Laios et al. (2008)	3 Primary serous/3 recurrent serous tumors	qRT-PCR	miR-9 and miR-223 can be biomarkers in recurrent ovarian cancer
Nam et al. (2008)	22 Serous tumors/6 normals	miRNA microarray	Ovarian cancer-specific miRNA signature
Zhang et al. (2008)	108 Tumors 109 Tumors 76 Tumors 504 Tumors 96 Tumors	miRNA microarray, aCGH, affymetrix cDNA microarray, tissue array, qPCR validation	miRNAs are downregulated in malignant transformation and tumor progression Genomic copy number loss and epigenetic silencing account for miRNA dysregulation
Dahiya et al. (2008)	34 Tumors and HOSE-B cell line	miRNA microarray	Ovarian cancer-specific miRNA signature
Sorrentino et al. (2008)	Drug-resistant vs. wild-type cancer cell lines	miRNA microarray	Paclitaxel and cisplatin resistance is associated with a specific miRNA fingerprint
Yang et al. (2008b)	69 Tumors (42 sensitive/27 resistant)	miRNA microarray	Let-7i is a modulator of platinum-based chemotherapy Let-7i is a biomarker to predict chemotherapy response and survival
Boren et al. (2009)	16 Ovarian cancer cell lines	miRNA microarray	miRNA signature associates to cell line drug response
Wyman et al. (2009)	33 Tumors/HOSE-B cell line	Deep sequencing	Ovarian cancer-specific miRNA signature Subtypes specific miRNA signature
Eitan et al. (2009)	19 Tumors (stage I/II)/38 tumors (stage III)	miRNA microarray	miRNA signature during progression miRNA expression associated with response to platinum-chemotherapy
Hu et al. (2009)	55 Advanced-stage tumors	miRNA microarray	miR-200b-429 are biomarkers for ovarian cancer outcome
Lee et al. (2009)	33 High-grade serous tumors 2 Low-grade serous tumors 2 Serous borderline tumors 3 Normal fallopian tubes	miRNA microarray	No abnormalities in miRNA expression correlated to BRCA1/2 status miR-34c and miR-422b are prognostic biomarkers
Nagaraja et al. (2010)	10 Human clear-cell ovarian cancer cell lines and 1 normal ovarian surface epithelial cultures	Deep sequencing	Clear-cell ovarian cancer-specific miRNA signature miR-101 inhibits mTOR pathway and increases rapamycin sensitivity
Creighton et al. (2010)	8 Serous tumors 4 Serous cancer cell lines 4 NOSE cell lines	Deep sequencing	miR-31 is downregulated in cancer Reduced levels of miR-31 are correlated with defects in the p53 pathway
Vaksman et al. (2011)	21 Tumors (13 effusions/8 primary tumors)	miRNA microarray	miRNA signatures for the primary tumors and effusions
Kim et al. (2010)	103 Tumors	miRNA microarray	miRNA signature is correlated with clinico-pathological parameters (subtype, grade, survival)
Marchini et al. (2011)	144 Tumors (stage I)	miRNA microarray	Ovarian cancer-specific miRNA signature miR-200c is a predictor of survival and relapse
Cancer Genome Atlas Research Network (2011)	489 Serous tumors	miRNA microarray	Global analyses of mRNA expression, miRNA expression, promoter methylation, and DNA copy number

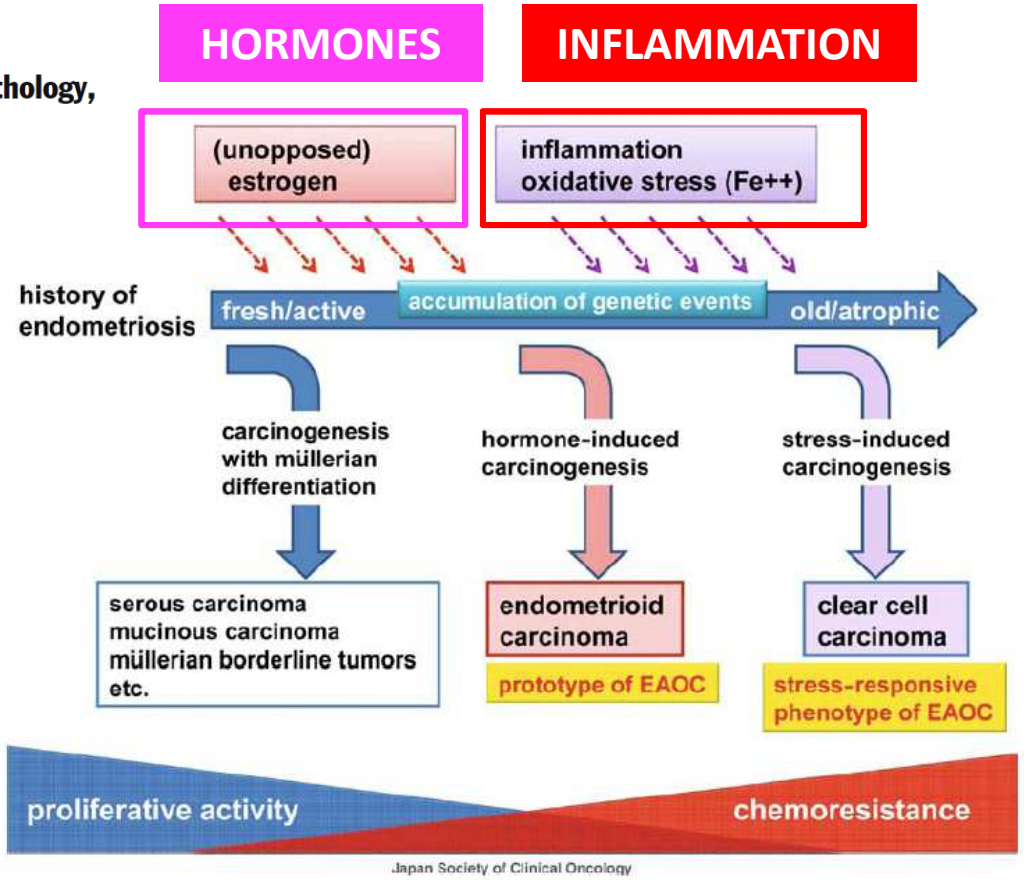
PATHOGENESIS: malignant transformation of endometriosis

Int J Clin Oncol (2009) 14:383–391
DOI 10.1007/s10147-009-0935-y

REVIEW ARTICLE

Masaki Mandai · Ken Yamaguchi · Noriomi Matsumura
Tsukasa Baba · Ikuo Konishi

Ovarian cancer in endometriosis: molecular biology, pathology, and clinical management



DIAGNOSIS: biomarkers - a way to detect CO earlier

ENDOMETRIOSIS

OVARIAN CANCER

CA 125 — elevated in 47% of early disease and in 80% to 90% of advanced case

HE 4 — Overexpressend in endometrioid and serous tumors

RO MA — Risk of ovarian malignancy algoritm

OVA 1 BLOOD TEST

Panel of 5 biomarkers in SUSPECTED OVARIAN MASSES:

1. CA-125,
2. b2 microglobulin,
3. apolipoprotein A1,
4. Prealbumin,
5. transferrin

There are NO BIOMARKERS that identify patients with endometriosis at elevated risk of ovarian cancer

DIAGNOSIS: biomarkers - a way to detect CO earlier

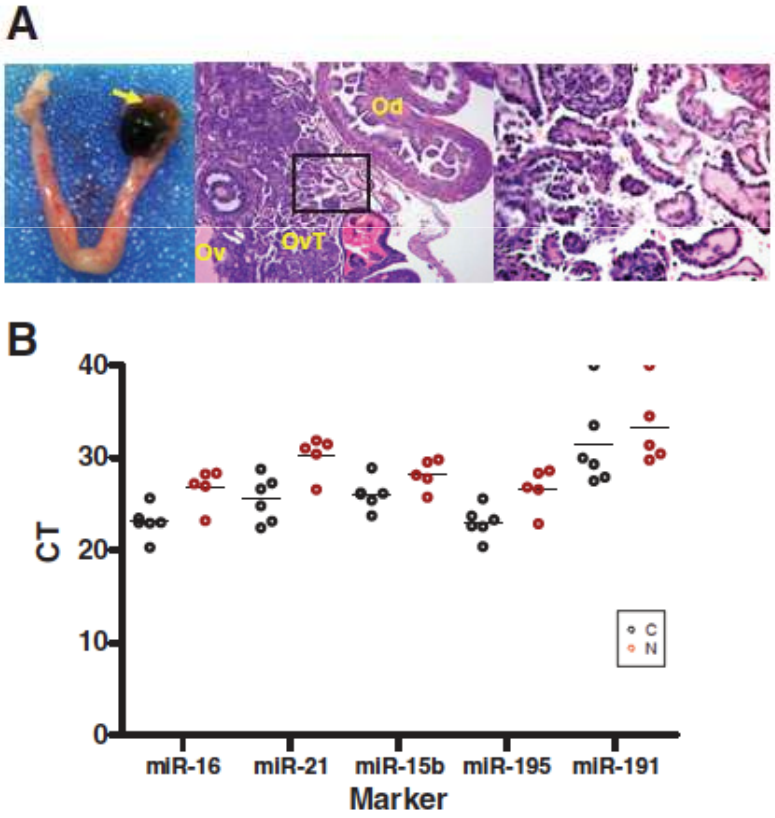
Clinical Cancer Research

AACR

Plasma MicroRNAs as Novel Biomarkers for Endometriosis and Endometriosis-Associated Ovarian Cancer

Swati Suryawanshi, Anda M. Vlad, Hui-Min Lin, et al.

Clin Cancer Res 2013;19:1213-1224. Published OnlineFirst January 29, 2013.



Found 4 miRNAs (miR-15b, 16, 21, and 195) differentially expressed in human EAOCs from healthy controls

circulating miRNAs may serve as promising biomarkers with high sensitivity and specificity FOR EARLY DETECTION and DIAGNOSIS OF ENDOMETRIOSIS AND EAOCS

DIAGNOSIS: ultrasound

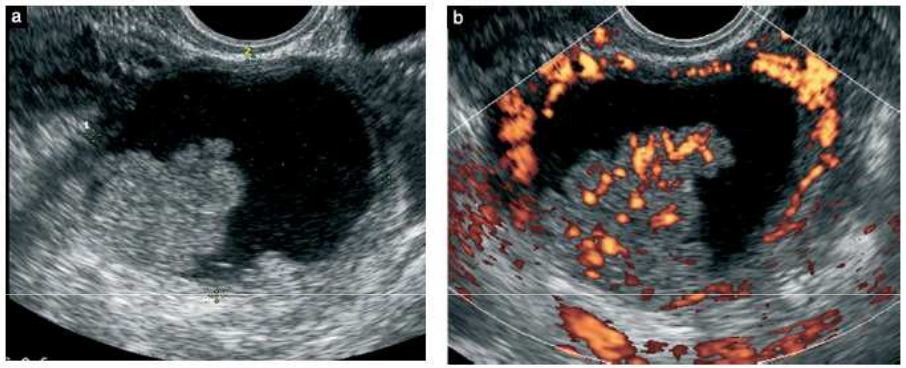


Figure 1 Endometrioid borderline tumor that developed in an endometrioid cyst in a 30-year-old patient. The ovarian lesion appeared as a unilocular-solid lesion (largest diameter of mass, 46 mm) with a papillary projection (height = 29 mm) (a), which was highly vascularized at power Doppler examination (b).

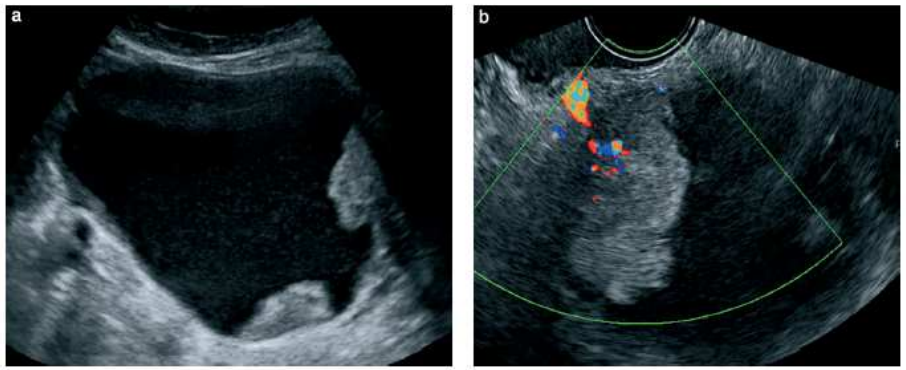


Figure 2 Grade 1 endometrioid ovarian carcinoma that developed in an endometrioid cyst in a 49-year-old-patient. The ovarian lesion appeared as a unilocular-solid lesion (largest diameter of mass, 134 mm) with a papillary projection (height = 60 mm) (a), which was moderately vascularized at color Doppler examination (b).

Ultrasound Obstet Gynecol 2011; 38: 99–106
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.8970

Ovarian cancer arising in endometrioid cysts: ultrasound findings

A. C. TESTA*, D. TIMMERMAN†, C. VAN HOLSBEKE‡, G. F. ZANNONI§, S. FRANSIS¶, P. MOERMAN**, V. VELLONE§, F. MASCILINI*, A. LICAMELI*, M. LUDOVISI*, A. DI LEGGE*, G. SCAMBIA* and G. FERRANDINA††

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Sonographic characteristics of MALIGNANT TRANSFORMATION in endometrioid cyst:

- Presence of solid tissue
- Heterogeneous cystic content
- Solid tissue with positive Doppler signals
- Papillary projection more frequent

PROGNOSIS

RESEARCH www.AJOG.org

ONCOLOGY

Prognostic analysis of ovarian cancer associated with endometriosis

Sanjeev Kumar, MD; Adnan Munkarah, MD; Haitham Arabi, MD; Sudeshna Bandyopadhyay, MD; Assaad Semaan, MD; Kinda Hayek, MD; Gunjal Garg, MD; Robert Morris, MD; Rouba Ali-Fehmi, MD

ENDOMETRIOSIS ASSOCIATED OVARIAN CANCER has a much better survival rate than OVARIAN CANCER

EAOC patients were more likely to have:

- Low grade
- Early stage tumors

TABLE 2
Survival analysis

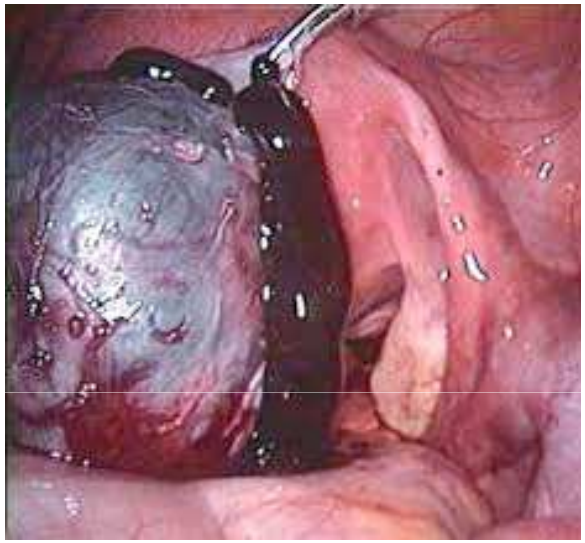
Variable	EAOC	OC
Early-stage survival		
5 y	75%	86%
Median	Not achieved	Not achieved
Late-stage survival		
5 y	50%	39%
Median	57 mo	38 mo
Overall survival		
5 y	62	51
Median	199 mo	62 mo

EAOC, endometriosis-associated ovarian cancer; *OC*, ovarian carcinoma without endometriosis.

Kumar. Ovarian carcinoma associated with endometriosis. Am J Obstet Gynecol 2011.

TAKE HOME MESSAGE

There is a **connection** between endometriosis and OC but ENDOMETRIOSIS IS NOT A PRECANCEROSIS



Pre-operative counselling and work-up is CRUCIAL in the clinical management of women with endometriosis

Pay attention to SUSPICIOUS SITUATION:

- Women > 40 years
- Suspicioud ultrasound
- CA 125 very high