Atomic Force Microscopy reveals how mechanical cues from the extracelular matrix modulate functional differentiation in mammary epithelial cells

Jordi Alcaraz[1,2,3], *Ren Xu*[1], *Hidetoshi Mori*[1], *Carlos Bustamante*[2] *y Mina J. Bissell*[1]

[1] *Lawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley CA 94720, US*

[2] *University of California Berkeley, 642 Stanley Hall, Berkeley CA 94720, US*

[3] *Dirección actual: Universitat de Barcelona, Casanova 143, Barcelona 08036, Spain*

jalcaraz@ub.edu

Resumen

In the mammary gland, epithelial cells are embedded in a 'soft' environment, and become functionally differentiated in culture when exposed to a laminin-rich extracellular matrix gel. Here we define the processes by which mammary epithelial cells integrate biochemical and mechanical extracellular cues to maintain their differentiated phenotype. We used cells cultured on top of gels in conditions permissive for β-casein expression using atomic force microscopy to measure the elasticity of the cells and their underlying substrata. We found that maintenance of β-casein expression required both laminin signaling and a 'soft' extracellular matrix as is the case in normal tissues in vivo, and biomimetic intracellular elasticity as is the case in intact primary mammary epithelial organoids. Conversely two hallmarks of breast cancer development, stiffening of the extracellular matrix and loss of laminin signaling, led to loss of β-casein expression and non-biomimetic intracellular elasticity. Our data indicate that tissue-specific gene expression is controlled by both the the tissues' unique biochemical milieu and the distinct mechanical properties of the extracellular matrix, processes involved in both maintenance of tissue integrity and protection against tumorigenesis.