Title of the project: Biomechanics of the Breast Cancer Microenvironment

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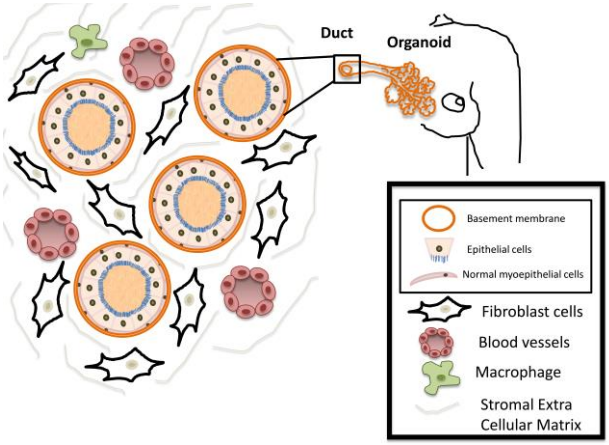
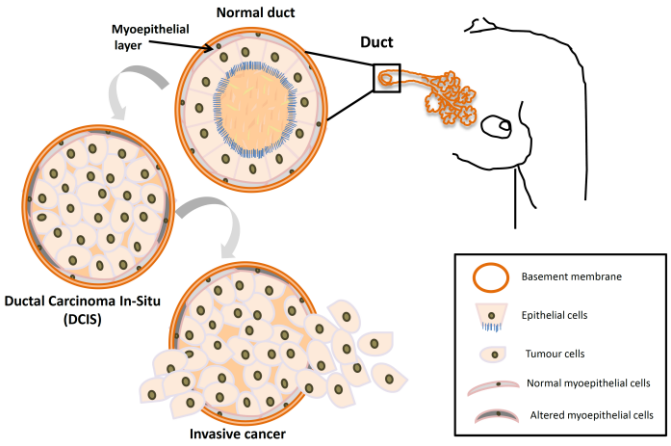
Normal Human Breast



From normal human breast to DCIS and invasive cancer



Project Description: Breast cancer starts as Ductal Carcinoma in Situ (DCIS), in which tumour cells are kept within the myoepithelial layer of the mammary ducts. The increasing intraductal pressure exerted by proliferating cells inside DCIS ducts may reach a limit at which the myoepithelial layer breaks, releasing previously confined tumour cells to the surrounding tissue. These cells can now invade and form metastasis in other organs, setting the progression from a localised and curable DCIS to a devastating invasive disease. The properties of the surrounding tissue (microenvironment) or stroma have a paramount role in the progression of this cancer.

Project Aims

This project will focus on the biomechanical characterization of the breast fibroblast, the main cellular component of the stroma. The specific aim will be to investigate how these fibroblasts mechanically communicate with their surroundings in physiological and pathological conditions, and how these cells influence the microenvironment to facilitate cancer cell invasion. These results will shed light on the biomechanics of breast cancer, and will set the ground for better choices of breast cancer diagnosis and treatments.

Key techniques: Biophysical and cell biology techniques: Magnetic tweezers, immunofluorescence, Western blot, tissue culture, organotypic cultures, elastic pillars.

- Calvo, F., et al., *Mechanotransduction and YAP-dependent matrix remodelling is required for the generation and maintenance of cancer-associated fibroblasts.* Nature Cell Biology, 2013. **15**(6): p. 637
- del Rio, A.; Perez-Jimenez, R.; Ruchuan, L.; R; Roca-Cusachs, P.; Fernandez, J. M. and Sheetz, M.P. (2009) Stretching Single Talin Rod Molecules Activates Vinculin Binding. *Science,* **323**, 638-641.
- Roca-Cusachs P**,** del Rio A, Puklin-Faucher E, Gauthier NC, Biais N, Sheetz MP (2013) Integrin-dependent force transmission to the extracellular matrix by alpha-actinin triggers adhesion maturation. PNAS, **110**(15):E1361-E1370