

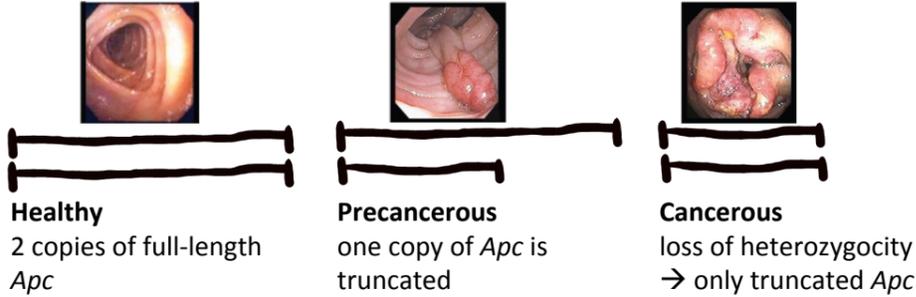


# A tumour associated APC fragment changes the response of MDCK cells to compression

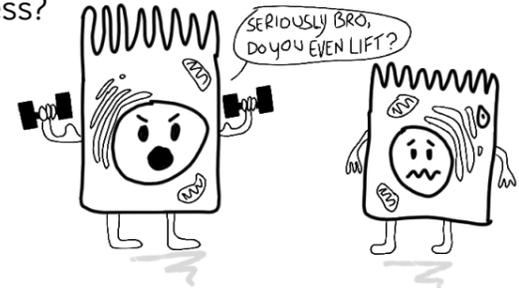
Valerie Bentivegna<sup>(1)</sup>, Sandy Cochran<sup>(2)</sup> and Inke Näthke<sup>(1)</sup>

## Introduction

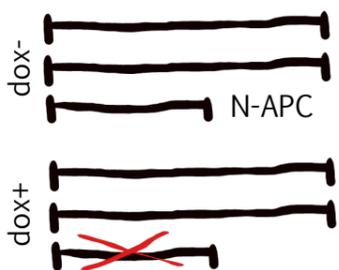
Truncation mutations in the tumour suppressor *Apc* (*adenomatous polyposis coli*) are found in >90% of colorectal cancers.



→ How do cells mimicking precancerous *Apc* status respond to mechanical stress?



## Methods

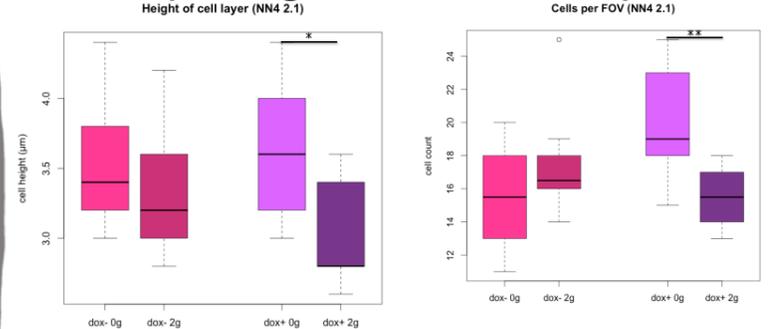


MDCK cells containing a doxycycline-repressible N-APC fragment



Confluent cells were subjected to mechanical compression for 30 minutes.

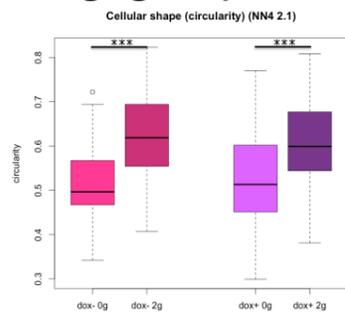
## N-APC expressing cells are less compressible



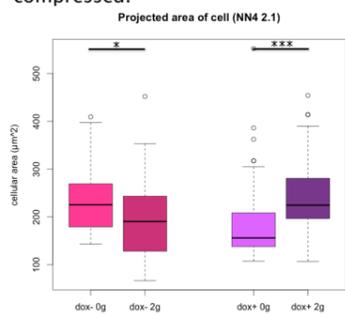
N-APC expressing cells compress less, which is consistent with cells being stiffer (~ previous AFM experiments).

Cells *not* expressing N-APC spread out when compressed, resulting in less cells for the same field of view.

## Cells respond to compression by changing shape



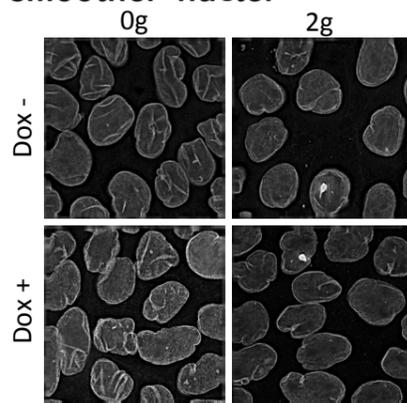
All cells become rounder when compressed.



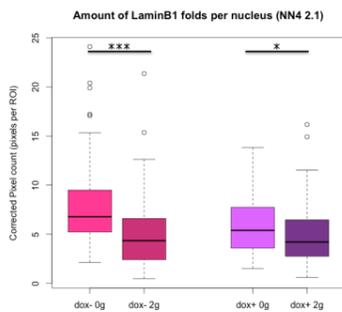
Control cells spread out when compressed, resulting in larger projected cell area.

TukeyHSD post hoc test \* p<0.05, \*\* p<0.01, \*\*\* p<0.001

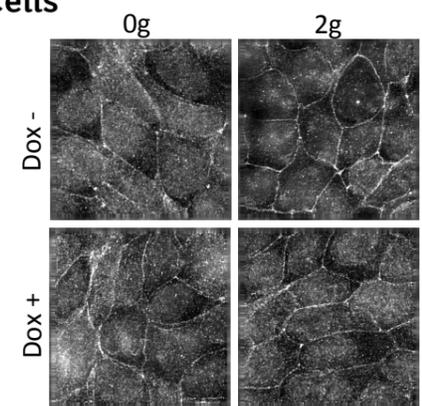
## Compression results in smoother nuclei



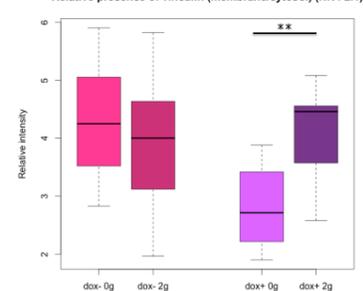
LaminB1 staining shows compressed nuclei are smoother.



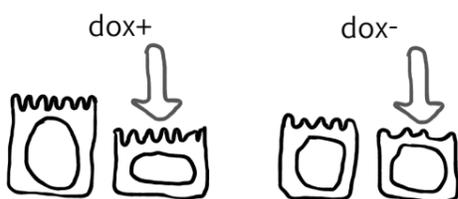
## Junctions are under more tension in N-APC expressing cells



Vinculin at the adherens junctions is an indication of junctions being under tension.



## Conclusions



Cells expressing N-APC respond differently to compression because:

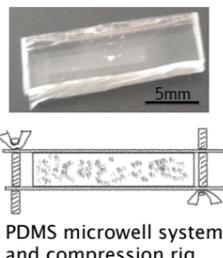
- the cytoplasm is stiffer?
- and/or
- the junctional cortex is under tension?

## Future directions

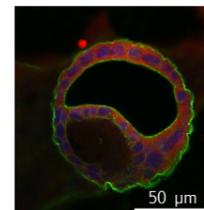
Compression with ultrasound



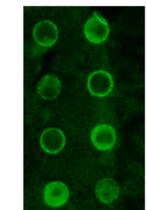
3D cell culture: MDCK cysts in PDMS wells



PDMS microwell system and compression rig.



MDCK cyst confined in a PDMS well.



MDCK cysts in PDMS wells before and during compression.

