The effect of matrix stiffness on vascular smooth muscle cell traction force

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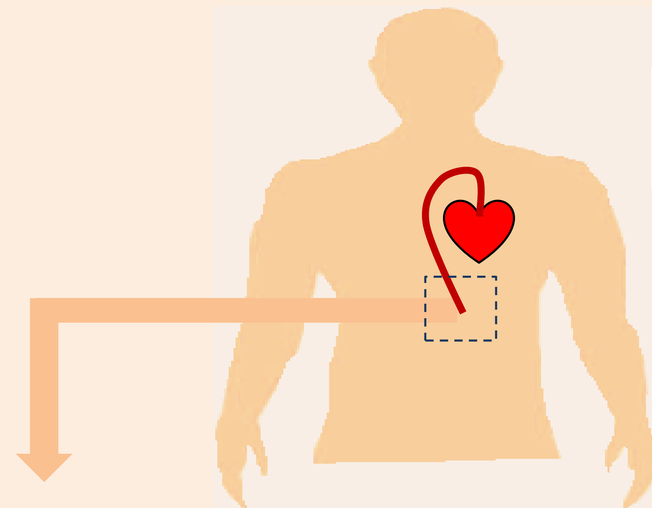
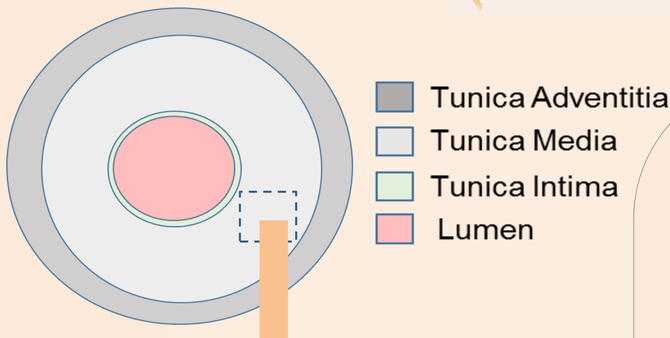
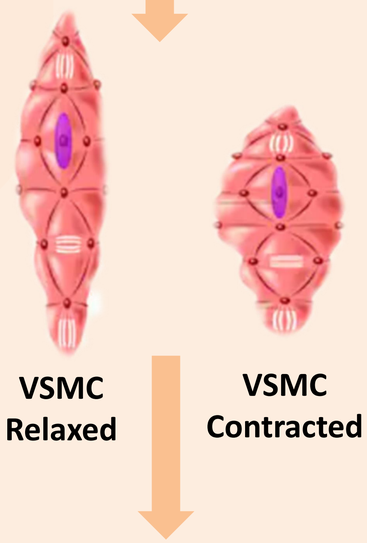
Background

- Decreased aortic compliance is associated with ageing and vascular disease.
- Changes in aortic compliance are driven by altered ECM composition.
- Vascular smooth muscle cells (VSMCs) are the predominant cell type in the vessel wall and VSMC contraction regulates vascular tone.
- Whether changes in ECM rigidity alter VSMC function remains poorly defined







- Cardiovascular disease (CVD) is the second highest cause of mortality within the UK

- Common physiological risk factors are ageing, hypertension, obesity and a rise in cholesterol

Introduction

- In this study, we investigate how matrix rigidity affects VSMC contractile response.
- Quiescent VSMCs were stimulated with AngII for 30 minutes to initiate contraction.
- Traction force microscopy (TFM) revealed that VSMCs generate increased traction force (TF) magnitudes on rigid hydrogels.
- This was abolished by stretch activated ion channel antagonist GsMTx4 or by depleting Ca2+ from the medium.
- On pliable hydrogels (12kPa), VSMCs contract, cell area is reduced but cell volume remains unchanged.
- On rigid hydrogels (72kPa), VSMCs fail to contract and cell area/volume is enhanced

Methods

- Our study fabricated polyacrylamide hydrogels of 12kPa (healthy) and 72kPa (diseased) stiffness
- Quiescent VSMCs were plated on these gels by crosslinking with collagen 1.
- Traction force microscopy (TFM) was performed on VSMCs plated on both 12kPa and 72kPa hydrogels.
- Immunofluorescence labelling was also performed by utilising a combination of primary and species specific conjugated AlexaFluor-secondary antibodies.
- Z stacks were captured using a Zeiss laser scanning confocal microscope.
- Data analysis was performed on Image J and statistical analysis was done on GraphPad Prism.

Results

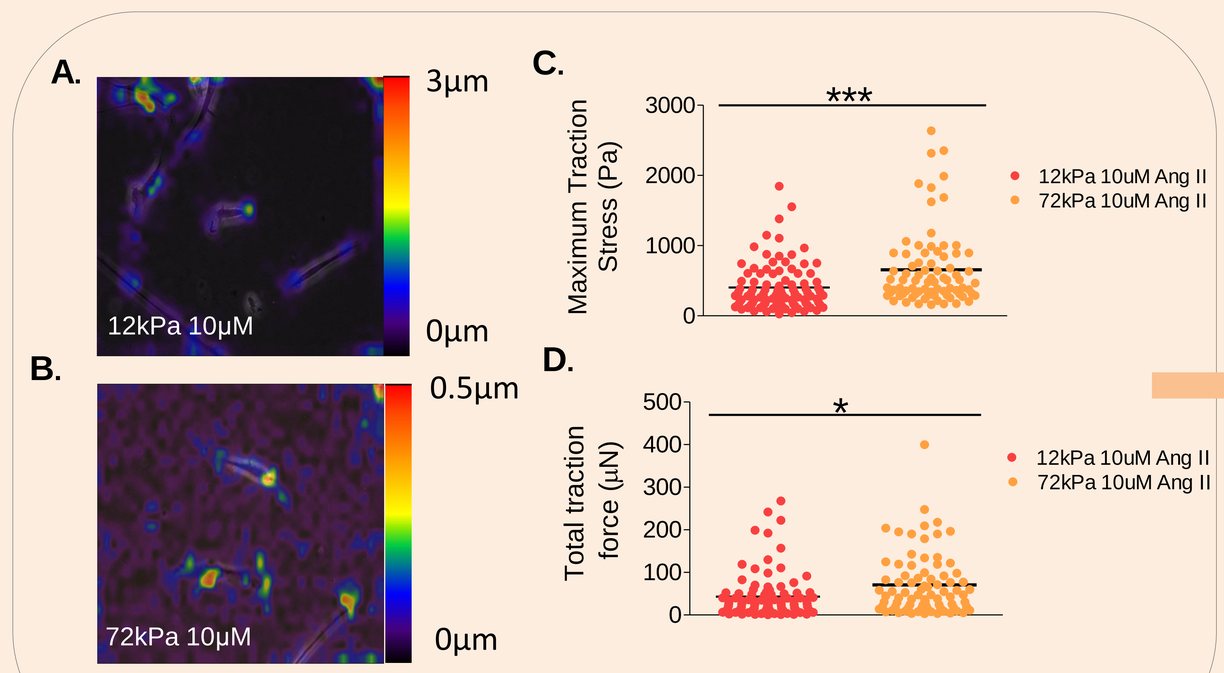


Figure 1. VSMC traction force increases in response to matrix rigidity

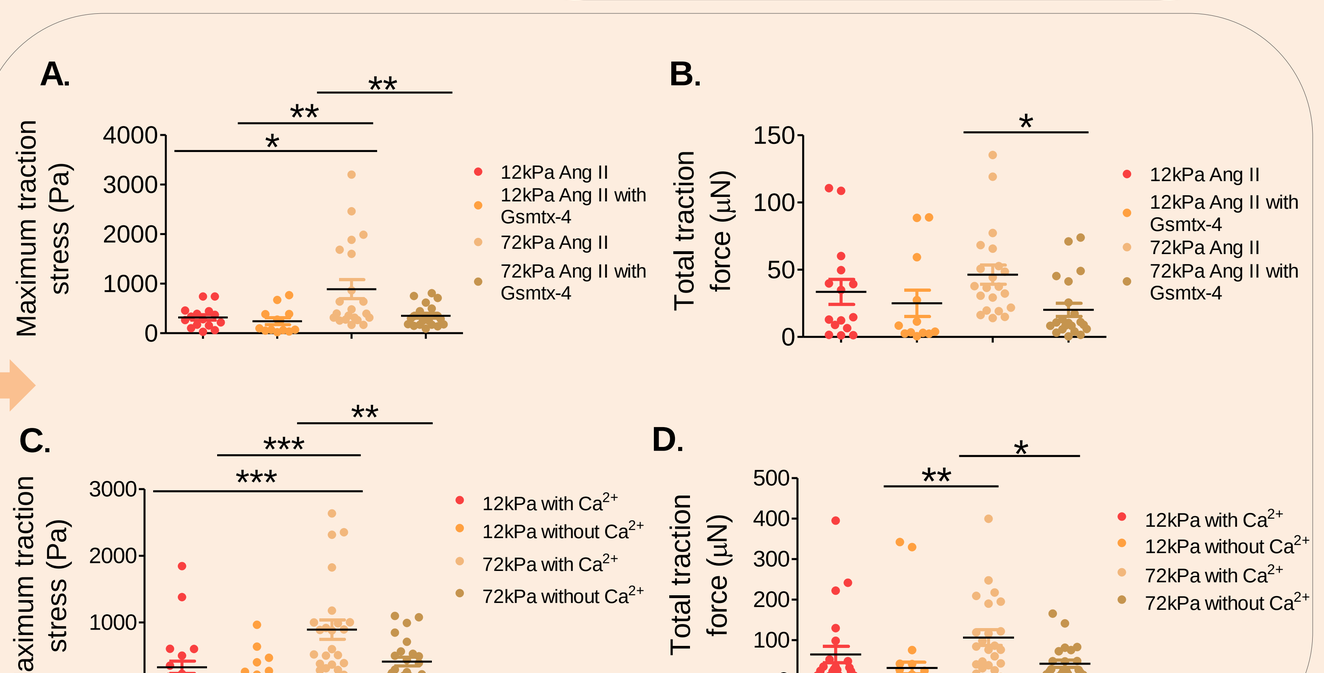


Figure 2. Matrix rigidity influences traction force via mechanical gated channels and Ca^{2+}

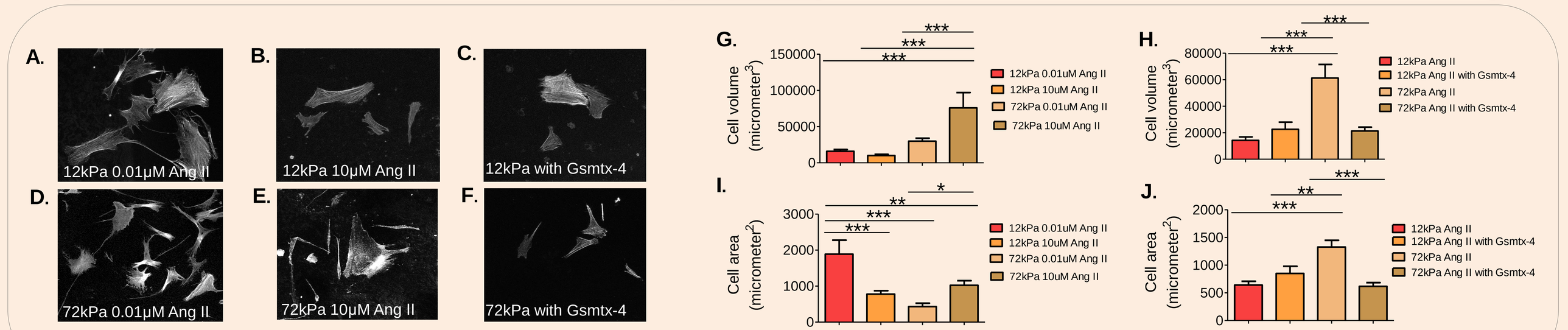


Figure 3. Matrix stiffness causes an increase in cell area/cell volume and this is abolished via mechanical gated channel antagonists

Future directions

- To identify which mechanical gated channels play a role in VSMC traction force and VSMC area/volume.
- To investigate whether ECM stiffness may alter VSMC function and serve as a migrational cue.

References

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- Ahmed, S., Warren D. (2018). Vascular smooth muscle cell contractile function and mechanotransduction. *Vessel Plus*.