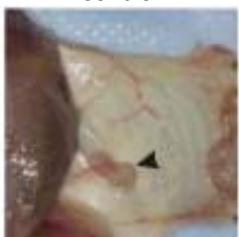



**Sensing matrix rigidity:
transducing mechanical signals from integrins to the
nucleus**

Pere Roca-Cusachs

Universitat de Barcelona

**Institute for Bioengineering of
Catalonia (IBEC)**

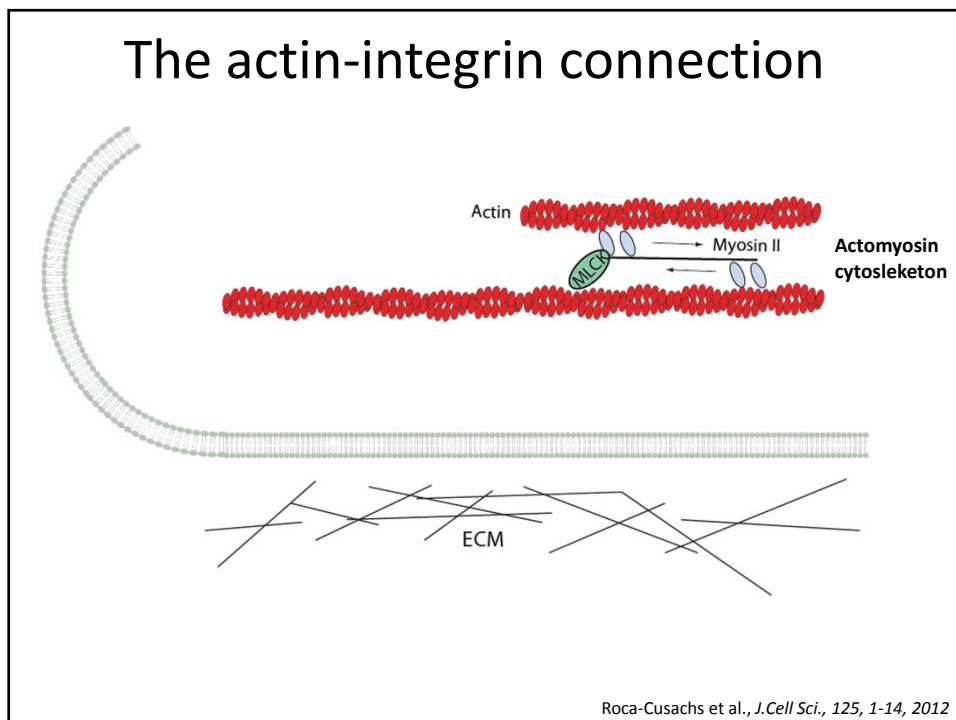
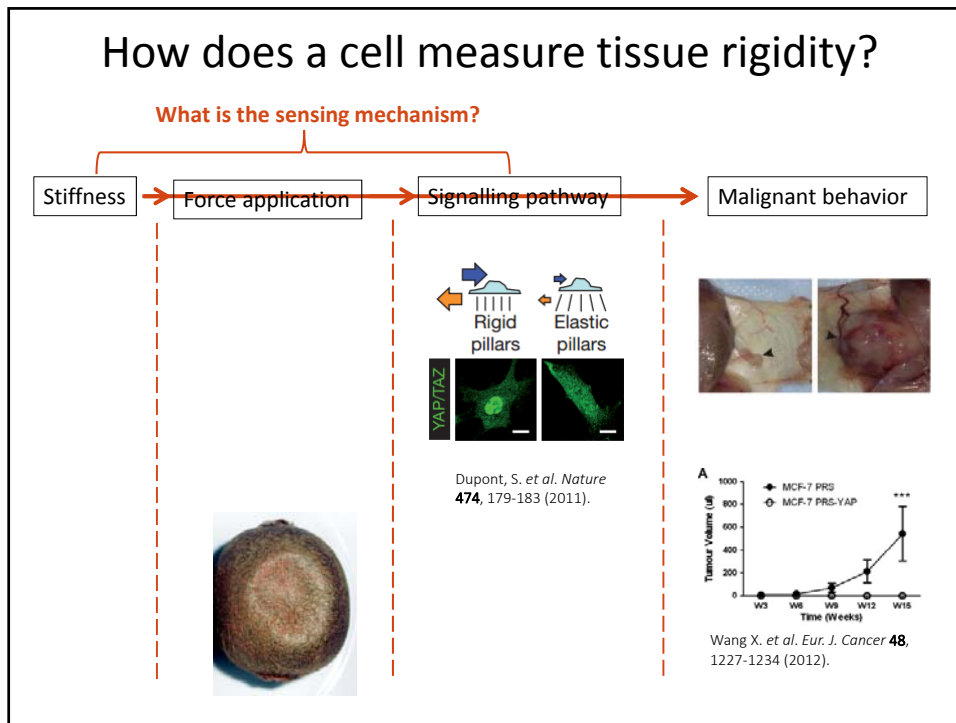
	Control	Increased stiffness
Mouse breast tumors		

Levental et al., *Cell* 139:891-906, 2009

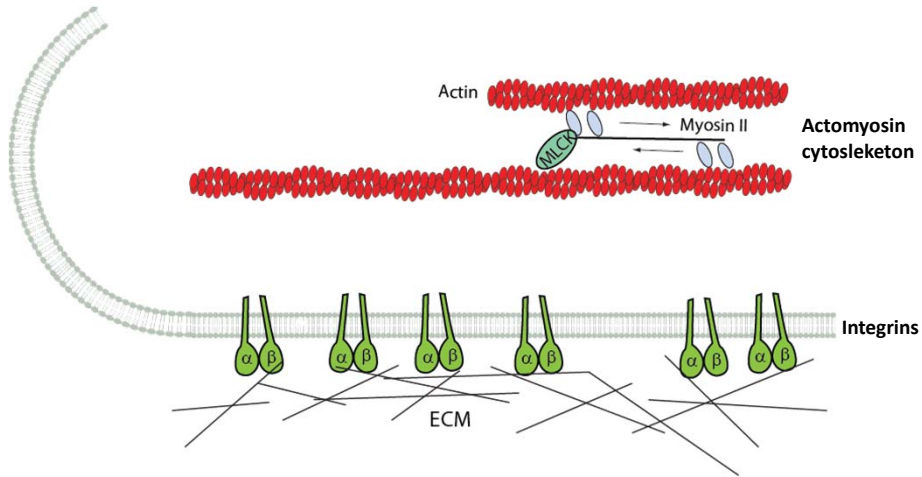
Mechanical factors are important in:

- Most solid tumors
- Development
- Wound healing
- ...

2

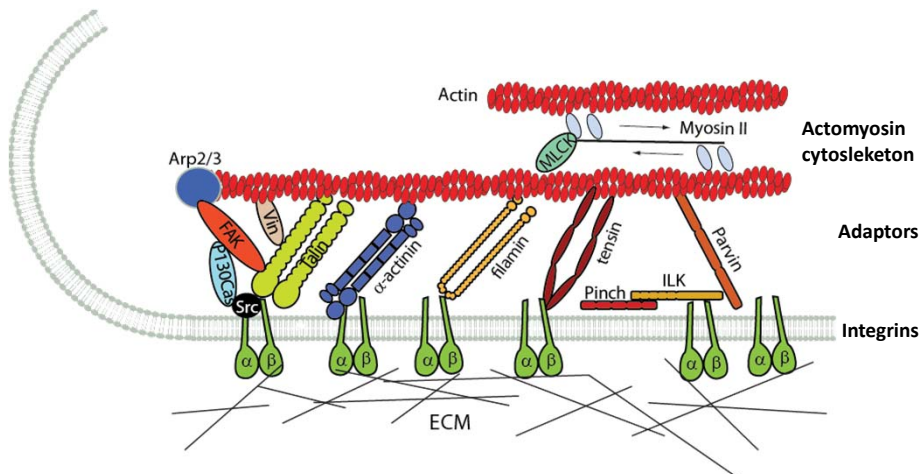


The actin-integrin connection



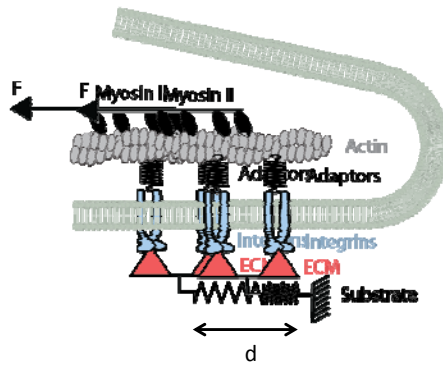
Roca-Cusachs et al., *J.Cell Sci.*, 125, 1-14, 2012

The actin-integrin connection



Roca-Cusachs et al., *J.Cell Sci.*, 125, 1-14, 2012

How does a cell measure tissue rigidity?

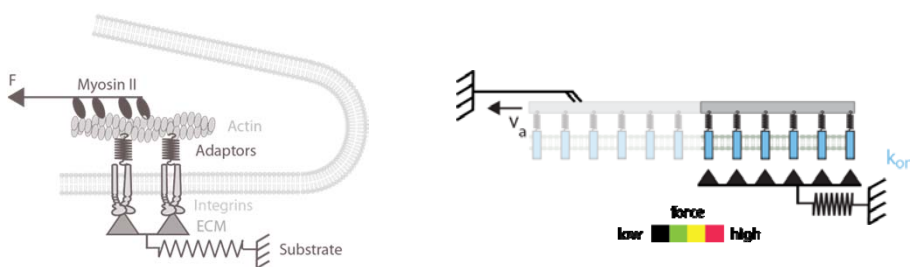


Substrate stiffness: $k = F/d$

Two fundamental questions:

1. How does rigidity regulate cell-matrix **force transmission**?
2. How is then this **force transduced** into a biochemical signal?

Step 1: force transmission



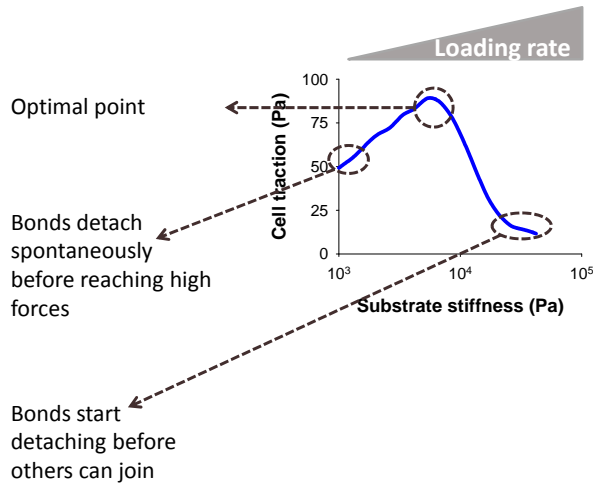
Actin flow

Deforms substrate

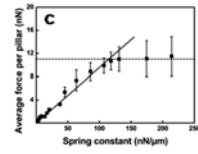
Soft substrate:
Slow force buildup
(low **loading rate**)

Stiff substrate:
Fast force buildup
(high **loading rate**)

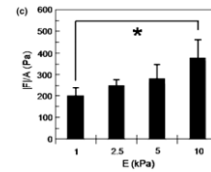
Step 1: force transmission



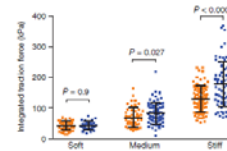
Based on Chan and Odde, *Science* **322**, 1687-1691 (2008).



Ghibaudo et al., *Soft Matter* **2008**, **4**:1836-1842

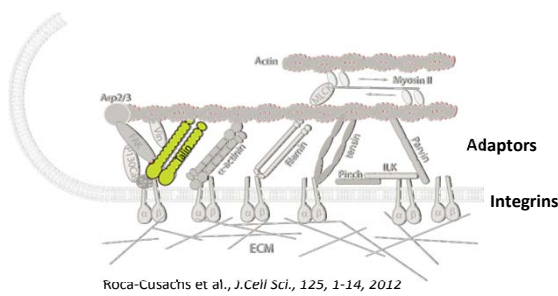


Califano et al., *Cell Mol Bioeng* **2010**, **3**:68-75

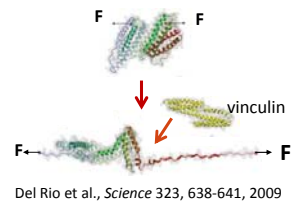


Schiller et al., *Nat Cell Biol* **2013**, **15**:625-636

Step 2: force transduction

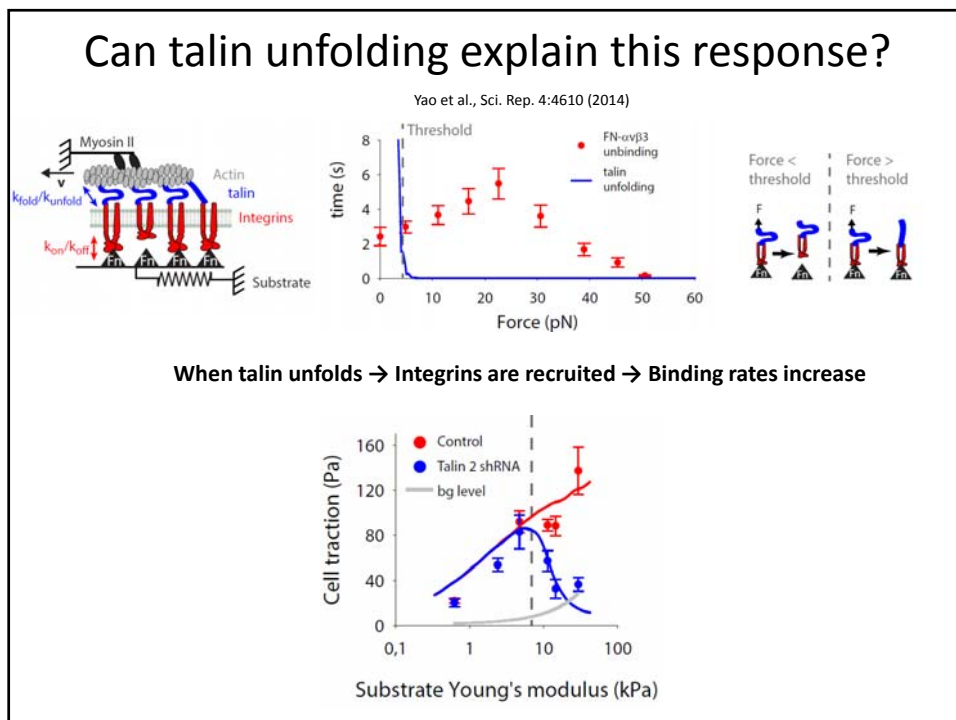
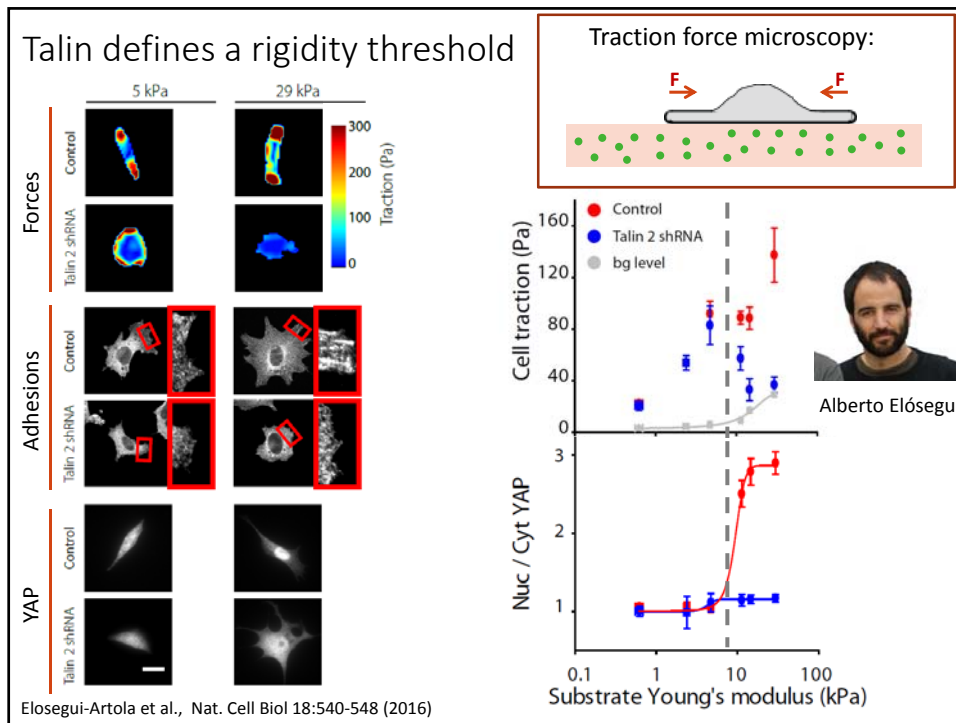


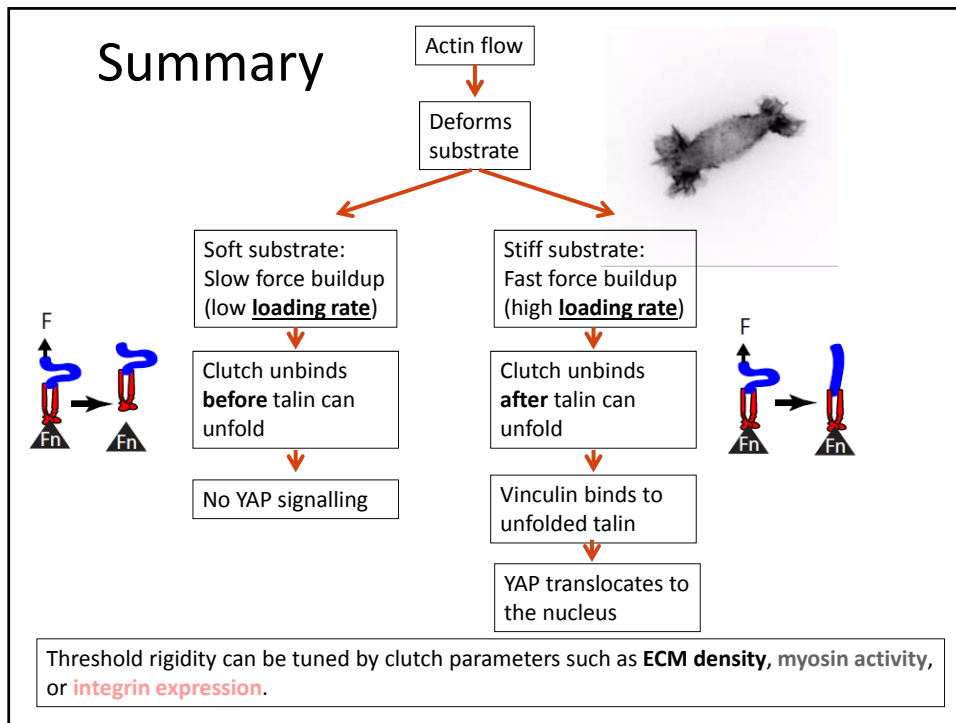
Roca-Cusachs et al., *J. Cell Sci.*, **125**, 1-14, 2012




Integrin recruitment, adhesion growth
Roca-Cusachs et al., *PNAS* **106**, 16245-16250, 2009

Does talin unfolding mediate rigidity sensing?






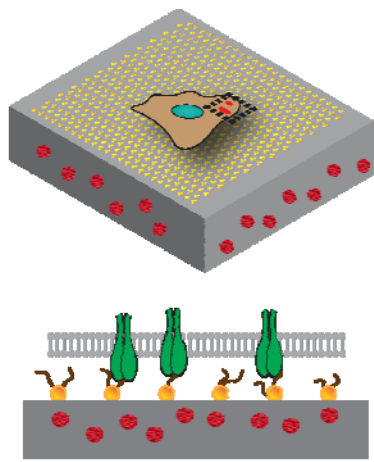
Sensing ligand density



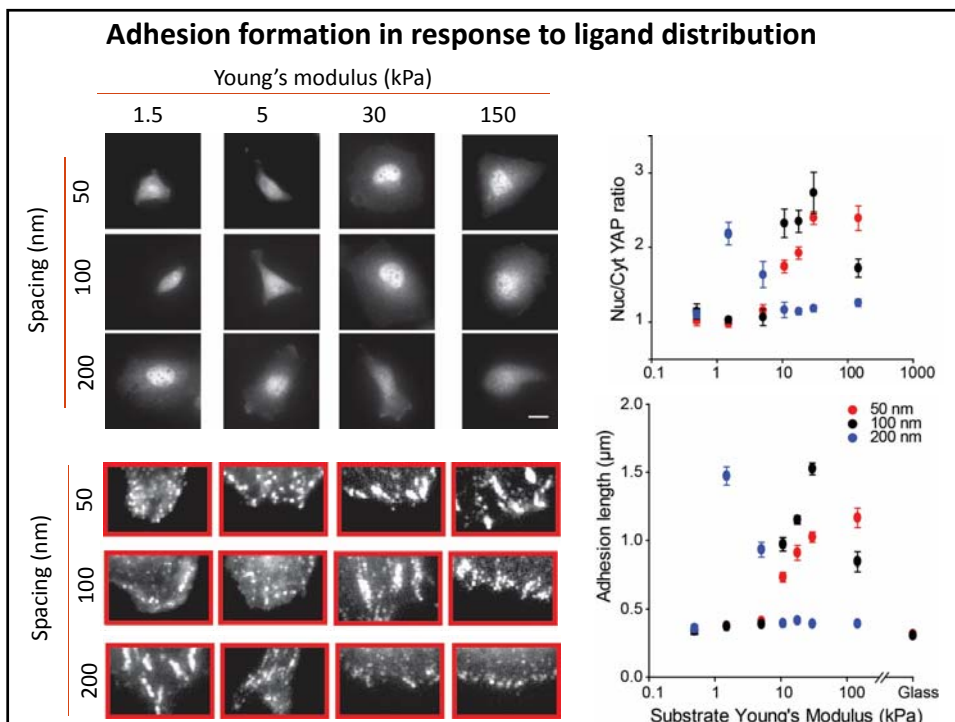
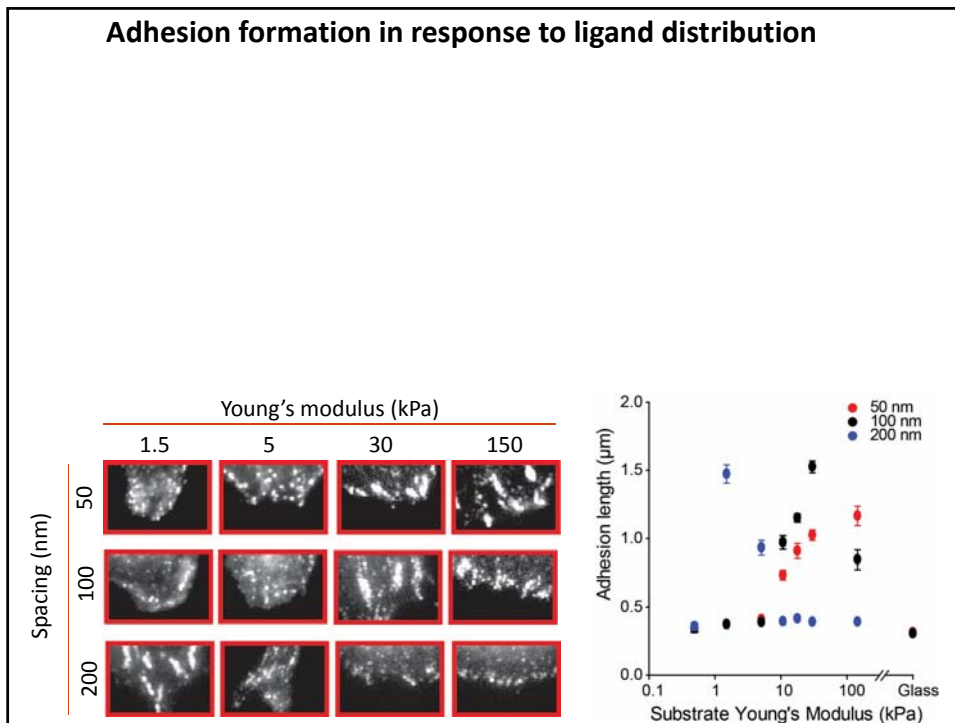
Ada Cavalcanti

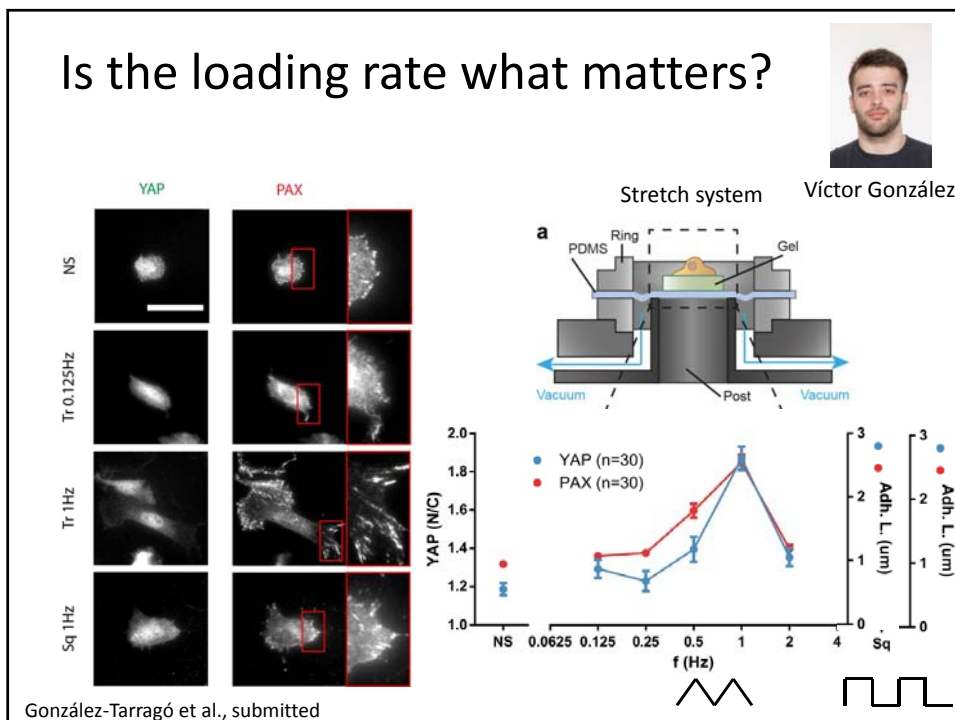
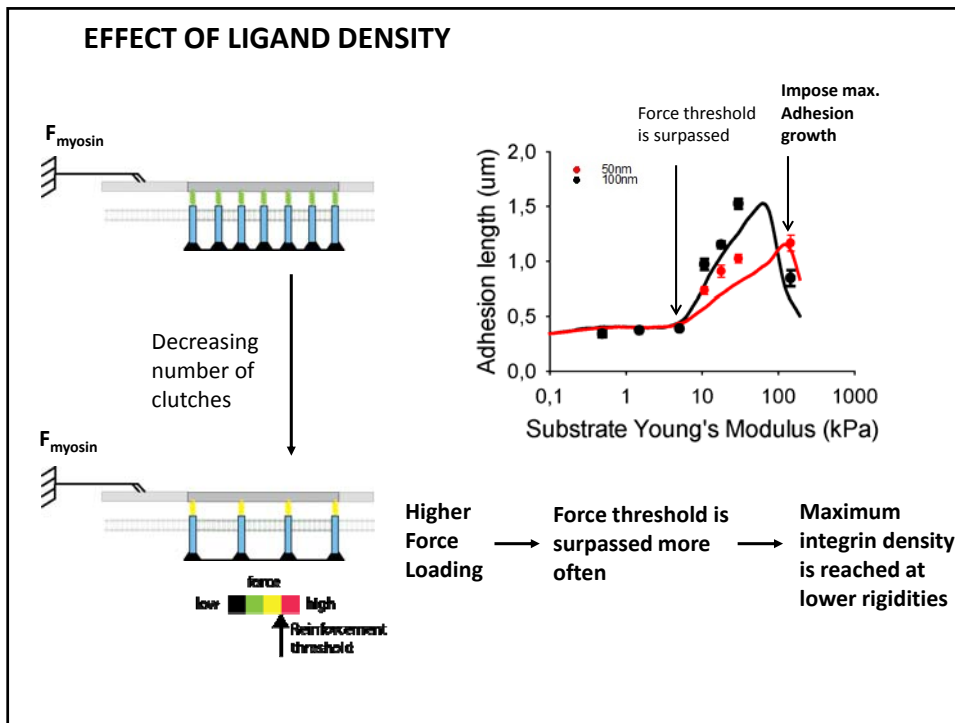


Tina Weigand

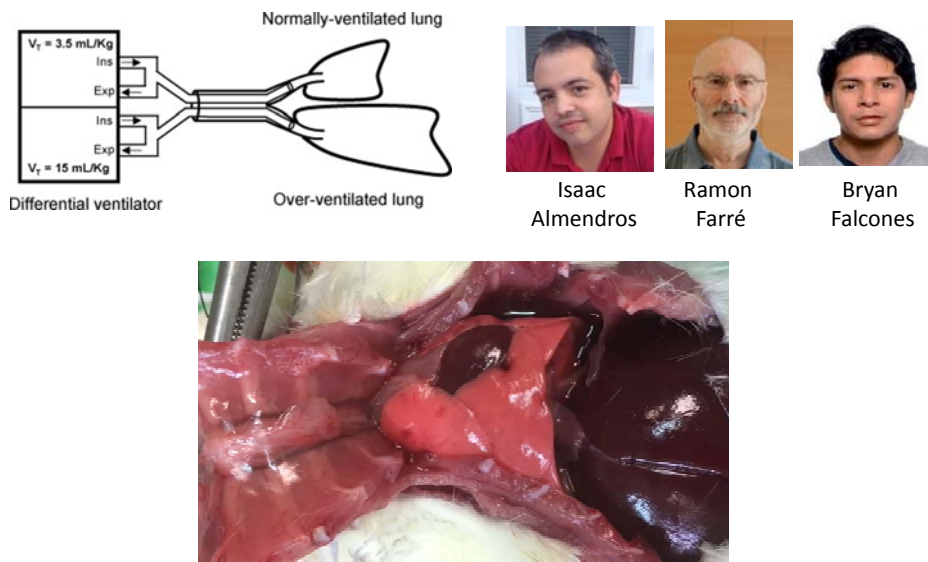


Oria et al., *Nature* 552:219-224 (2017)

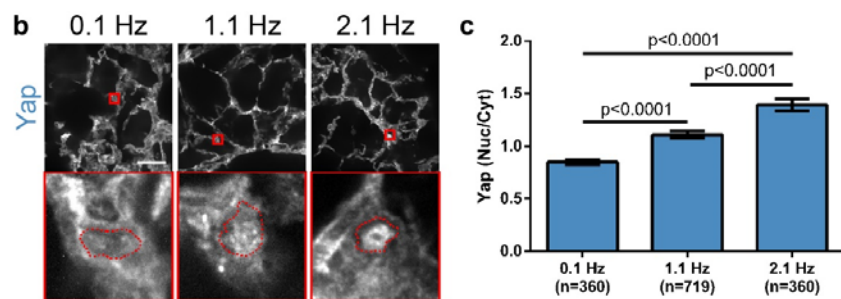


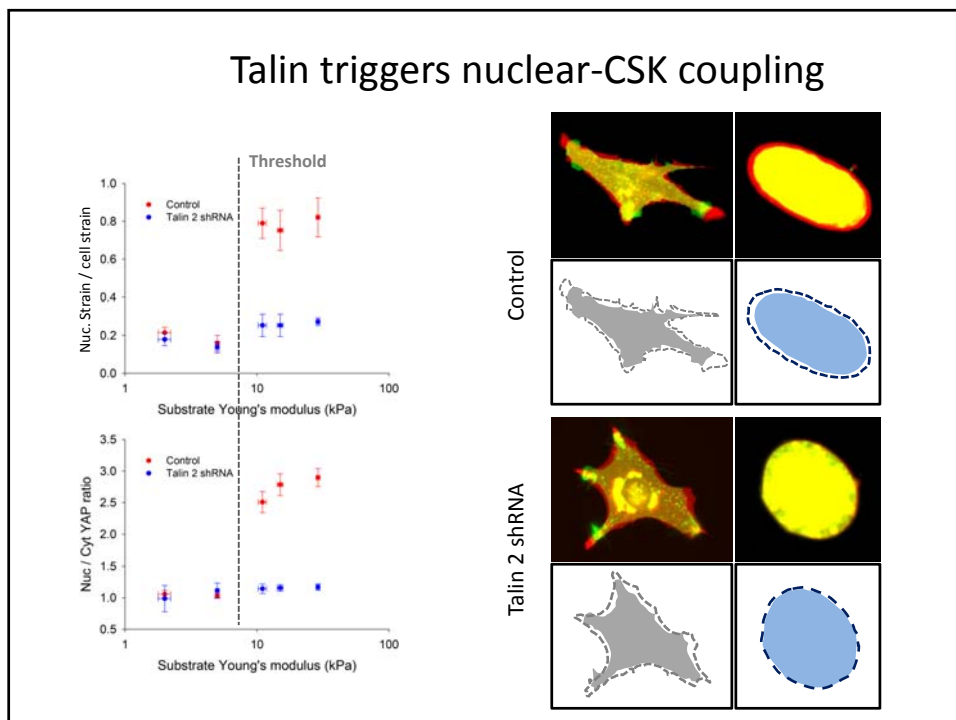
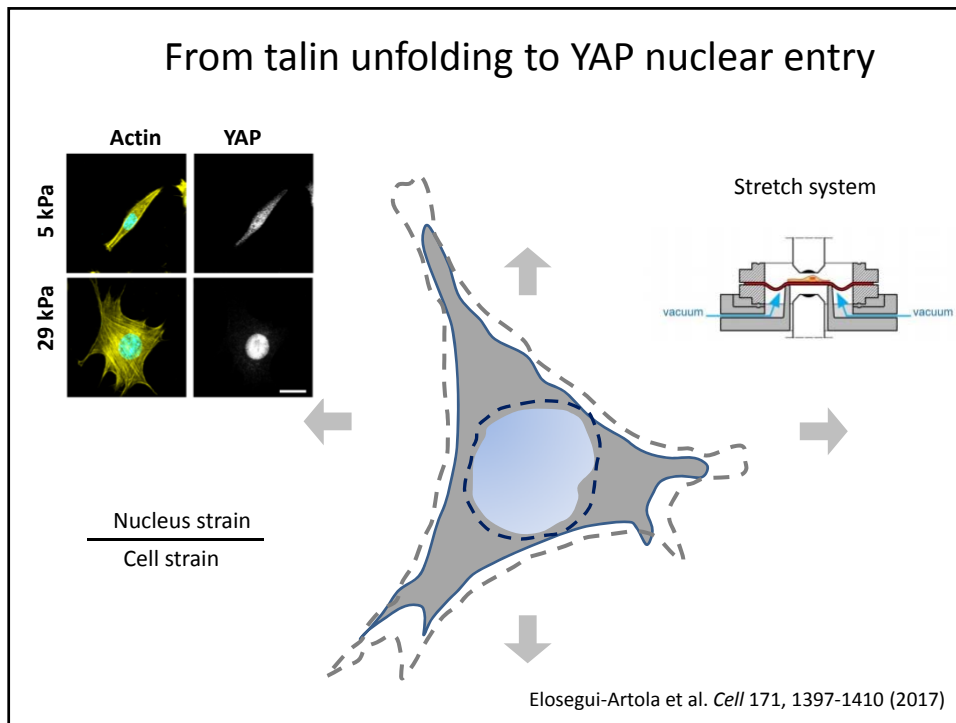


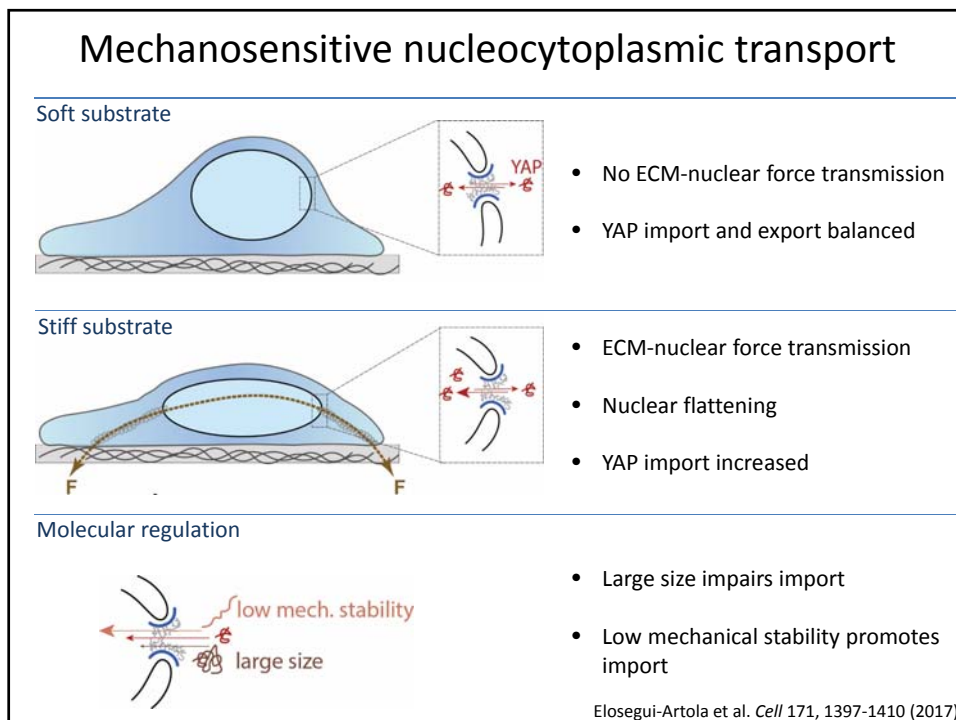
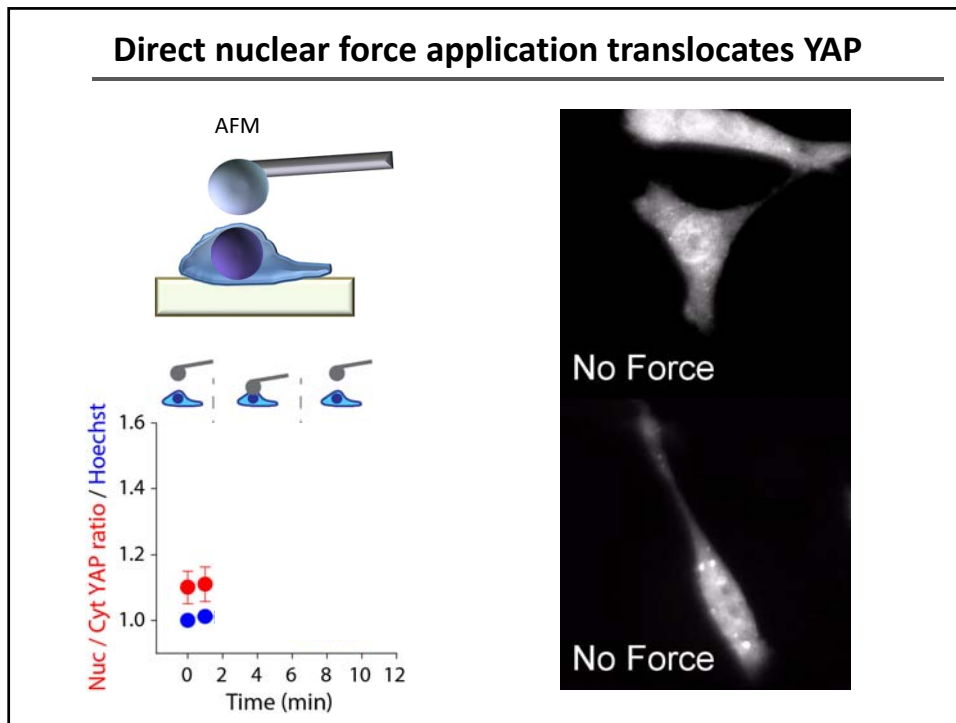
Loading rat(e)s in vivo



Loading rat(e)s in vivo







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