



- Dipartimento di Ricerca Traslazionale e Nuove Tecnologie in Med & Chir
- DAI di Medicina di Laboratorio

VIRUSES and GENES in HUMAN BREAST CANCER

Generoso Bevilacqua

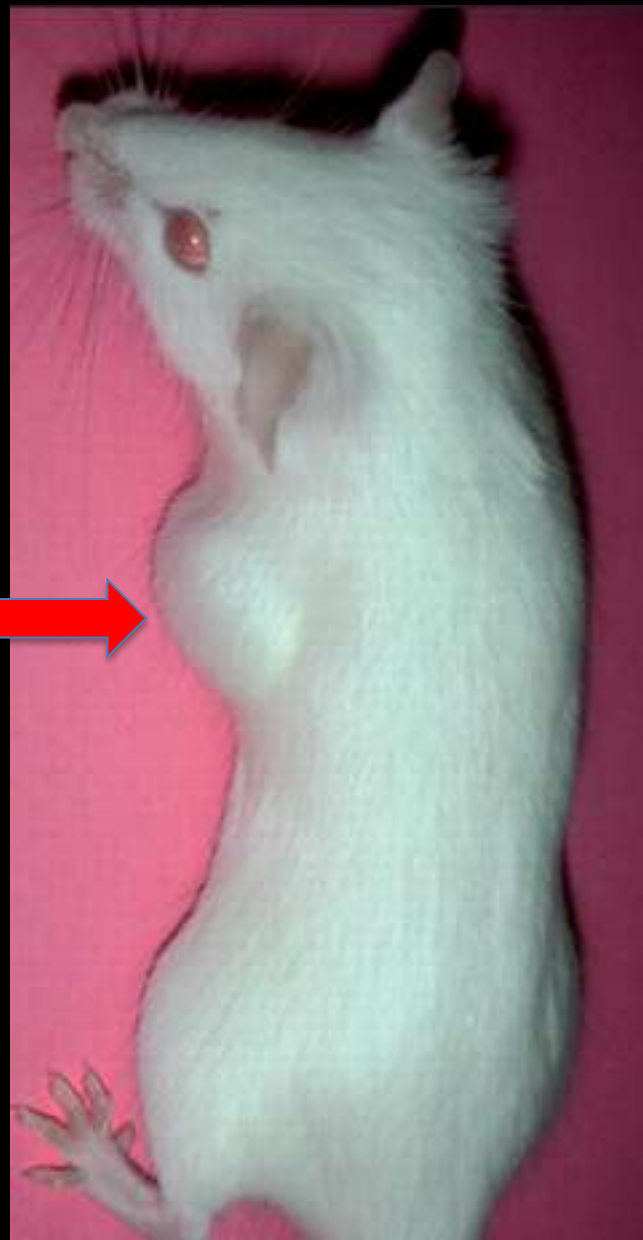
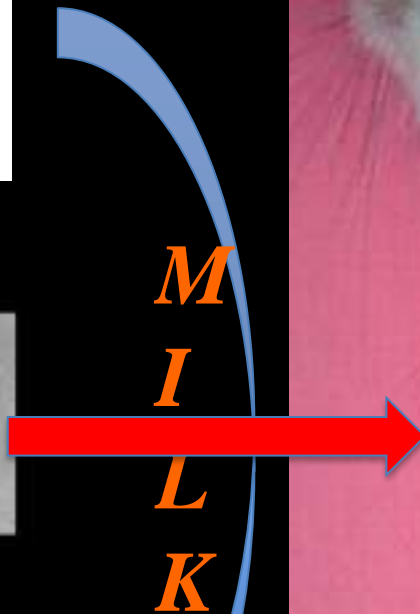
- Viral etiology of BC: in collaboration with **Chiara Mazzanti**, Fondazione Pisana per la Scienza, Pisa
- Germ line and somatic genetic alterations in BC: on behalf of **Adelaide Caligo**, AOUP



MMTV



***Murine Mammary
Tumor Virus***





MMTV



MMTV-like sequences
in human breast cancer:
a fluorescent PCR/laser
microdissection

**NATURAL HISTORY of
approach
HUMAN BREAST**

Zanmarchi F et al
CANCER

J Pathol: 209:436, 2006



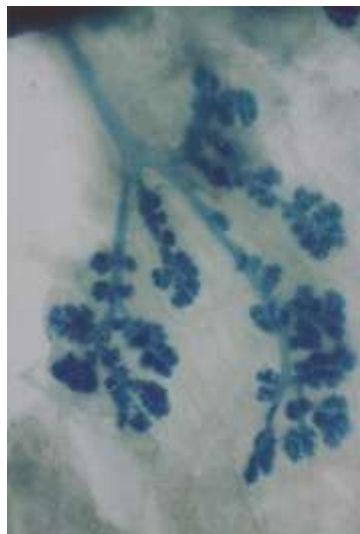
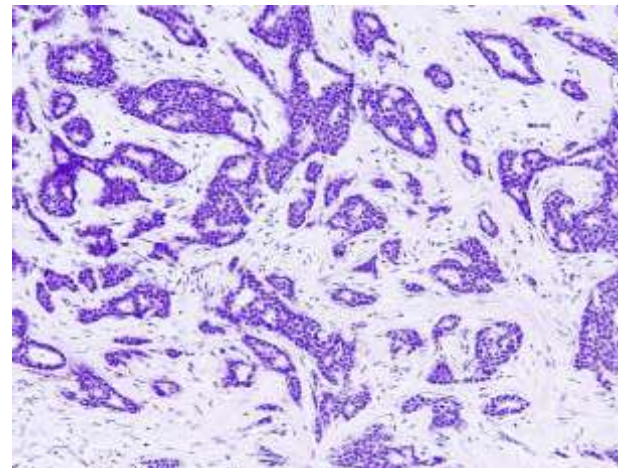
35% of human breast carcinoma

A mouse mammary tumor virus env-like exogenous sequence is strictly related to progression of human sporadic breast carcinoma.

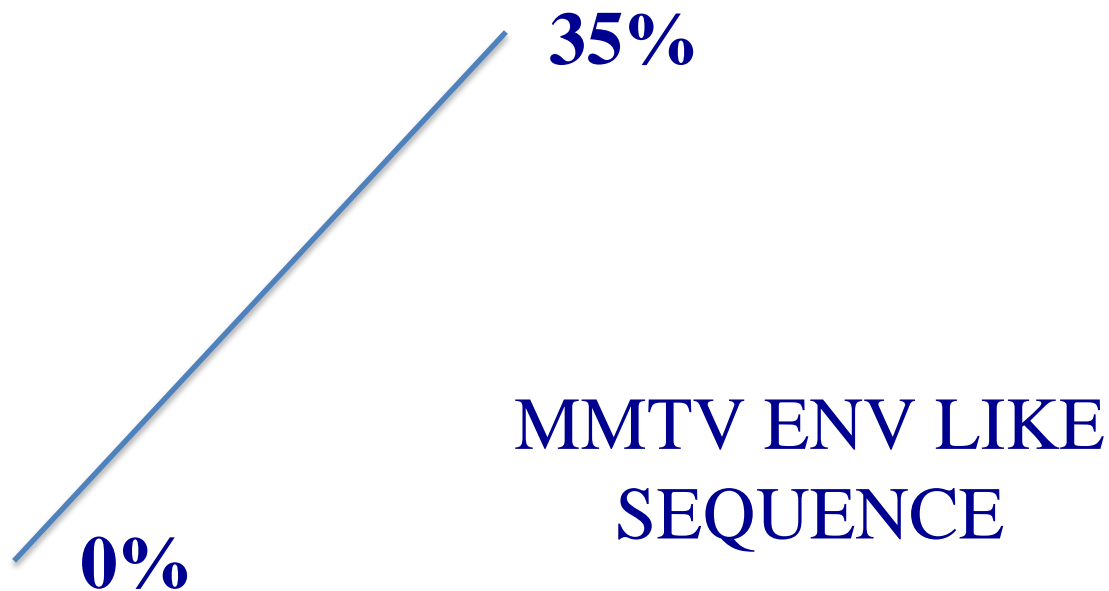
Mazzanti CM1 et al

Am J Pathol: 179: 2083, 2011

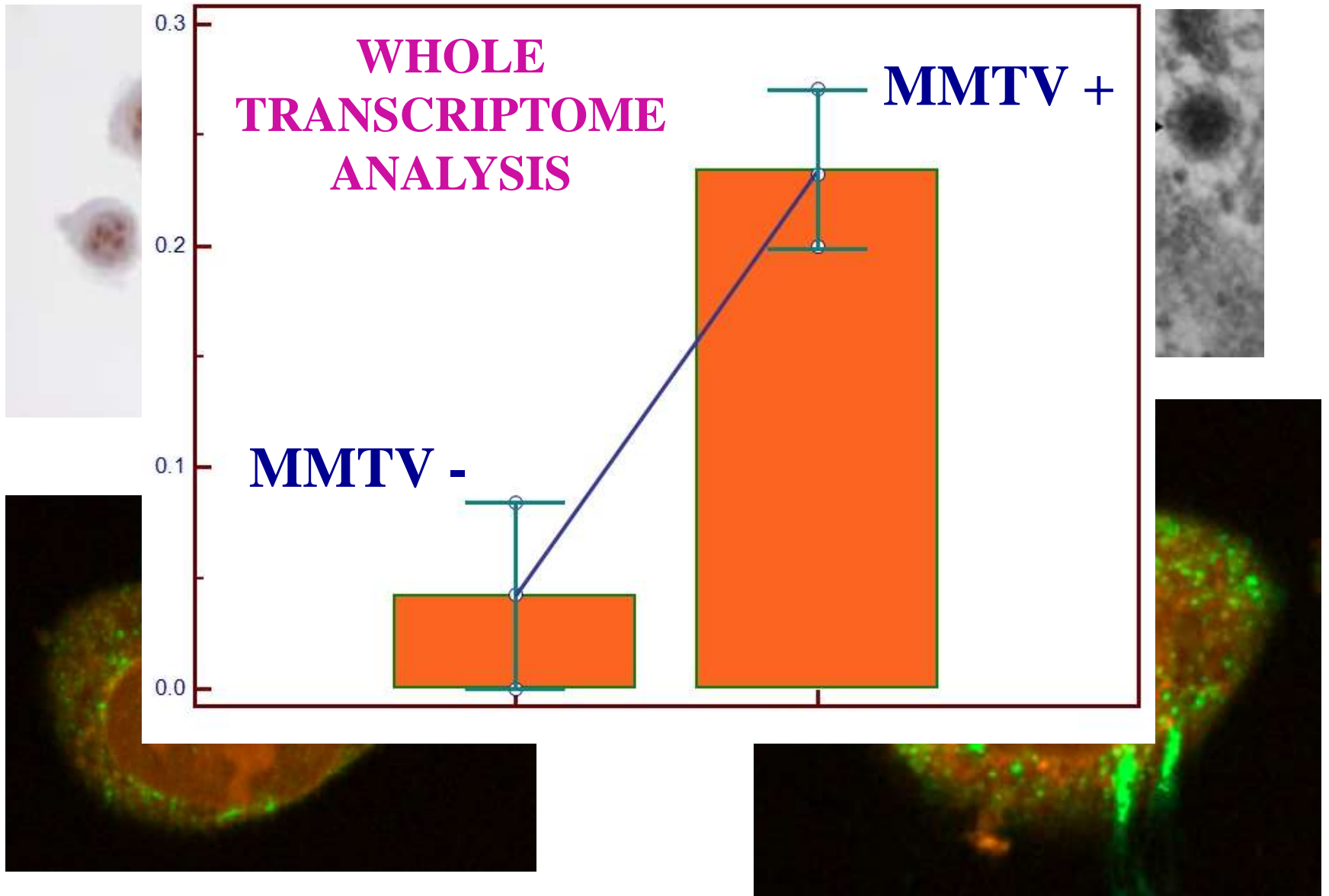
infiltrating breast carcinoma



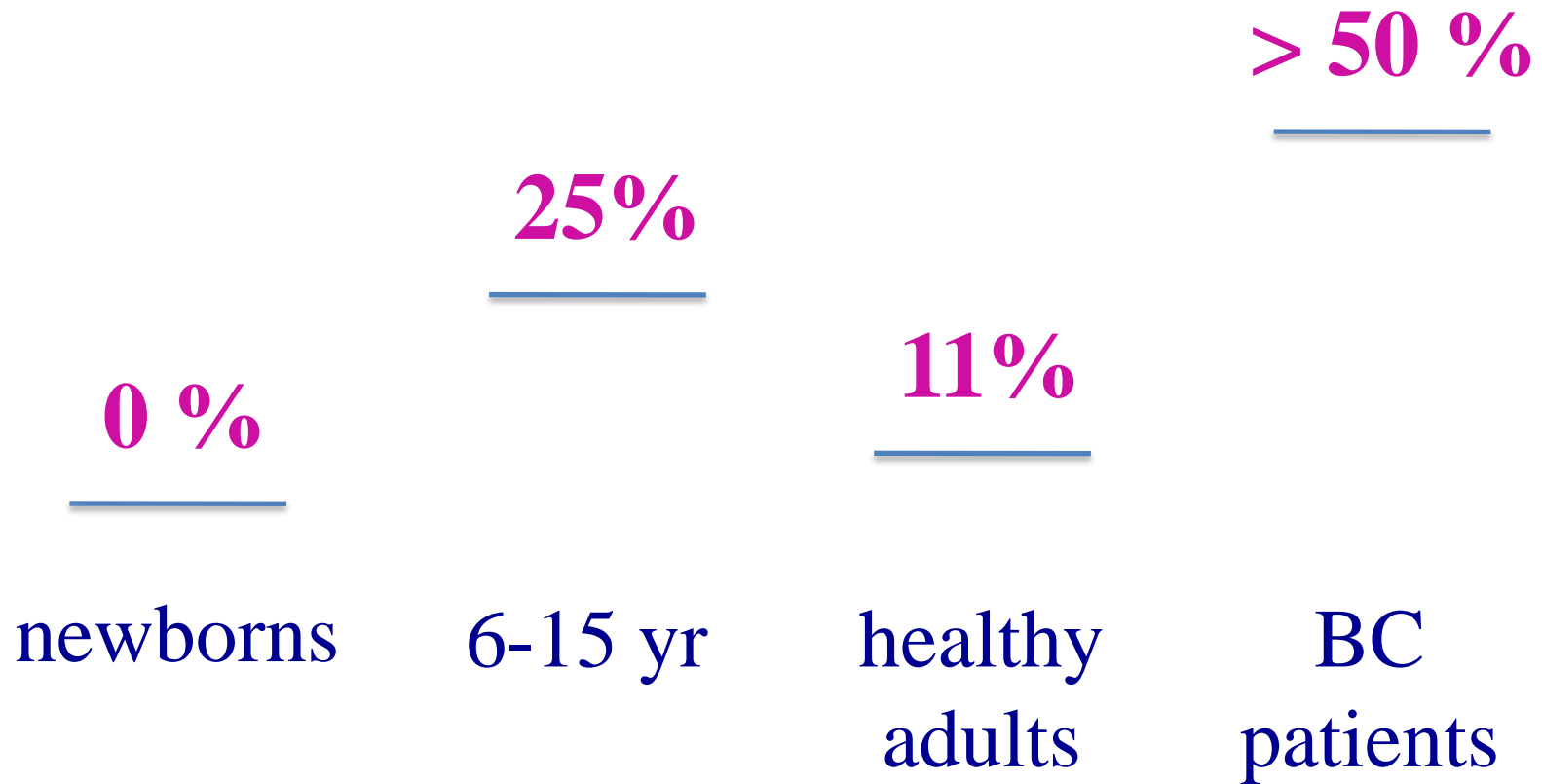
normal breast



MMTV in HUMAN PRIMARY CELL CULTURE



MMTV ENV in HUMAN SALIVA



STRONG EVIDENCE



MMTV

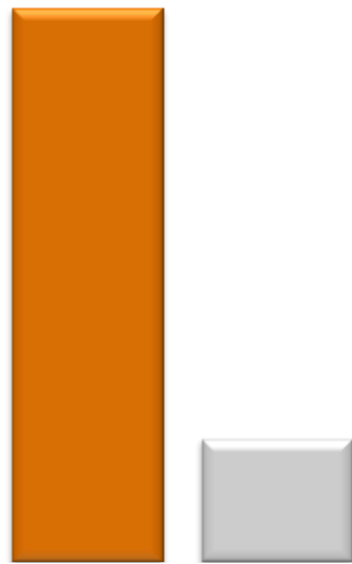


VACCINE ??

NGS analysis of DNA repair genes in Triple Negative Breast Cancer as a basis for a therapeutic approach

BRCA1, BRCA2, CHEK2, BRIP1, PALB2, TP53, ATM, BARD1, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, PMS1, PMS2, RAD50, RAD51c, RAD52, 53BP1, ERCC1 - - - **PARP1, CDH1, PTEN, STK11**

GERM LINE MUTATIONS



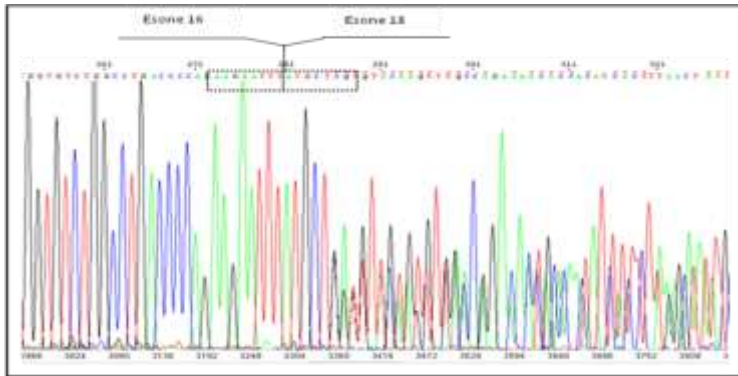
RESPONDERS

neoadjuvant therapy with
anthracyclines and taxanes

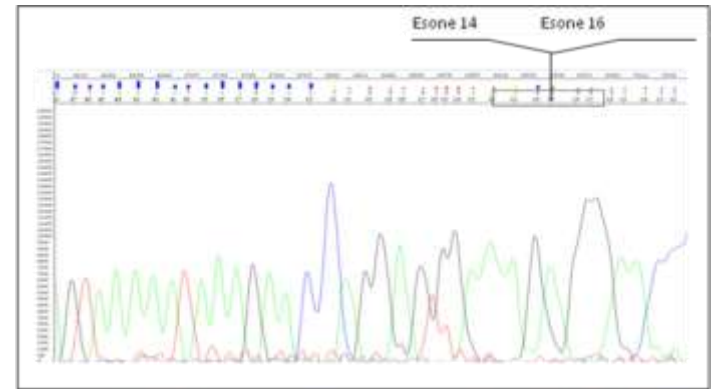


NON - RESPONDERS

Alternative aberrant splicing as inactivation mechanism of *BRCA1* and *BRCA2* genes in breast and/or ovarian cancer families



deletion of exon 17 > abnormal stop signal at codon 1673
(**p.Val1665Serfs*8**) > truncated protein



deletion of exon 15 > 194 abnormal stop signal at codon 1510 (**p.Ser1496Glyfs*14**) > truncated protein

The investigation of alternative transcripts of *BRCA1* and *BRCA2* genes reveals the presence of 15% of pathogenic isoforms not showed by classic methods of mutation screening

BRCA1 RELATED DNA REPAIR GENES IN BREAST CARCINOGENESIS

Previous experiment showed in yeast that *MSH6*, *MRE11*, *RAD50* and *RAD51* genes might have a role in genomic instability induced by human BRCA1 gene

MSH6 and RAD50 are frequently mutated in breast tumors of BRCA1 UV carrier patients

MOLECULAR ONCOLOGY / MEDICINE



TECHNOLOGY

**MOLECULAR
PATHWAYS**

