

Project Title:

Bioengineered 3D Breast Cancer Models to Study ECM–TRP Mechanosensing and Nanotherapeutic Response

PI: Nora Bloise

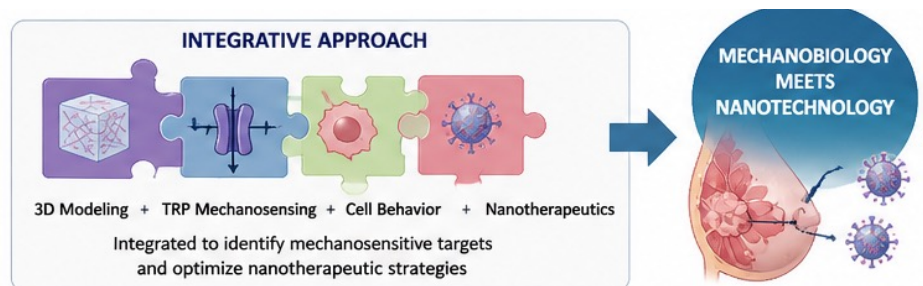
Laboratory: “Cells and biomaterials interactions: nanotechnology”, Unit of Biochemistry of Department of Molecular Medicine.

Background:

Extracellular matrix (ECM) remodeling is a hallmark of breast cancer progression, leading to increased tissue stiffness and altered tumor architecture¹. These mechanical changes regulate key cellular processes—including proliferation, migration, and invasion—through mechanotransduction pathways. Among mechanosensitive elements, transient receptor potential (TRP) channels play a critical role in calcium signaling and cellular responses to mechanical stimuli². However, their contribution to ECM-driven tumor progression and their influence on nanotherapeutic delivery and efficacy remain poorly understood. **Aim:** This PhD project aims to elucidate how ECM remodeling and TRP channel-mediated mechanosensing regulate breast cancer progression and response to nanotherapeutics.

Objectives: 1. Develop and characterize engineered 3D breast cancer models with

tunable ECM stiffness and architecture. 2. Investigate the expression and activity of TRP channels under varying mechanical conditions. 3. Determine how ECM mechanics and TRP signaling influence cancer cell behavior (proliferation, invasion, mechanotransduction pathways). 4. Evaluate the impact of ECM remodeling and TRP activity on nanoparticle transport, cellular uptake, and therapeutic efficacy. **Methodology Overview:** The project will employ advanced 3D culture systems (e.g., hydrogels with controlled stiffness and composition) to mimic the tumor microenvironment. Mechanical properties will be systematically modulated to study their effects on TRP channel activity using molecular, imaging, and electrophysiological approaches. Nanoparticle-based drug delivery systems will be introduced to assess how biomechanical cues affect transport and uptake. Functional assays will link these findings to therapeutic outcomes. **Expected Outcomes and Impact:** This study will provide mechanistic insight into how ECM stiffness and TRP-mediated mechanosensing jointly regulate tumor progression and nanotherapeutic response. The findings are expected to identify novel mechanosensitive targets and inform the design of more effective nanomedicine strategies for breast cancer treatment.



Bibliography: 1) Mierke CT. Extracellular Matrix Cues Regulate Mechanosensing and Mechanotransduction of Cancer Cells. *Cells*. 2024 Jan 2;13(1):96. doi: 10.3390/cells13010096. PMID: 38201302; PMCID: PMC10777970. 2) Giannaccari M, Florindi C, Bloise N, Moccia F, Lodola F, Visai L. TRP channels and cancer modulation: a voyage beyond metabolic reprogramming, oxidative stress and the advent of nanotechnologies in targeted therapy. *J Exp Clin Cancer Res*. 2025 Aug 14;44(1):240. doi: 10.1186/s13046-025-03495-4. PMID: 40813985; PMCID: PMC12351952.