

Investigating vimentin's role in cell migration and mechanics

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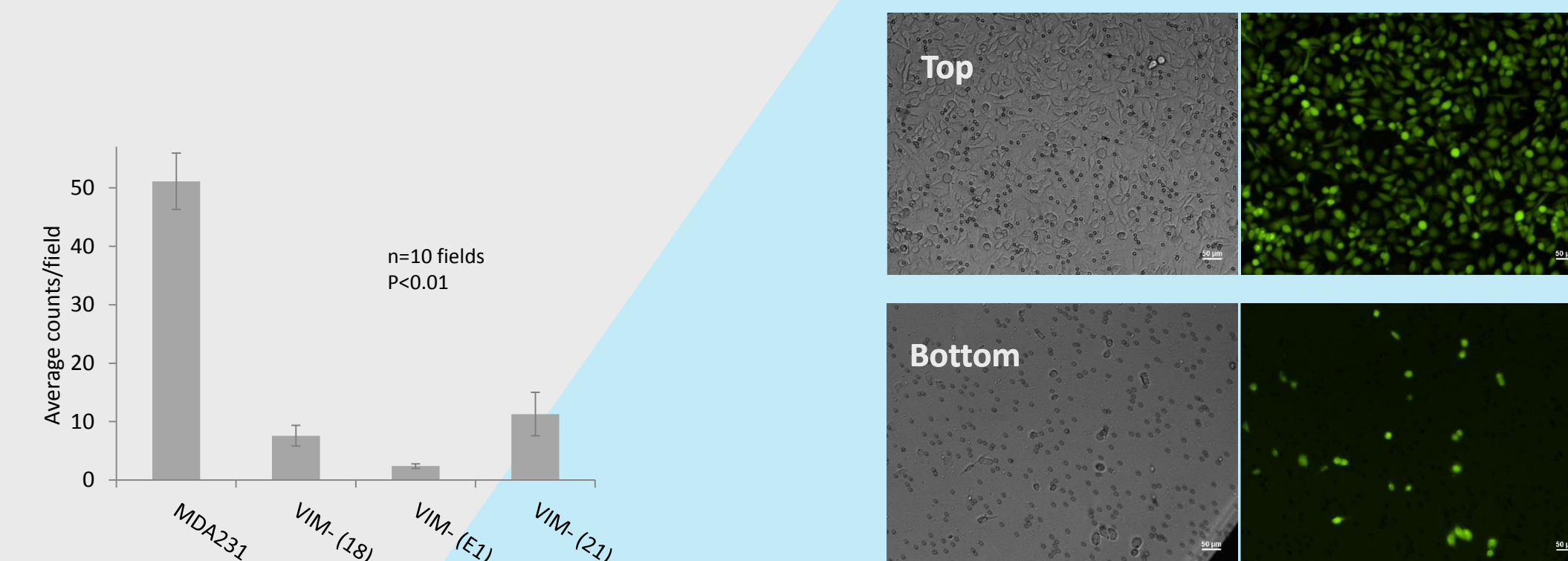
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Abstract

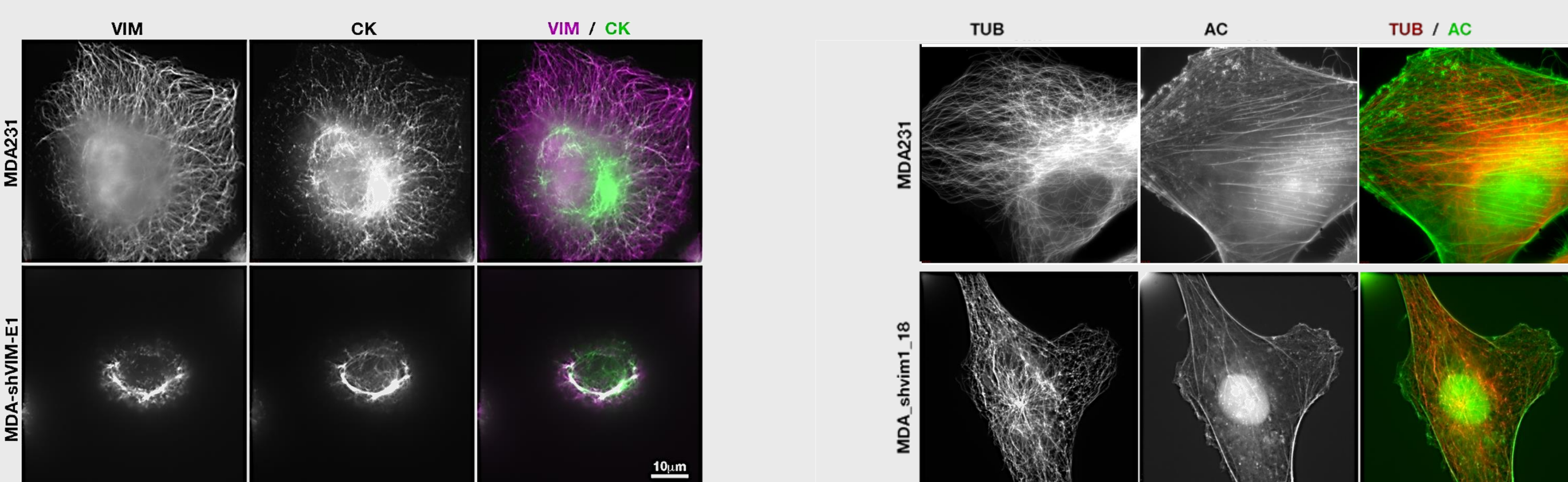
The cytoskeleton is deeply related to cell motility characteristics – cell migration and invasion capabilities. From the cytoskeleton components, a lot of research had been made about actin and microtubules. However, less is known about the role of the intermediate filaments. We study the role of the intermediate filament vimentin, which is a known EMT marker, on the mechanical and motility properties in a metastatic breast cancer cell line (MDA231). Native MDA231 express both vimentin and cytokeratins intermediate filaments as well as microtubules and actin. Using shRNA we have cloned MDA231 variants with no expression of vimentin and showed that it regulates the cell's motility, the intermediate filament structure and the elasticity of the cell.

Transwell migration



The WT cell line (containing vimentin) migrated at a significantly larger rate.

Cytoskeleton structure

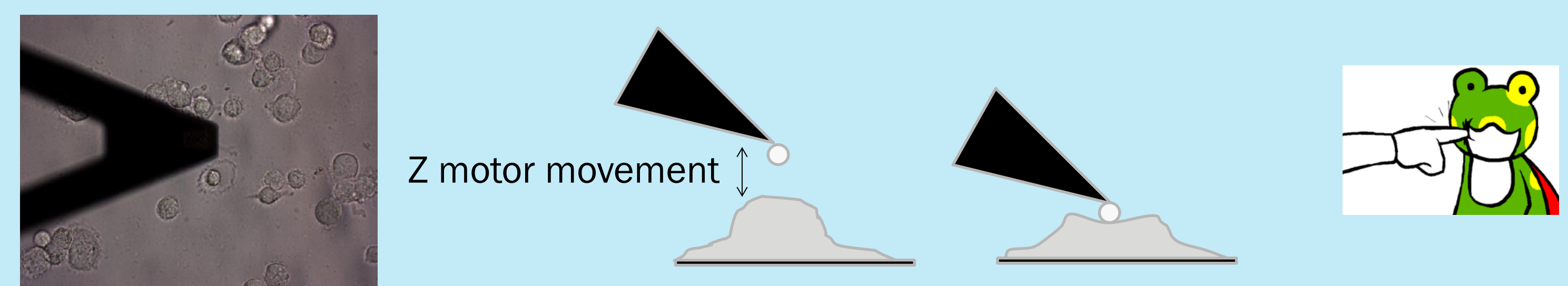


In MDA^{VIM-} cells the cytokeratins collapse to the nucleus. No dramatic changes are observed in the microtubules and actin networks.

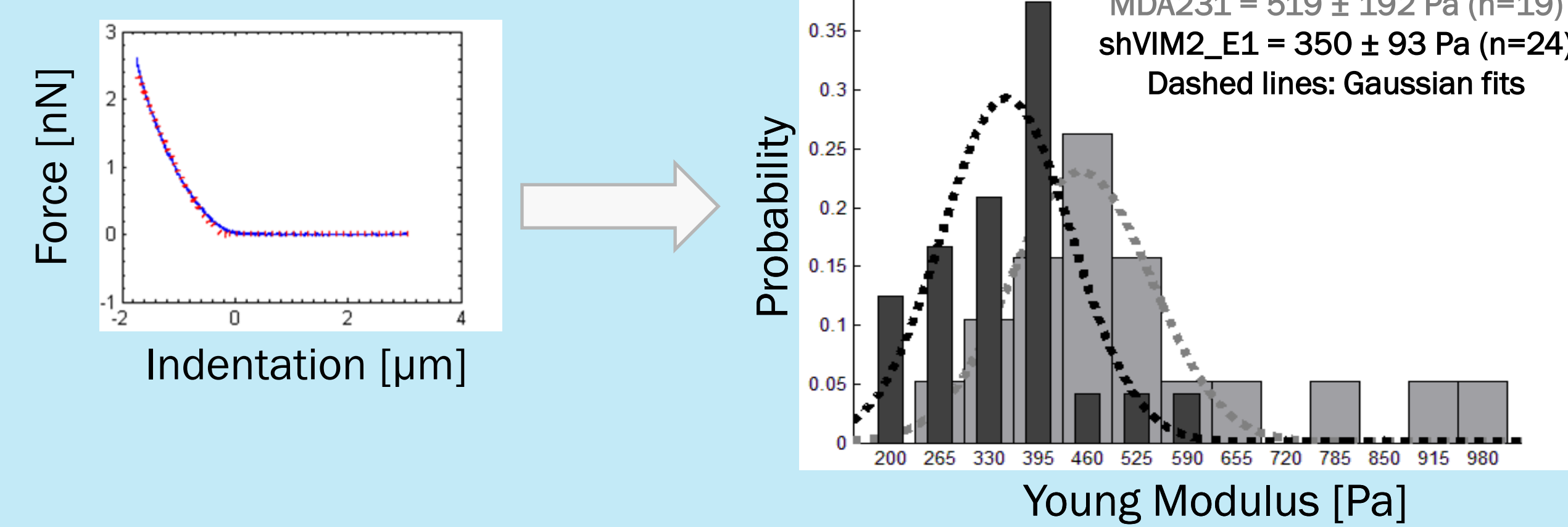
Atomic Force Microscope (AFM) force spectroscopy

The cell is roughly approximated as a homogenous material with a specific Young's modulus, which describes its resistance to deformation:

$$E = \frac{\sigma_{zz}}{\epsilon_{zz}} = \frac{\text{stress}}{\text{compression}}$$



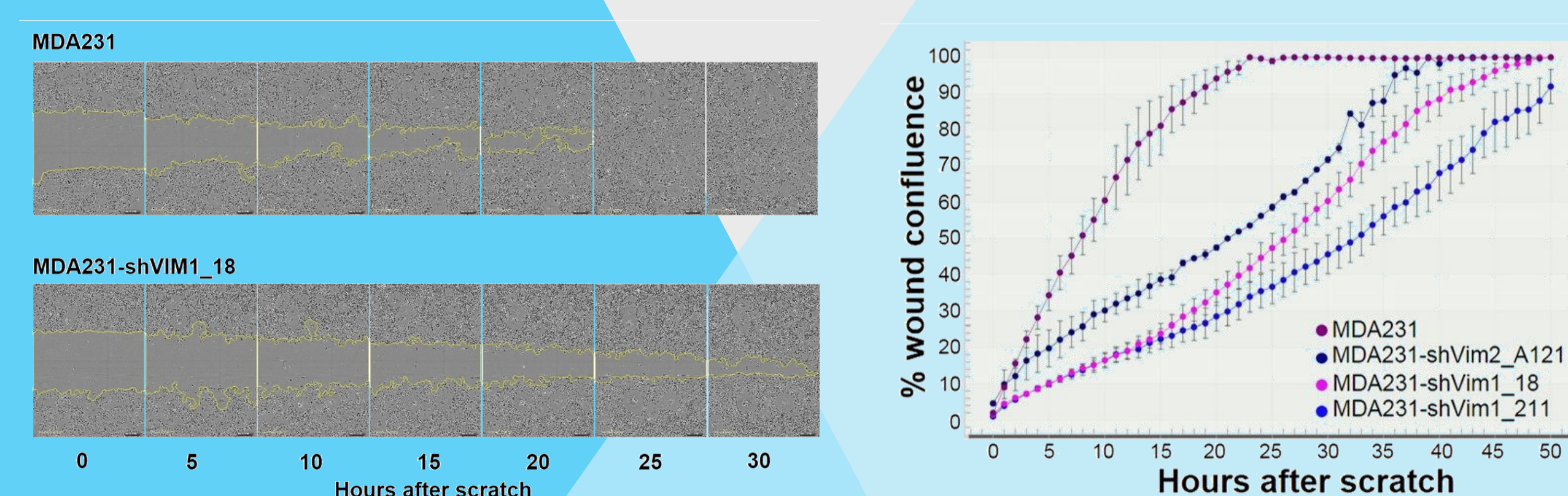
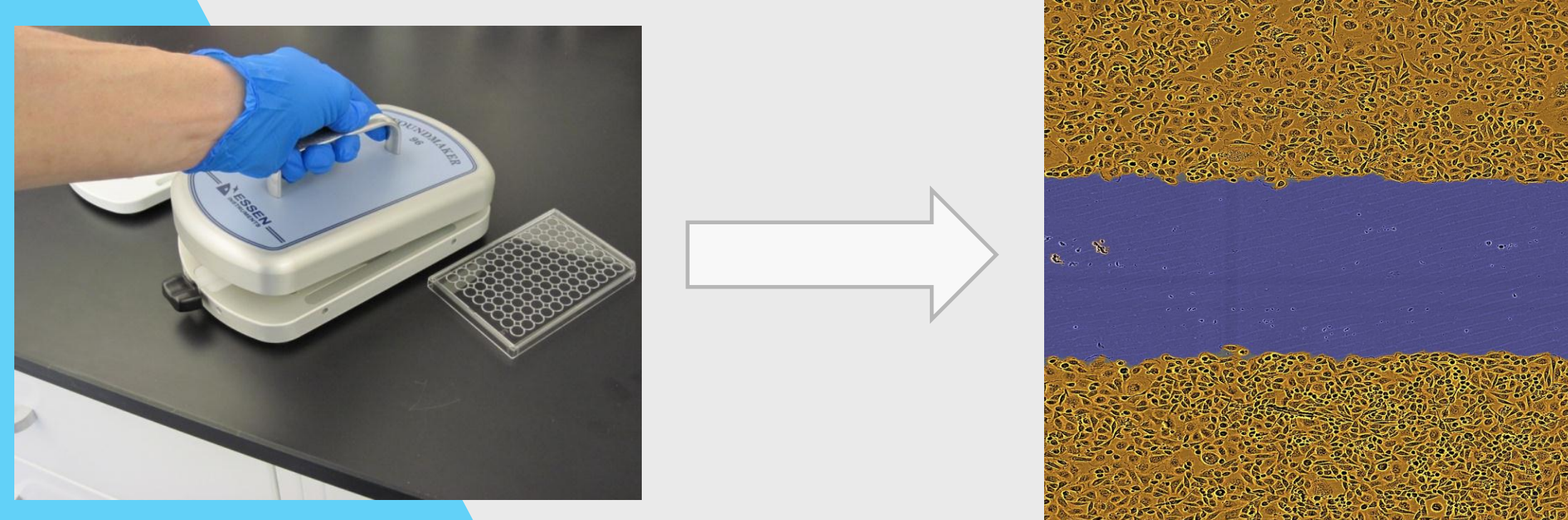
Young Modulus distribution



The MDA^{VIM-} clones became softer compared to the vimentin expressing WT.

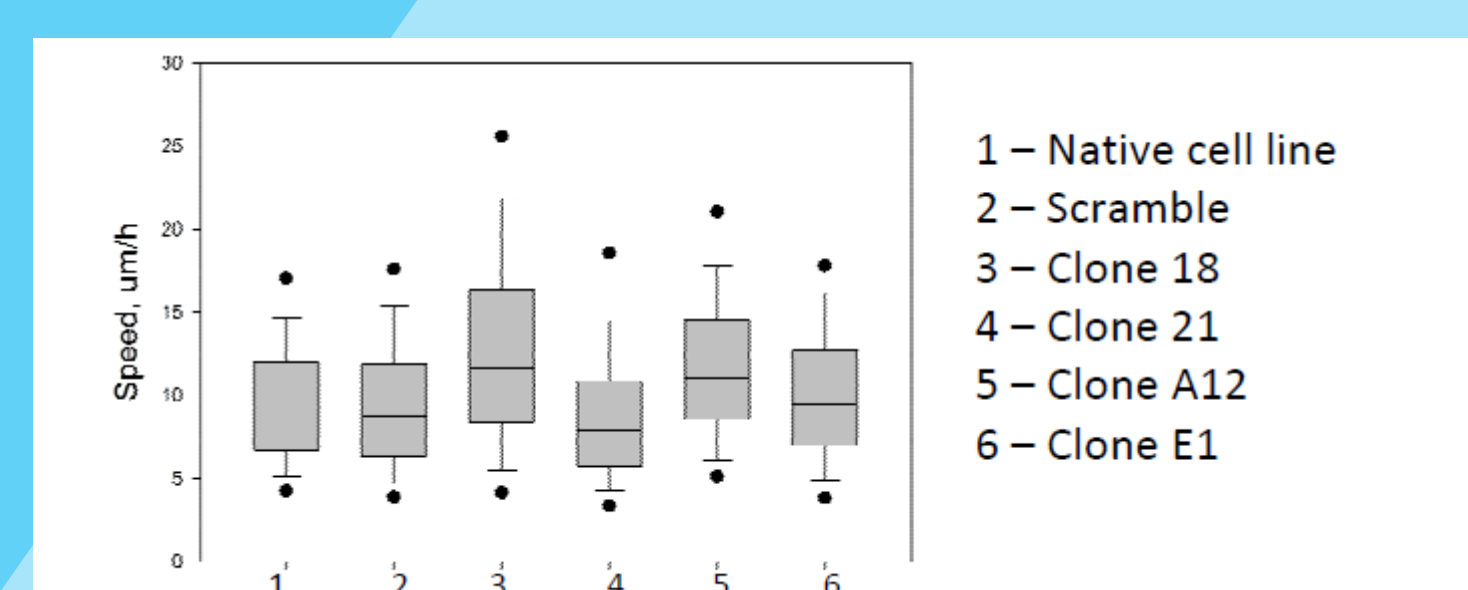
Cell motility – migration assays

Scratch assay (wound healing)



The MDA^{VIM-} clones show a significantly reduced migration rate.

Single cell velocity



Single cell velocity measurements show no difference between WT and MDA^{VIM-} variants – Difference only arises in the group behavior.

Conclusions and discussion

Softer cell ≠ higher motility, but softer cells → lower motility in colony!

Why? Softer cells produce a softer environment that the migrating cells sense.