European Institute of Oncology experiences in radiobiology

Barbara Vischioni,
Div. Radioterapia, Istituto Europeo di Oncologia,
Istituto FIRC di Oncologia Molecolare, Milano

RADIOBIOLOGY:

FROM A MORPHOLOGIC TO A FUNCTIONAL APPROACH

AND FROM BENCH TO BEDSIDE

Brescia - May 9th, 2008

The radiobiology lab at the European Institute of Oncology

AIMS:

- to promote research in the field of radiobiology

- to transfer knowledge from the lab to the clinic

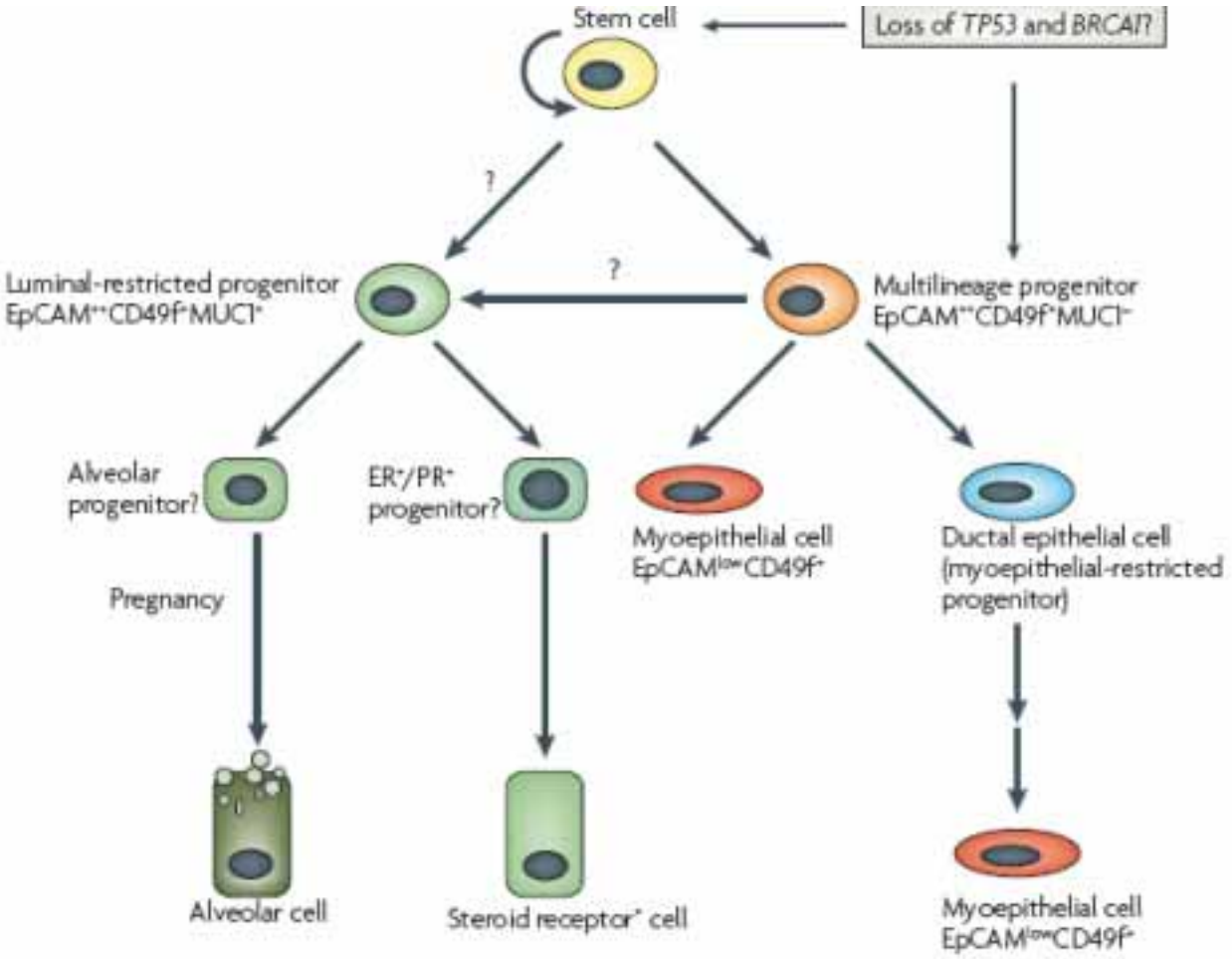
ONGOING COLLABORATIONS AND PROJECTS:

- Sensitivity of breast stem cells to radiation (*PG Pelicci, Experimental Oncology*)

- Screening on patient samples for the radiation activated genes identified by using the yeast Saccharomyces Cerevisiae as a model system (*M Foiani, Genome Integrity*)

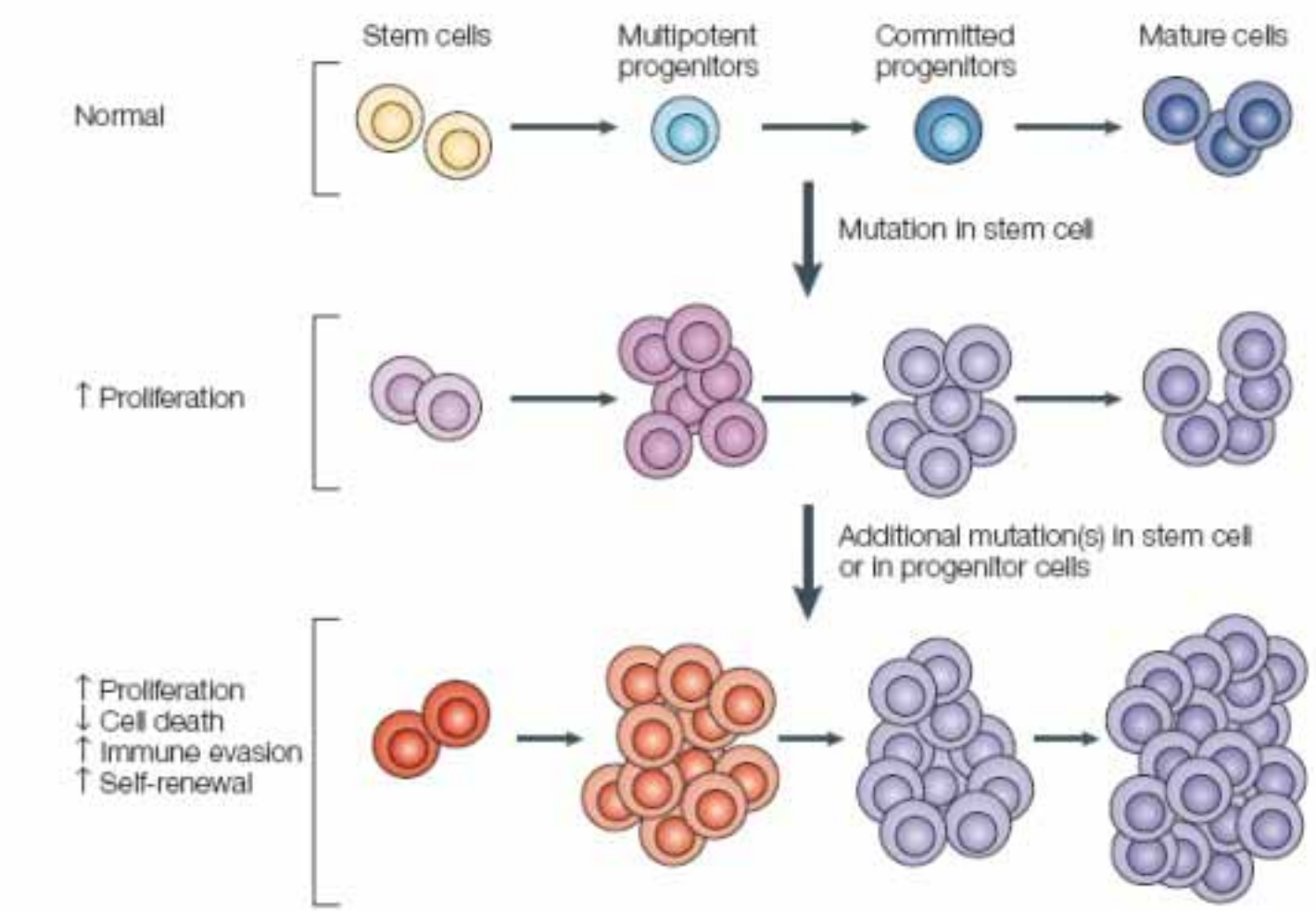
- Salmonella typhimurium systemic antitumor response directed by a low dose radiation protocol *(M Rescigno, Immunotherapy)*

Role of stem cells in normal mammalian breast development



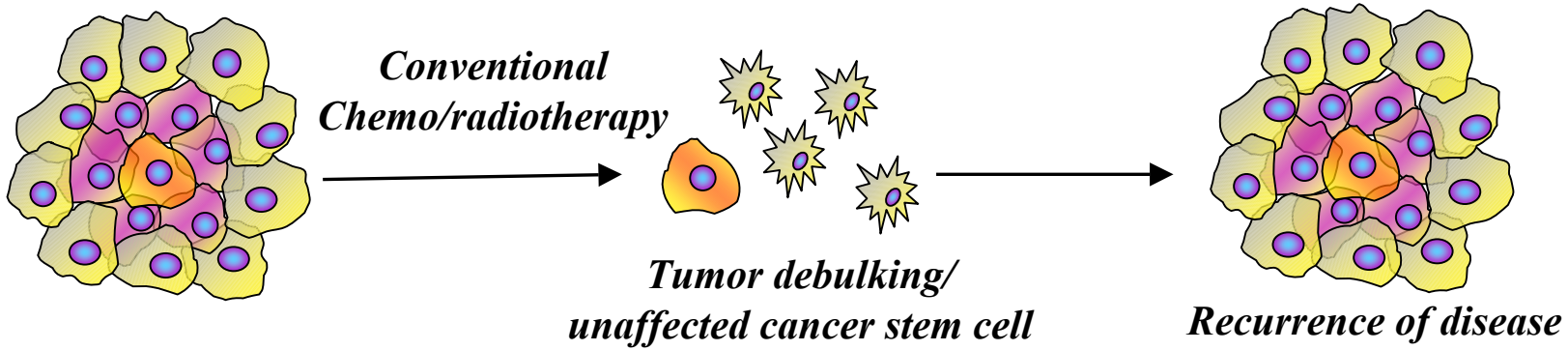
Stingl and Carlos, *Nature Reviews Cancer* 2007, 7:793

From normal stem cells to cancer stem cells



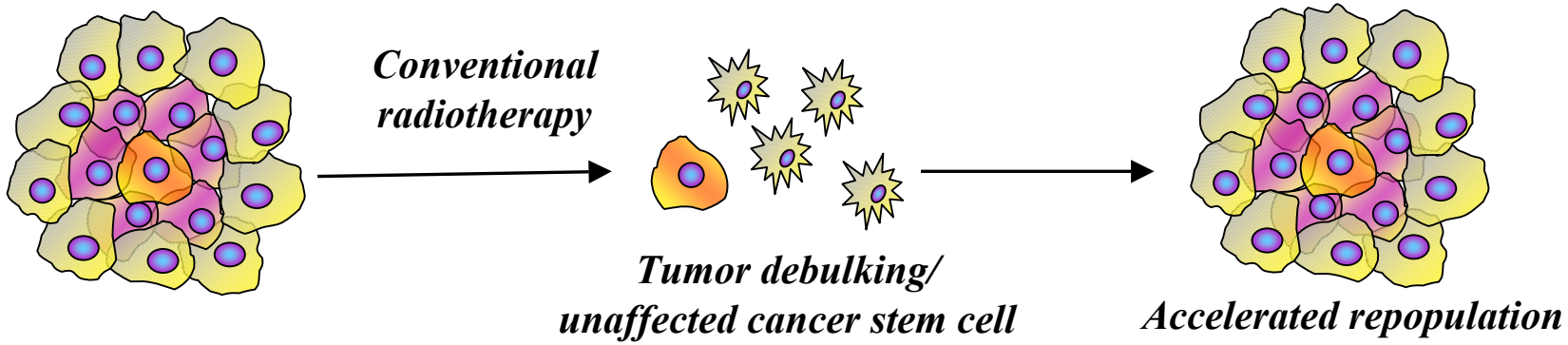
Dean et al., *Nature Reviews Cancer* 2005, 5:275

The stem cell model of carcinogenesis



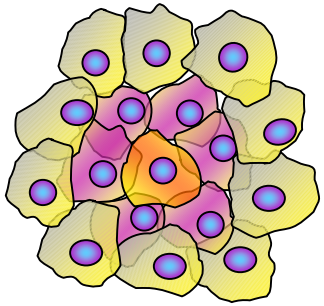
Cancer stem cells are endowed in the breast tissue with the potential to re-initiate tumor formation

Stem cells and accelerated repopulation during fractionated radiotherapy

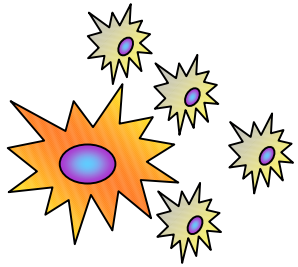


Each day of a treatment gap decreases the efficacy of RT by approximately 0.6 Gy, making it one of the major reasons for local failure of RT

Cancer stem cells: conventional anti cancer treatments and the need for molecular targeted therapies



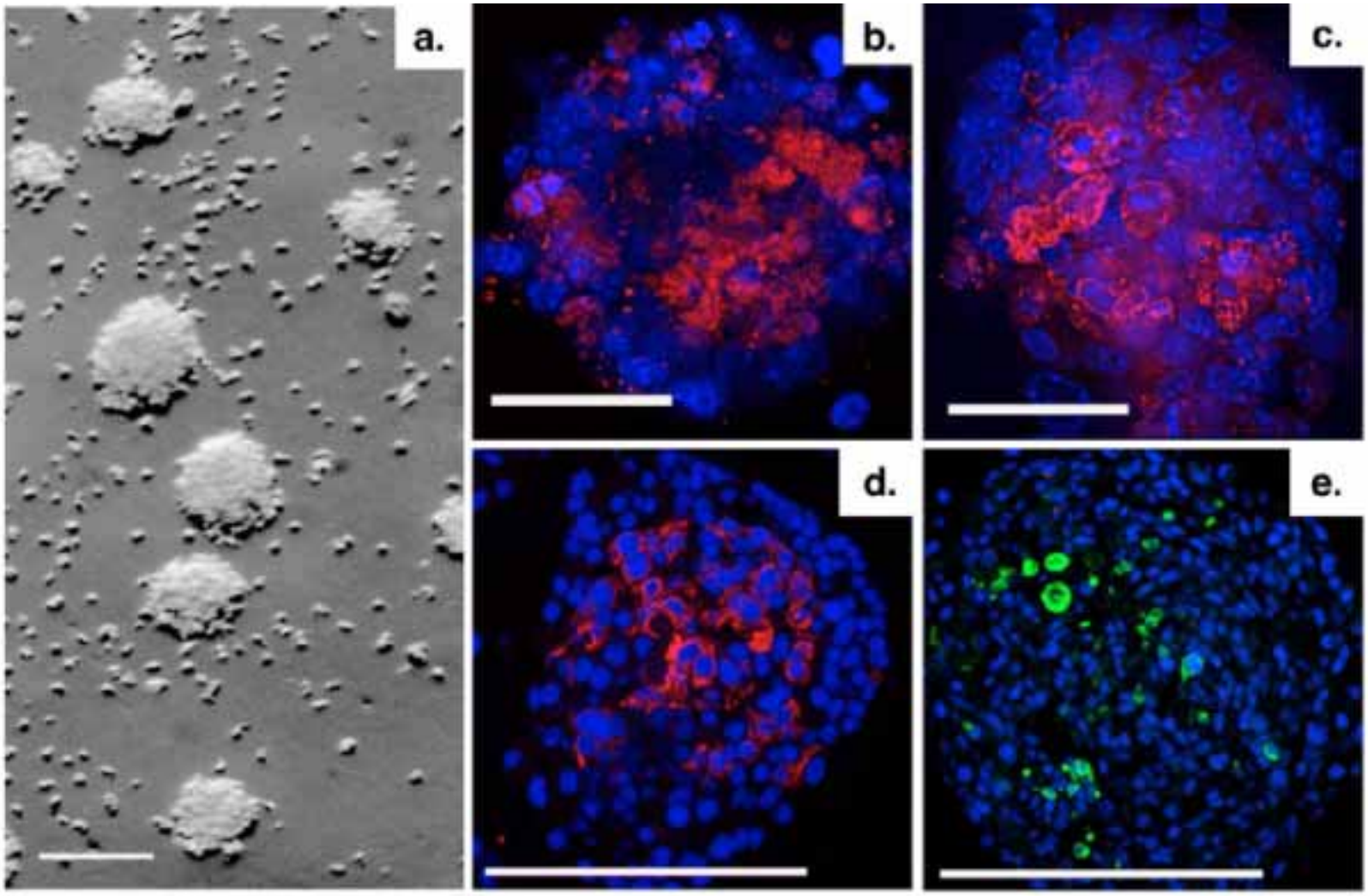
Conventional Chemo/radiotherapy
\+
Anti-cancer stem cells agents



Tumor debulking/ targeted cancer stem cell

Remission of disease

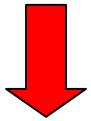
Mammary stem cells form mammospheres *in vitro*



Chen et al., *Journal of Cell Science* 2006, 120:468

Experimental design to investigate stem cell radiosensitivity

- separate breast stem cells (BSCs) and breast cancer stem cells (BCSCs) from the mammary glands of WT mice and transgenic mice overexpressing Erb2 oncogene
- disaggregate mammosphere
- count cell number and irradiate
- grow stem cells
- count stem cells and plate
- draw BSCs and BCSCs survival curves



Different sensitivity of BSCs and BCSCs to radiation

Conclusions

- **Different projects are being implemented at the IEO radiobiology lab**

- **Future plans concerning the project on radiosensitivity of breast stem cells**

  - **investigate the molecular mechanisms of radiosensitivity of BSCs and BCSCs, progenitor and stem cells (in terms of apoptosis, cell cycle regulation and senescence)**

  - **set up of a mouse model system recapitulating different steps of breast carcinogenesis in order to study in vivo the effects of different radiotherapy regimens**

Aknowledgements

IEO Department of Radiotherapy: Prof R Orecchia

IFOM-IEO Campus: PG Pelicci