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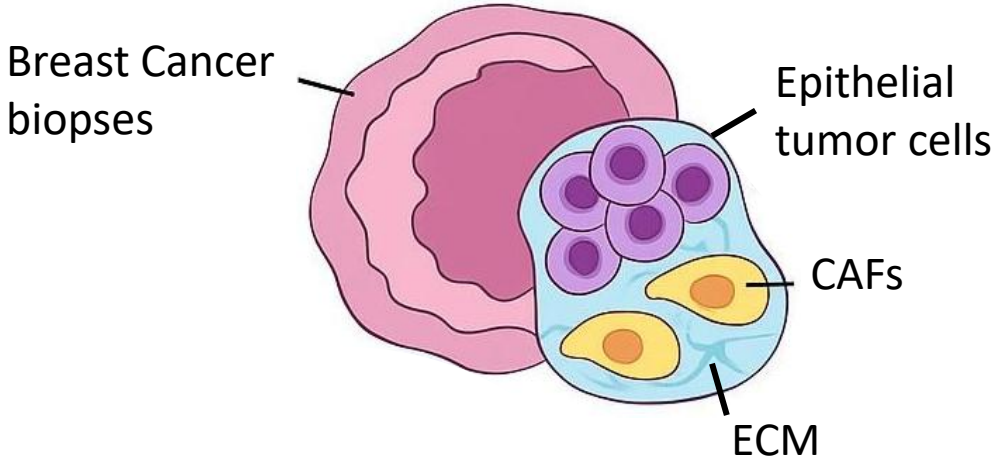
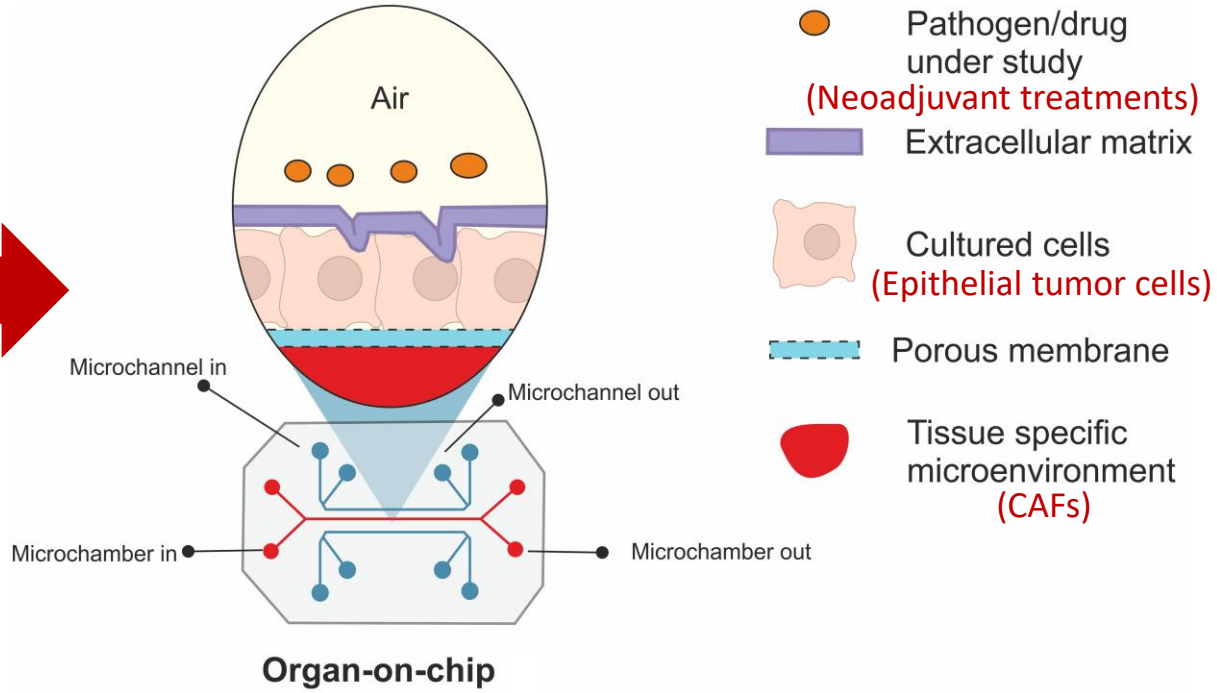
Nuova Proposta #2

Presentatrice:
Sara De Martino, PhD

Realizzazione di una piattaforma Organ-on-Chip Derivata da Paziente per Modellare la Senescenza Terapia-Indotta nel Microambiente del Carcinoma Mammario- Studio Pilota

Organ-on-Chip (Step I)



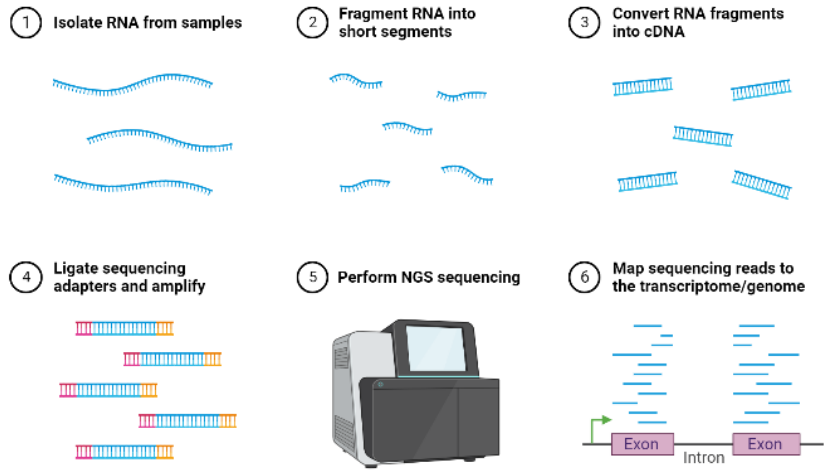


Nayak S et al, Organs-on-chips Provide Insights into Molecular Mechanisms of Disease and Facilitate the Design of Newer Treatment Strategies: A Concise Review. J Explor Res Pharmacol. 2024;9(2):116-123. doi: 10.14218/JERP.2023.00006S.

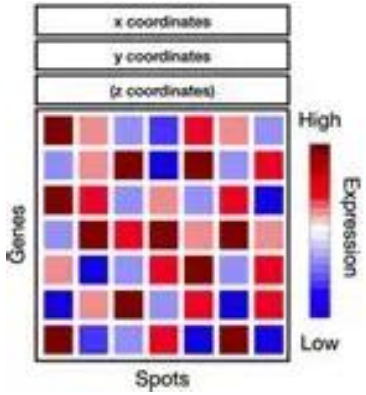
SenMAYO gene set to identify senescent cell state (Step II)

Blood sample from patients **pre- and post**-neoadjuvant treatments

RNA-seq



SenMAYO gene set analysis*



Van den Berge et al. (2019). RNA sequencing data: Hitchhiker's guide to expression analysis. Annual Review of Biomedical Data Science, 2, 139-173. https://doi.org/10.7287/peerj.preprints.27283v1

AIM

- **Develop patient-derived Transwell co-cultures and advanced Organ-on-Chip (OoC) platforms and characterize Therapy-Induced Senescence after neoadjuvant (NAD) treatments**

- **Correlate ex vivo responses with blood biomarkers, particularly the senMAYO transcriptional profile, derived from pre- and post-NAD patients to establish the clinical relevance of the model.**

*Saul, D. et al. A new gene set identifies senescent cells and predicts senescence-associated pathways across tissues. Nat Commun 13, 4827 (2022). https://doi.org/10.1038/s41467-022-32552-1

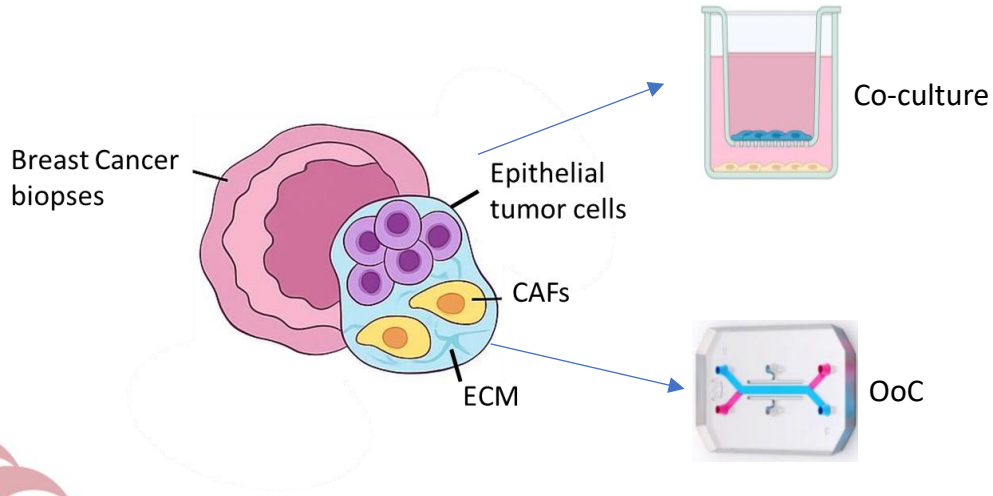
Objectives

- Develop co-culture models and OoC from pre-NAD patient biopsies
- Characterize *ex-vivo* TIS after NAD treatments
- Correlate *ex vivo* data with blood biomarkers (in pre- and post-NAD patients) from SenMAYO analyses.

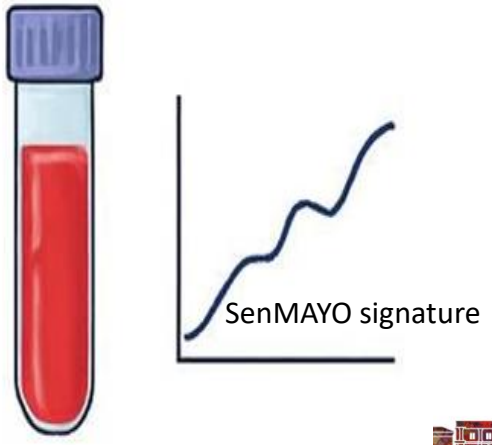
Methods

- N. 5 samples from biopsy/subtype: Luminal, HER2+, Triple Negative. **Total: 15 patients**
- **TIS upon NAD** treatments and multiparametric senescence markers validation (SA-β gal, p16, p21, γH2AX, SASP) in *ex-vivo* models
- **Parallel analysis** of peripheral blood derived from pre- and post-NAD patients to evaluate the MAYO signature (***putative multi-center study***)

I



II



Expected Impact

- Patient-derived platform to model TIS and, in future, to test drugs efficacy (e.g. K5) in Breast Cancer.

- Identification of predictive clinical biomarkers (SenMAYO) for future clinical trials.

- Towards a **precision oncology** that integrates Ooc and biomarkers to reduce recurrences and resistances

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