Cancer Care Center
Numero Verde
800 143 143
Numero per la Cura del Tumore

Sacro Cuore
Don Calabria
CCC
Cancer Care Center
Negrar - Verona

BRCA1/2 e carcinoma ovarico: caratteristiche patologiche

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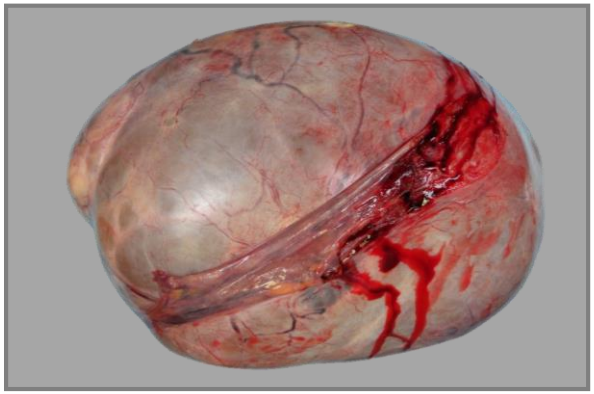
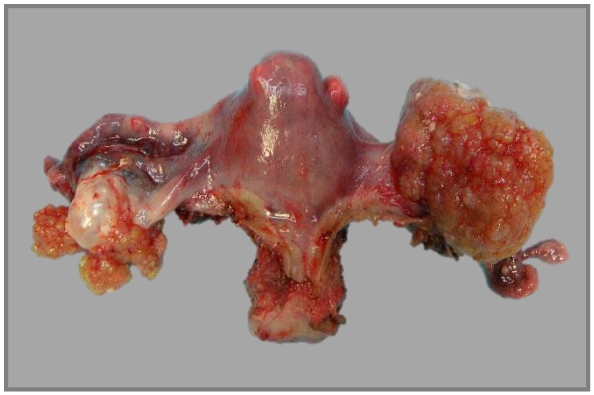
Carcinoma ovarico

1- Termine generico che definisce patologie diverse che condividono la stessa sede anatomica





2- In assenza di un precursore credibile, non è possibile una prevenzione primaria

Il modello dualistico del carcinoma ovarico

Typo I

Typo II

Basso grado
Stadio iniziale
Outcome favorevole

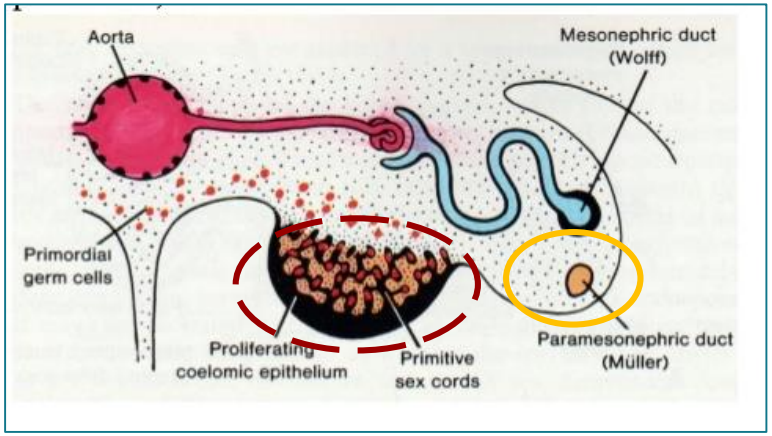
Alto grado
Stadio avanzato
Prognosi infausta

Adenocarcinoma endometriode EOC
Carcinoma a cellule chiare CC
Carcinoma sieroso basso grado LGSC
Carcinoma mucinoso MC
Tumore di Brenner BT

Carcinoma sieroso di alto grado HGSC
Carcinosarcoma MMMT
Carcinoma indifferenziato

Am J Pathol 2004, 164:1511-1518

Paradosso delle neoplasie epiteliali ovariche
Perché pur non essendo di derivazione mulleriana esprimono marcatori di tipo mulleriano (PAX8) ?



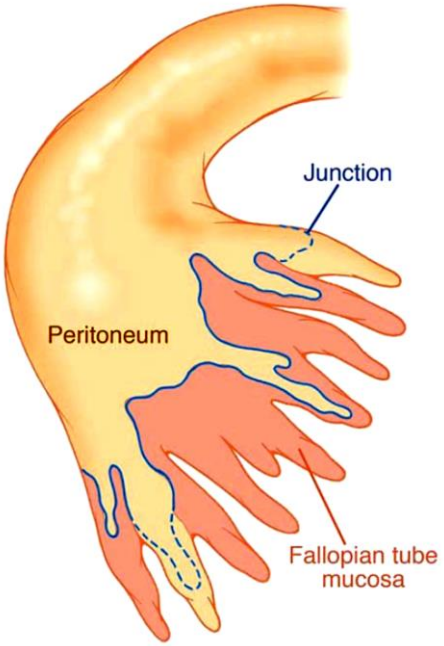
OVAIO

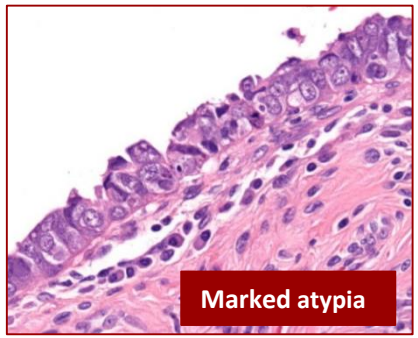
TUBE
UTERO
Fondo
Corpo
Cervice
Fornici vaginali

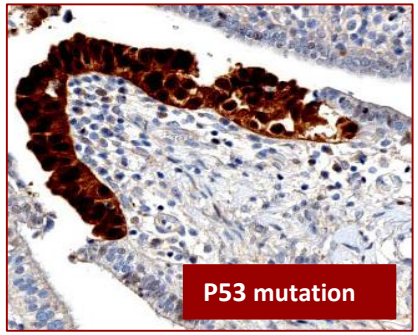
Identificazione di un precursore nelle paziente BRCA1/2 mut+

The Tubal Fimbria Is a Preferred Site for Early Adenocarcinoma in Women With Familial Ovarian Cancer Syndrome

Am J Surg Pathol • Volume 30, Number 2, February 2006







Sectioning and **E**xtensively **E**xamining the **FIM**briae

Serous Tubal Intraepithelial Carcinoma (STIC)

1. STIC in 8-10% pts con BRCA1 or BRCA2 mut+
2. STIC in 1% pts a basso rischio
3. Diagnosticato fino al 60% dei casi HGSC
4. Non identificati precursori credibili in ovaio
5. ***Biologia molecolare supporta questa ipotesi***

Evoluzione del modello dualistico

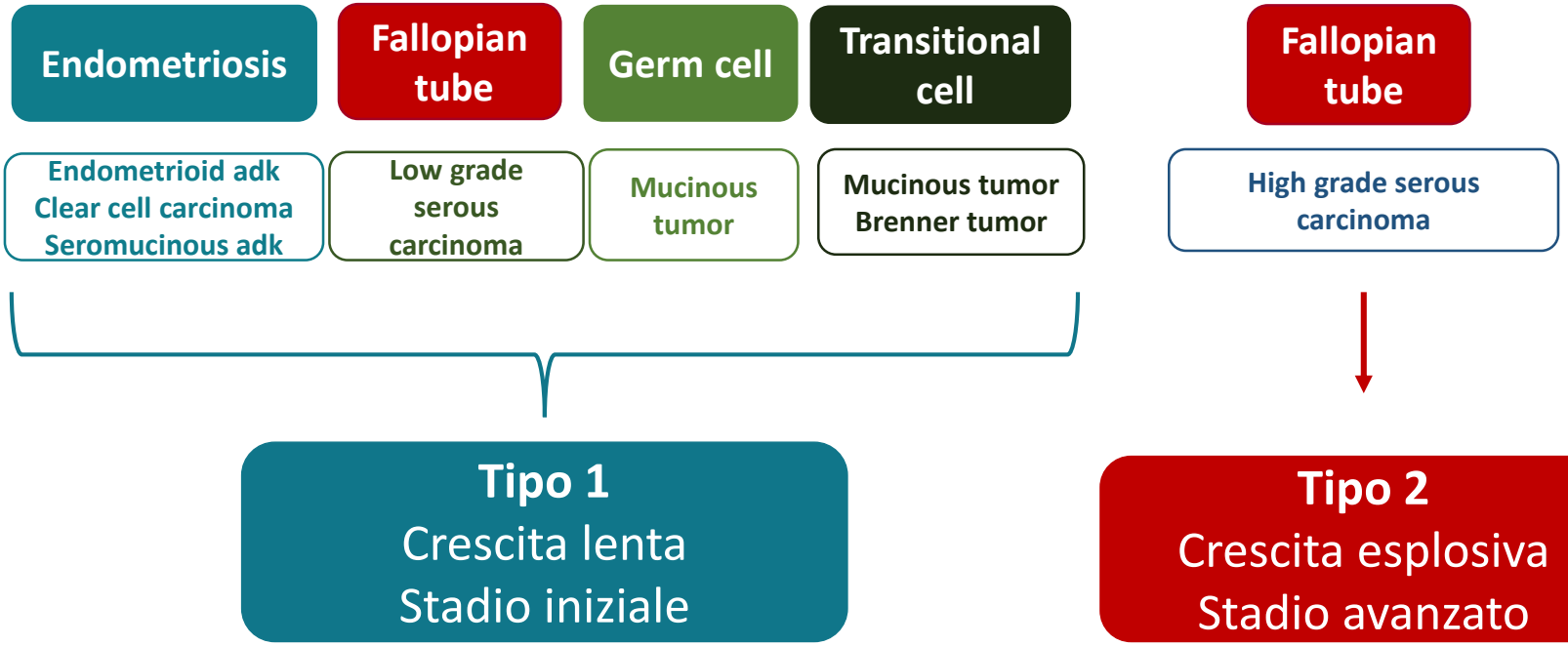
REVIEW

The Dualistic Model of Ovarian Carcinogenesis

Revisited, Revised, and Expanded

Robert J. Kurman and Ie-Ming Shih

The American Journal of Pathology, Vol. 186, No. 4, April 2016

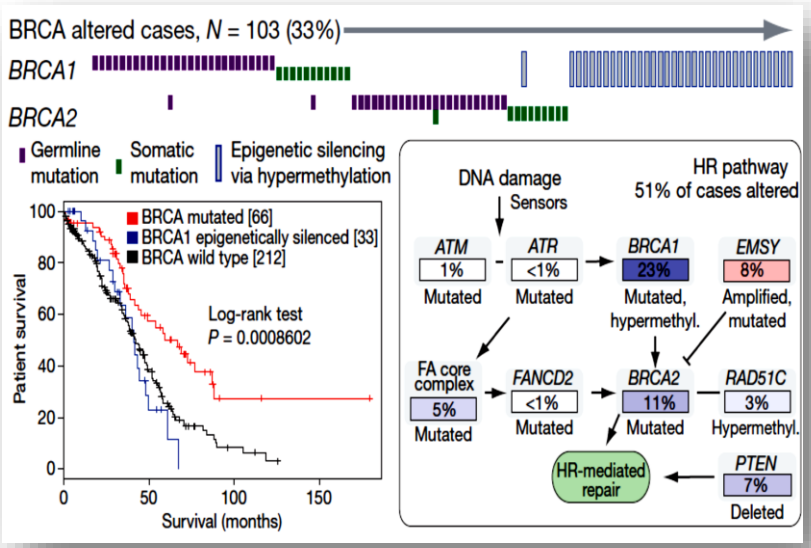


Integrated genomic analyses of ovarian carcinoma

The Cancer Genome Atlas Research Network*

30 JUNE 2011 | VOL 474 | NATURE | 609

HR alterations

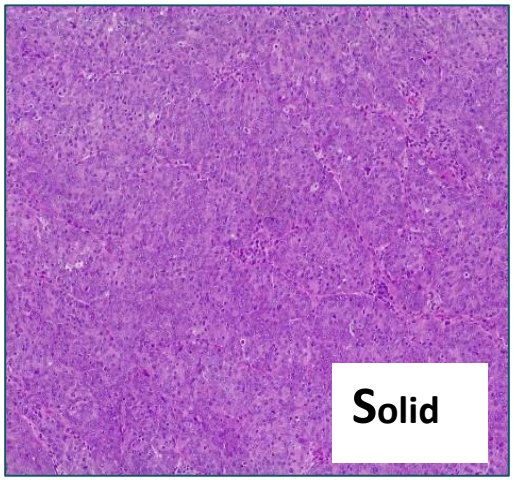


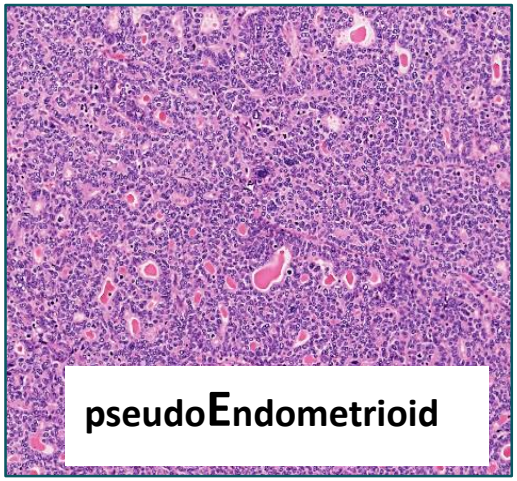
- *20% BRCA1/2 germline or somatic mutation*
- *11% BRCA1 promoter methylation*
- *20% EMSY, PTEN or mutation in the Fanconi Anaemia genes*

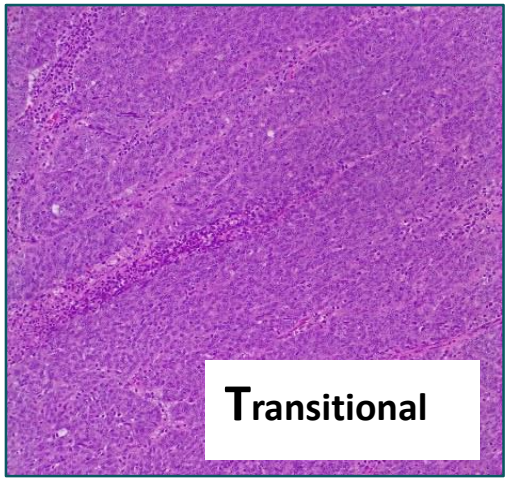
51% dei casi hanno alterazione in uno dei geni della ricombinazione omologa (HR)

Esistono caratteristiche morfologiche che correlano con l'assetto molecolare?

Solid pseudoEndomertrioid Transitional carcinomas







I carcinomi sierosi di alto grado con difetto in uno dei geni della ricombinazione omologa sono frequentemente a morfologia SET

Morphologic correlates of molecular alterations in extrauterine Müllerian carcinomas
Modern Pathology (2016) 29, 893–903

Morphologic patterns associated with *BRCA1* and *BRCA2* genotype in ovarian carcinoma
Modern Pathology (2012) 25, 625–636

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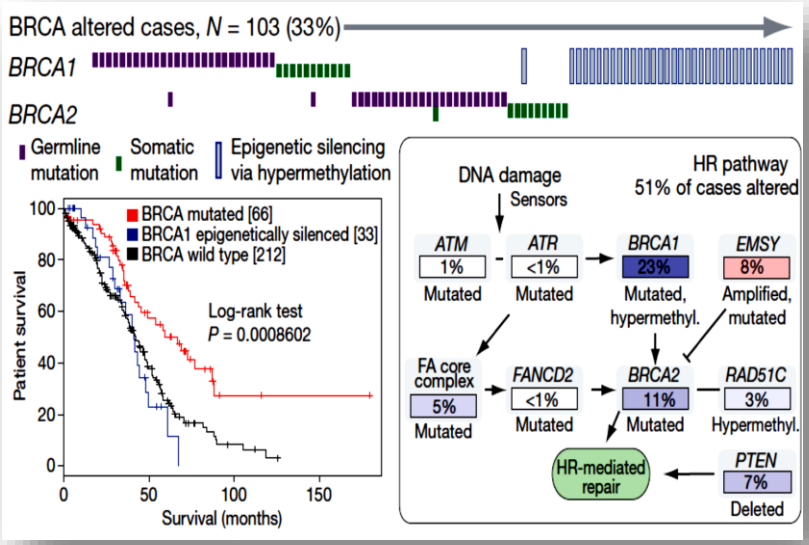
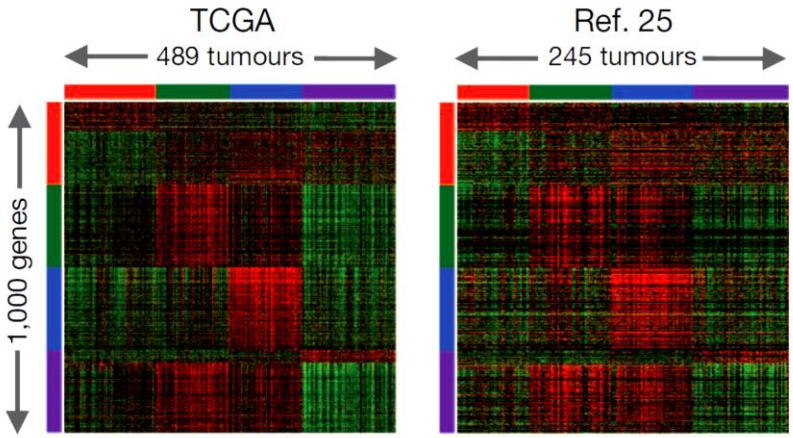




Tumour/gene groups

- Differentiated
- Immunoreactive
- Mesenchymal
- Proliferative

Gene expression

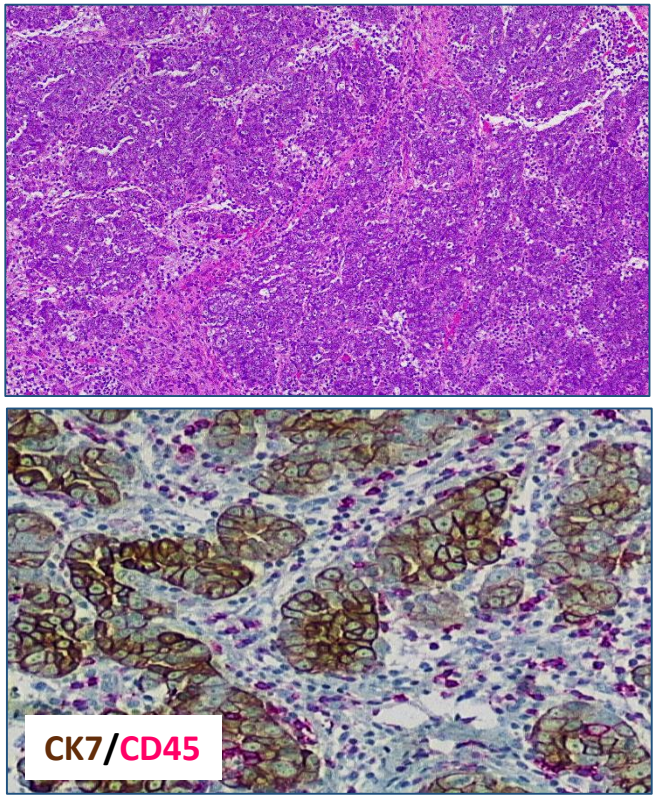
Low — High

- *20% BRCA1/2 germline or somatic mutation*
- *11% BRCA1 promoter methylation*
- *20% EMSY, PTEN or mutation in the Fanconi Anaemia genes*

51% dei casi hanno alterazione in uno dei geni della ricombinazione omologa (HR)

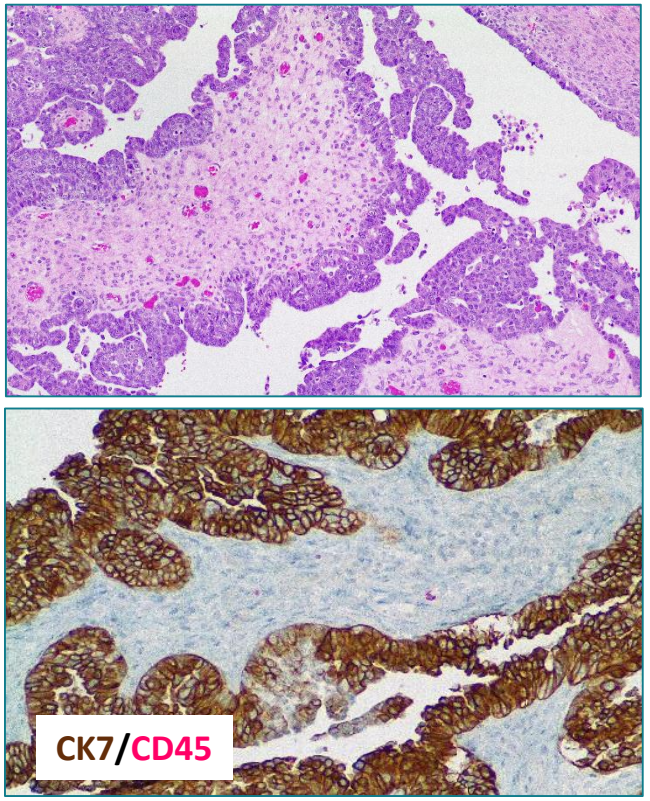
Immunoreactive group

BRCA germline mutation
sensitivity to platinum CHT
most favorable clinical outcome



Mesenchimal group

Less BRCA germline mutation
insensitivity to platinum CHT
very poor clinical outcome



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Conclusioni

1. *Il carcinoma ovarico è una categoria eterogenea dal punto di vista clinico, patologico e molecolare*

2. *Lo studio, nelle pazienti BRCA-mutate, ha consentito di identificare la tuba come sede di origine del carcinoma "ovarico" sieroso di alto grado*

3. *Esiste una relazione, anche se non assoluta, tra genotipo e fenotipo (SET)*