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Nuova Proposta #1

*Riunione Annuale*

**GIM** GRUPPO  
ITALIANO  
MAMMELLA

Presentatrice:  
Sara De Martino, PhD

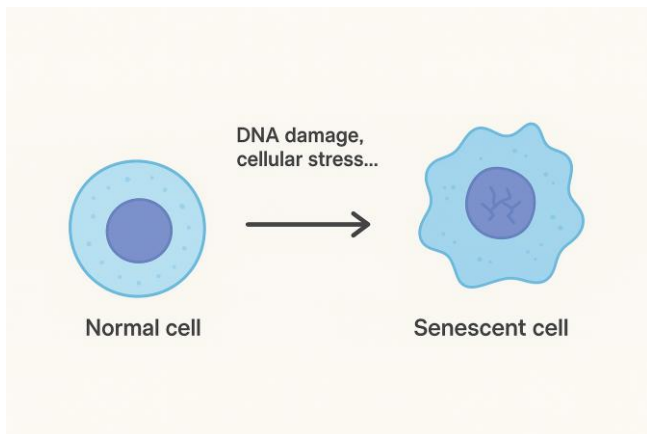


**26-27 SETTEMBRE 2025 BERGAMO**

**HOTEL EXCELSIOR SAN MARCO**

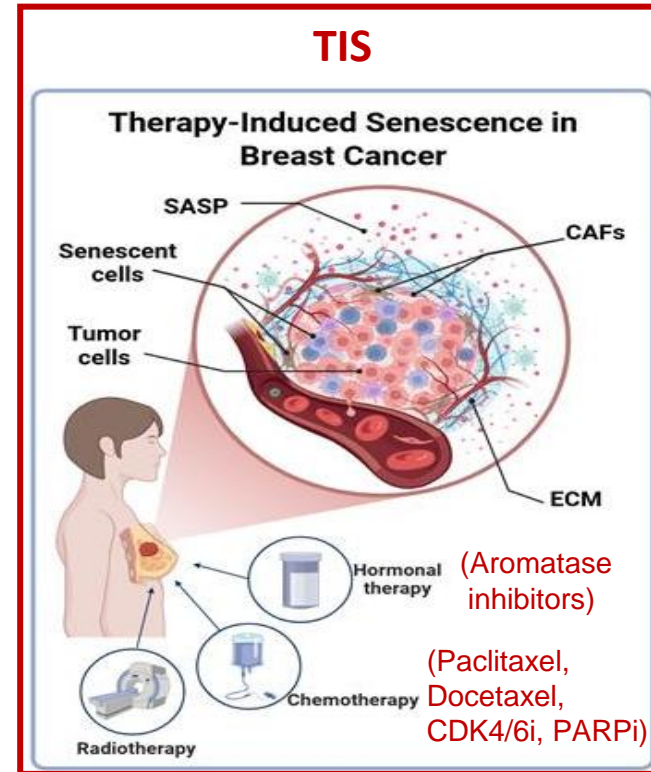
PIAZZA DELLA REPUBBLICA, 6

# Silenziamento del IncRNA HOTAIR e Terapia Senolitica nel tumore della mammella localmente avanzato Luminale, HER2+ e TN - Studio Pilota



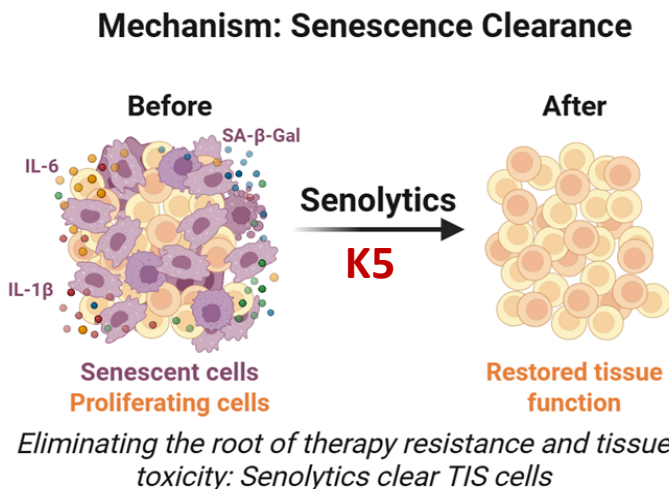
- Cell cycle arrest
- Dysregulated metabolism
- Macromolecular damage
- Resistance to apoptosis
- **Senescence-Associated Secretory Phenotype** (SASP, pro-inflammatory cytokines and chemokines).

Replicative Senescence  
 Oncogene-induced Senescence  
**Therapy-induced Senescence (TIS)**

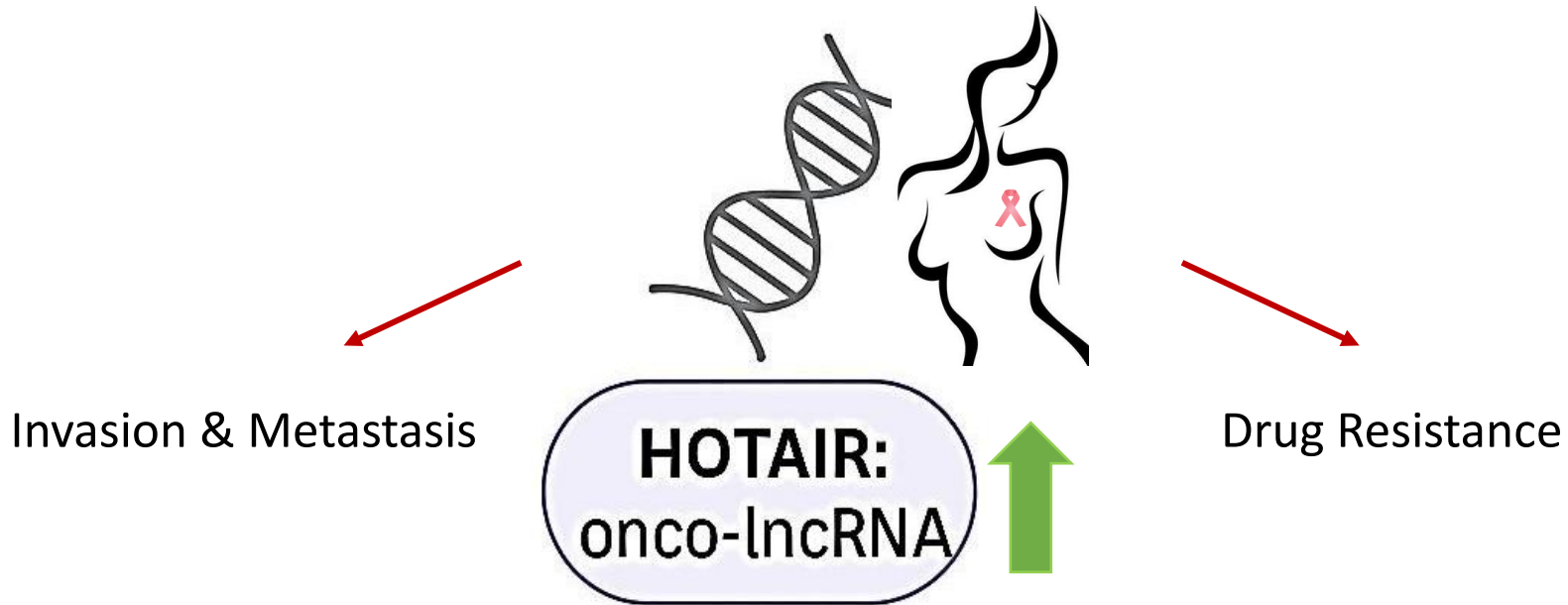


**Escaping from TIS:**

- Relapse
- Drug Resistance



**«One-two punch approach»**



## AIM

**Simultaneously targeting the oncogenic driver  
HOTAIR and the senescent niche**

*«Multiple approach»*

## Experimental design for Breast Cancer cell senescence

Breast Cancer  
Primary cultures  
or cell lines

Transfection with  
**HOTAIR *gapmers***

**TIS induction:**

- NT: solvent
- Aromatase inhibitors or targeted therapy (e.g.)

**Senolytic treatment:**

- Vehicle: DMSO
- Senolytic: **K5** 10  $\mu$ M



## Objectives & Methods

### Objectives

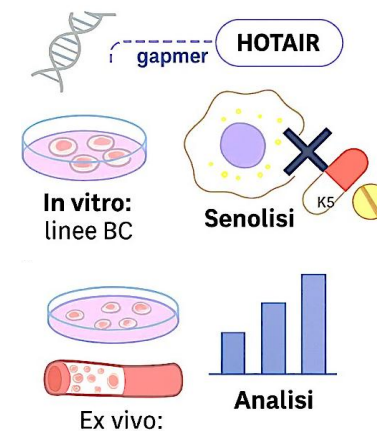
- HOTAIR silencing (anti-sense gapmers)
- K5 senolytic treatment (HSP90 $\alpha$  inhibitor)

### Methods

- *In vitro*: Breast Cancer cell lines (Luminal A and B, HER2+, TN)
- *Ex-vivo*: Patient-derived\* epithelial Primary Cultures from biopsy

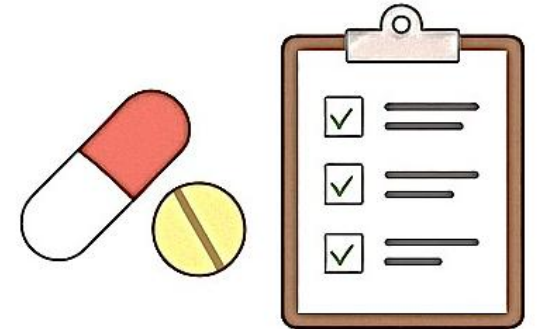
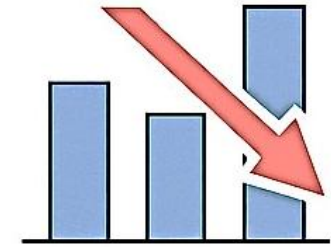
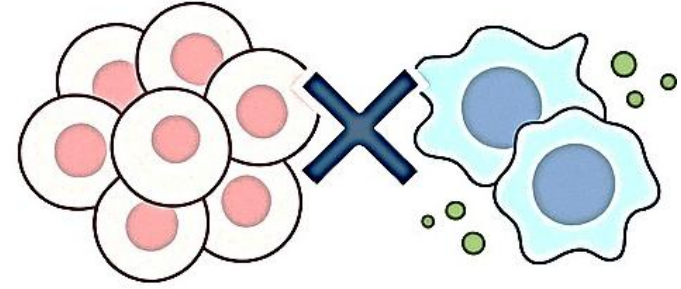
### Analysis

- Proliferation
- Apoptosis
- Senescence markers
- Molecular analysis (RNA-seq)



# Expected Impact

- Synergic elimination: Proliferant cells + TIS cells
- Reduction of recurrence and therapeutic resistance
- New combined therapeutic paradigm for BC
- Basis for future translational clinical trial



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