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Biomimetic Modeling of Preeclamptic Conditions

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Introduction

Background:
- Preeclampsia is a condition often diagnosed around 20 weeks of pregnancy
- Preeclampsia results in 18% of US maternal deaths and 15% of premature US births
- Results in high blood pressure, headaches, nausea, and breathing difficulties

Hypothesis:
Placental stiffness shares a direct correlation with the adverse progression of preeclampsia.

Aims/Objectives:
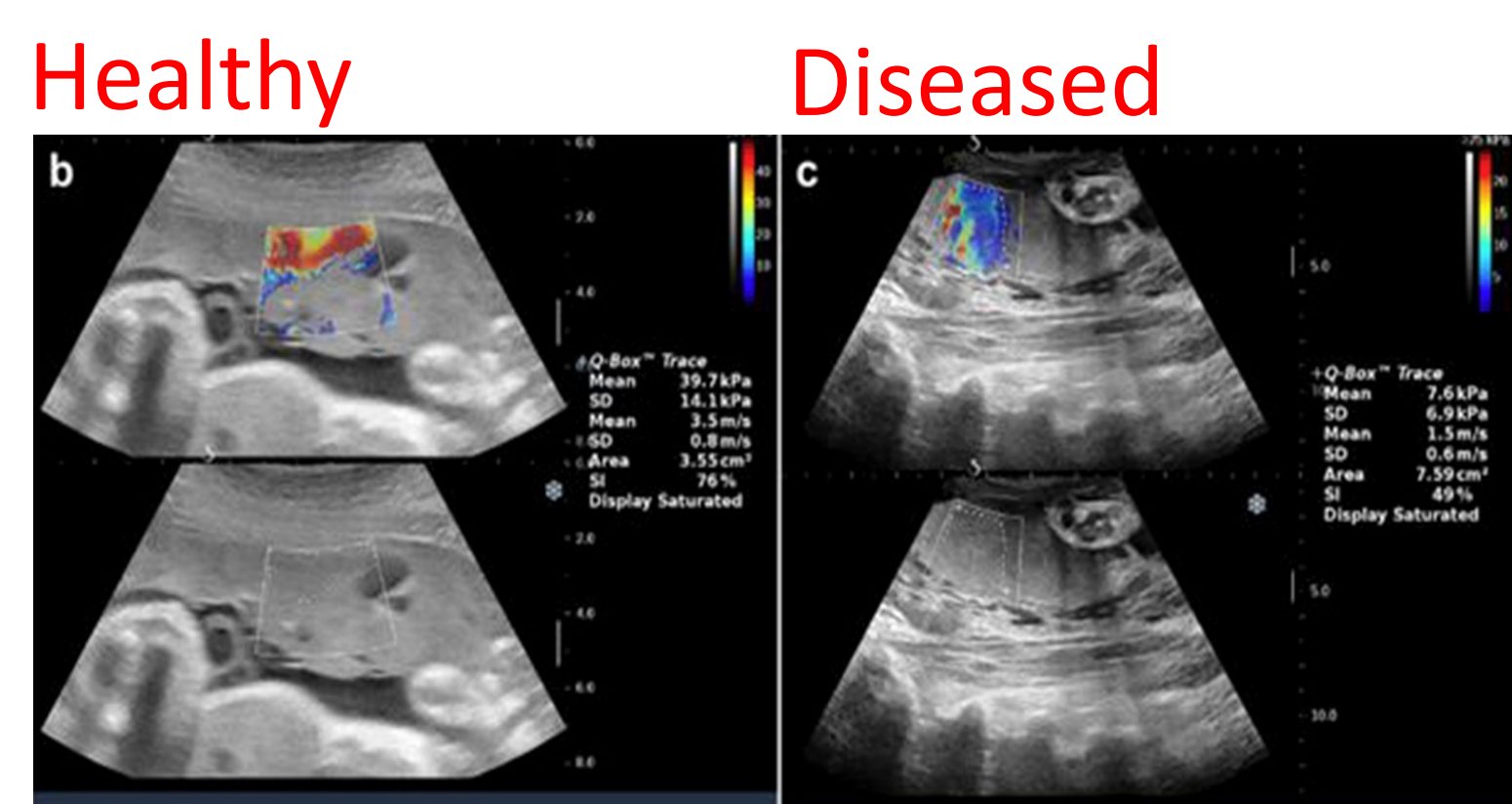- Characterize the relationship between stiffness and alterations to placental cell morphology, metabolism, and function

Healthy   Diseased

Figure 1. Clinical data shows a relationship between increasing stiffness and a diseased state
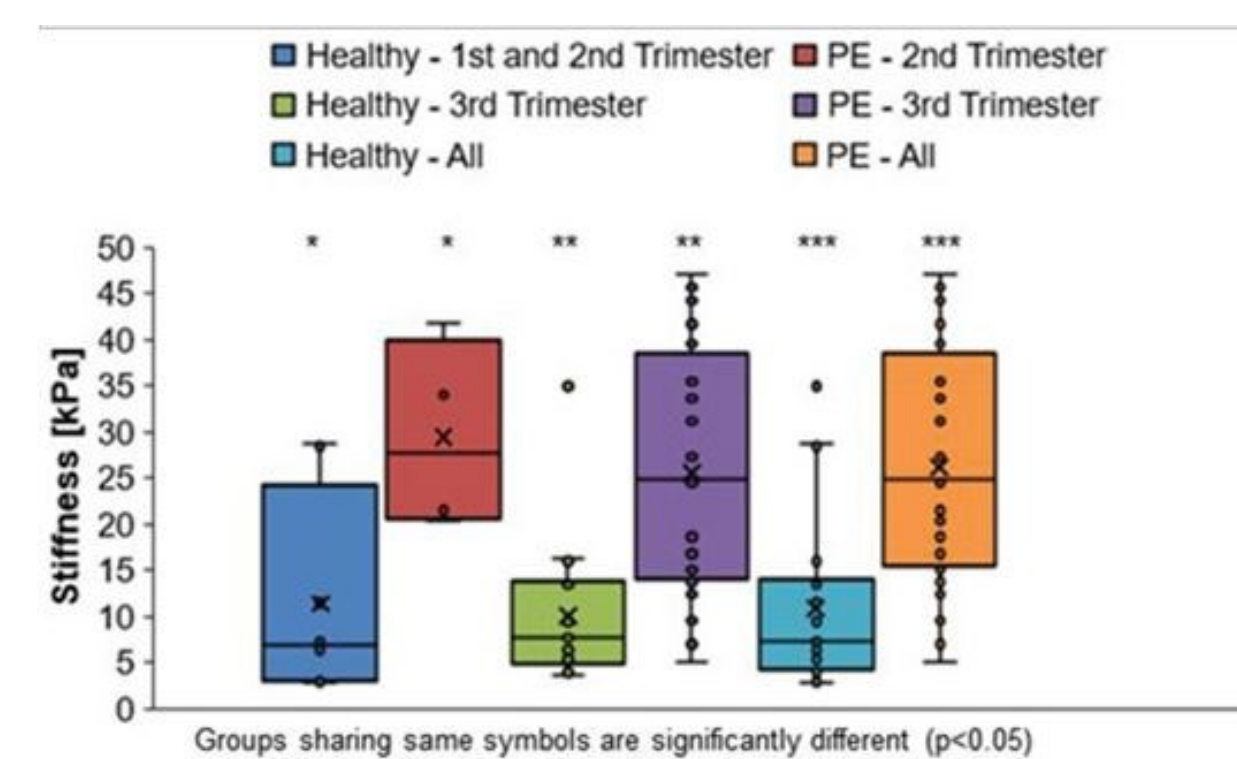

Figure 2. Quantification of stiffness data can be applied to the creation of *in vitro* models

Experimental Design

To model *in vivo* stiffness placenta cells (HTR8) are cultured on "**BEASTS** (*Bio-Engineered Adhesive Siloxane substrate with Tunable Stiffness*)" at 3 different stiffnesses: 8kPA, 25kPa, and 55kPa

Cell Culture:

HTR8 Cells

8kPa Healthy   25kPa Preeclampsia   55kPa Severe Preeclampsia
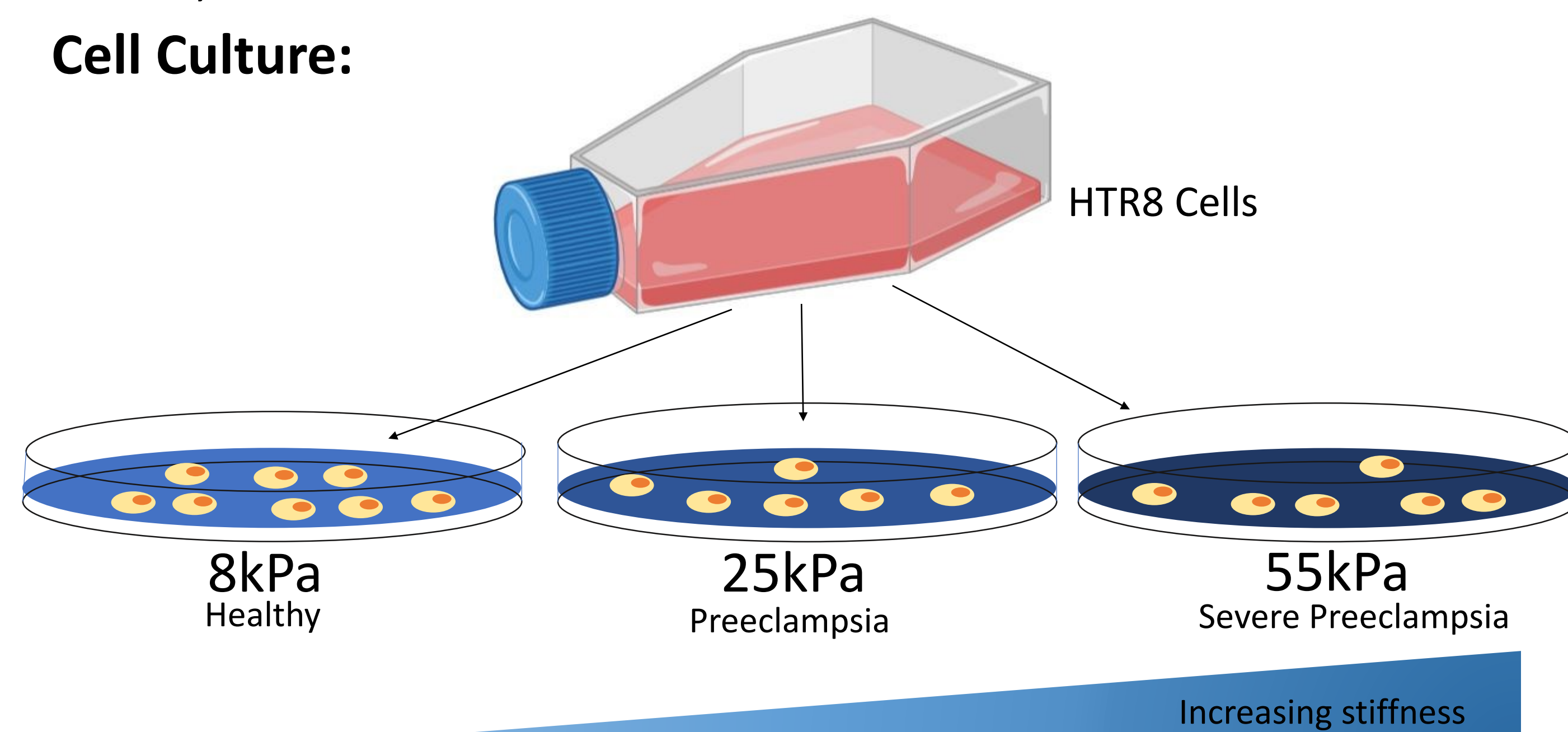
Increasing stiffness

Figure 3. Cells are cultured in T-75 flasks and 8-10mL HTR8 media. The media is changed daily until 90% confluence is reached, then cells are seeded onto stiffness plates. The remaining cells are split into new flasks or frozen for later use.

BEASTS Preparation

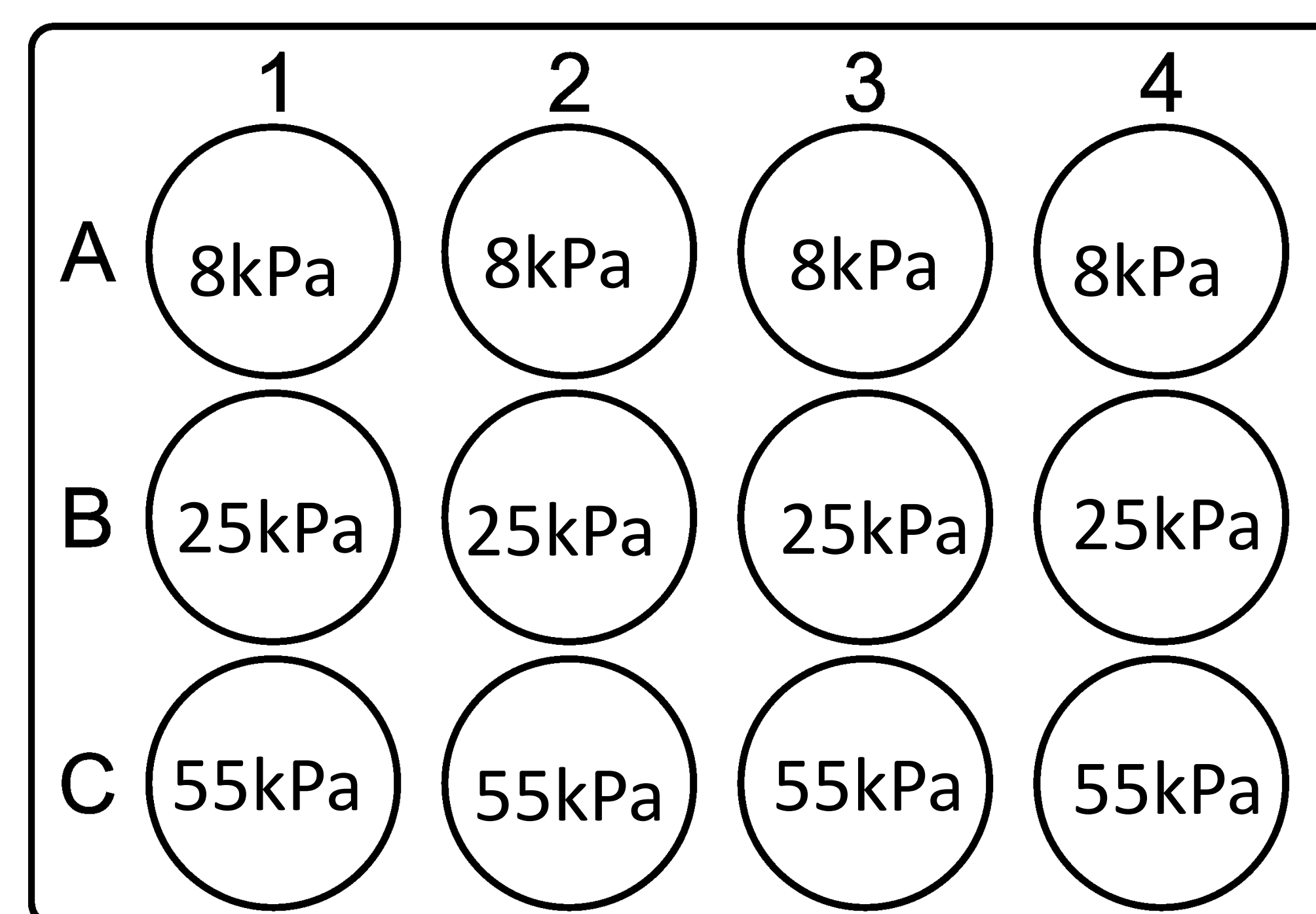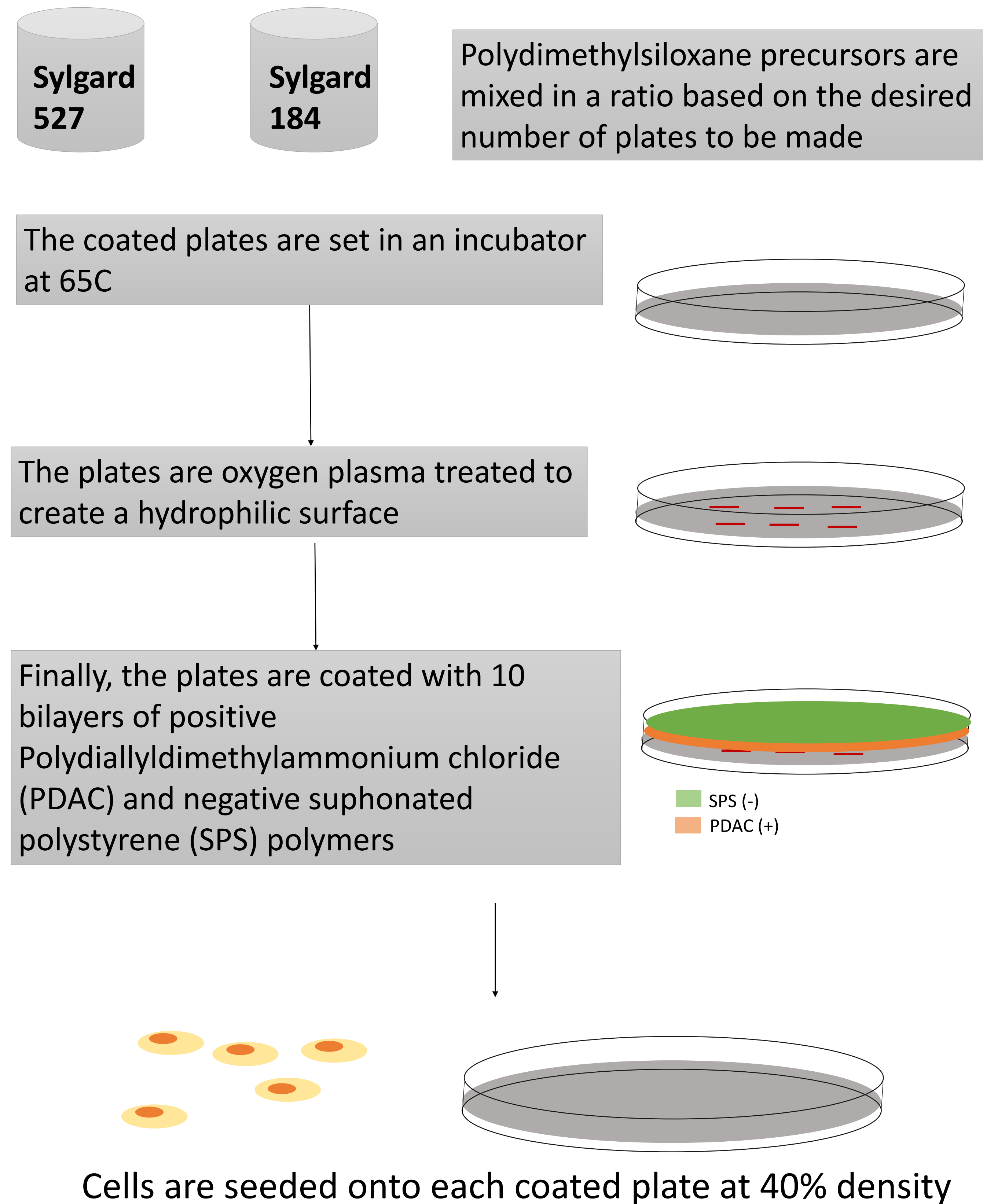The plates are coated in a prepared substrate that constitutes the BEASTS platform

Sylgard 527   Sylgard 184   Polydimethylsiloxane precursors are mixed in a ratio based on the desired number of plates to be made

The coated plates are set in an incubator at 65C

The plates are oxygen plasma treated to create a hydrophilic surface

Finally, the plates are coated with 10 bilayers of positive Polydiallyldimethylammonium chloride (PDAC) and negative suphonated polystyrene (SPS) polymers

SPS (-)   PDAC (+)

Cells are seeded onto each coated plate at 40% density

	1	2	3	4
A	8kPa	8kPa	8kPa	8kPa
B	25kPa	25kPa	25kPa	25kPa
C	55kPa	55kPa	55kPa	55kPa

Figure 4. 12-well plates are prepared in the shown stiffness orientation

Results

Morphology: Once the plates have been seeded they are monitored for several days, when they reach adequate confluence they are imaged for changes in morphology. The images show cell elongation with increasing stiffness.
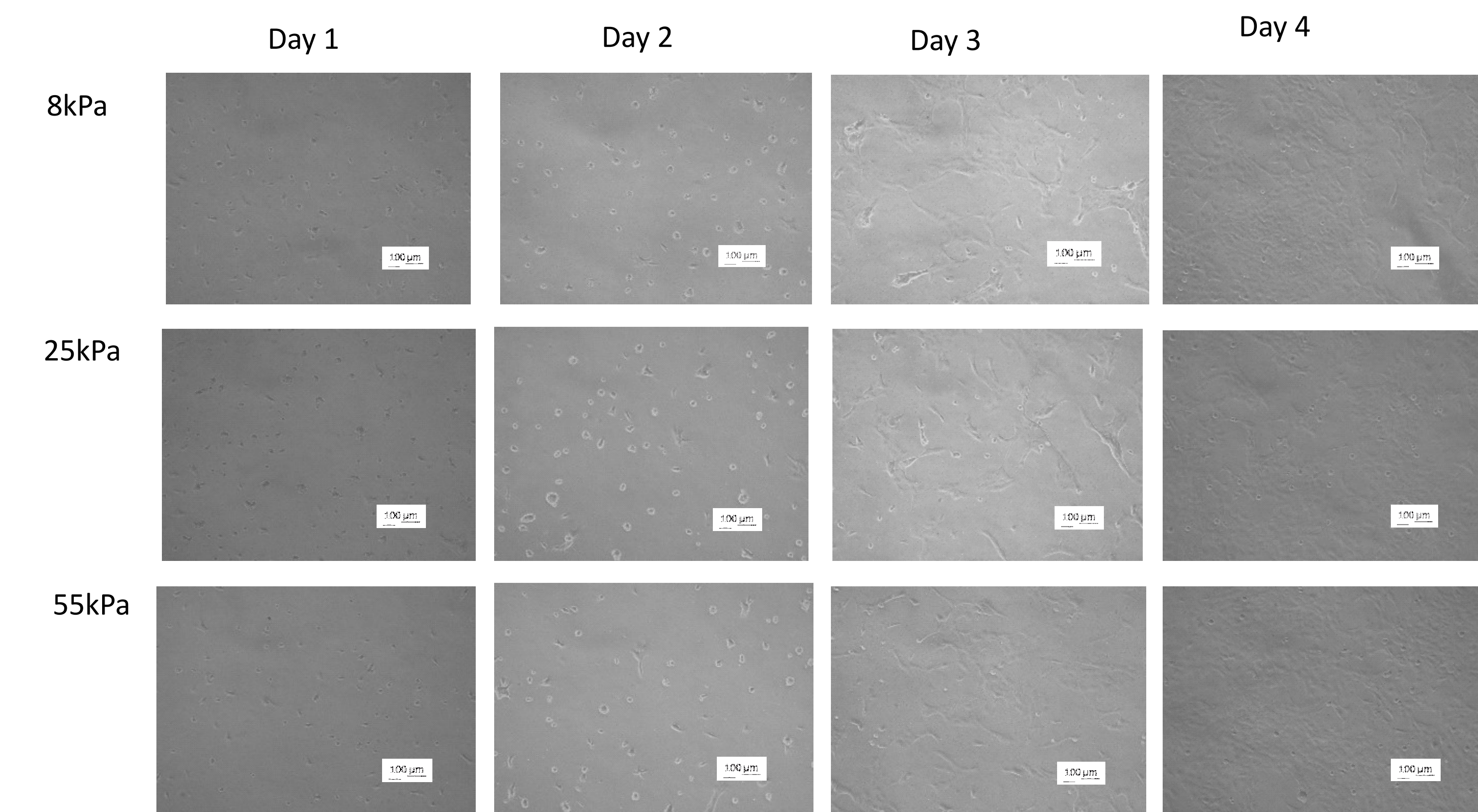

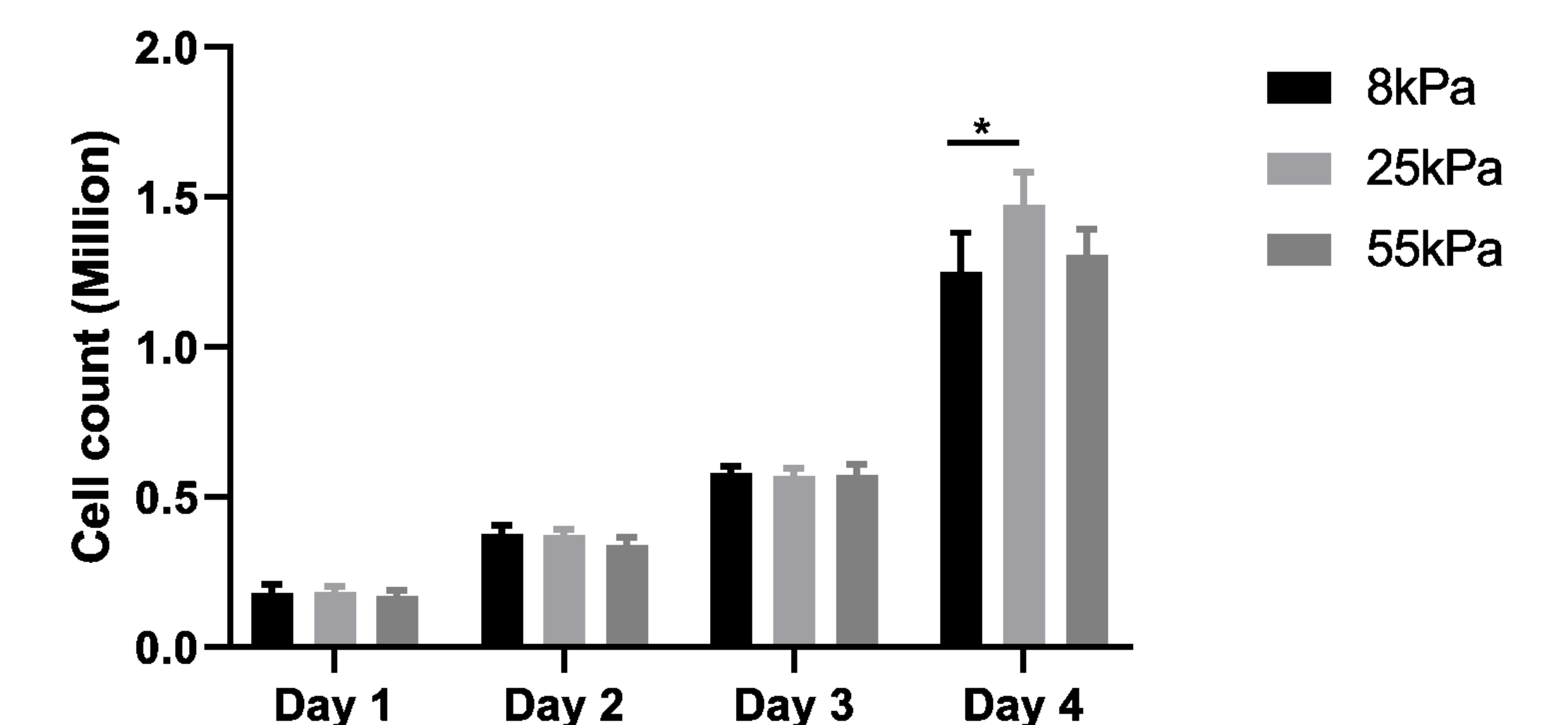**Figure 5.** Morphological analysis of placenta cells on increasing stiffnesses

Figure 6. Cell count of plates over the course of 4 days at different stiffnesses. Counted using a hemocytometer   n=4

Future Work

- Preform *in vitro* migration assays on various substrate stiffnesses
- Conduct and analyze experiments to analyze metabolic activity and gene expression at varying stiffnesses
- Eventually work towards implementing the research as a targeted method of exploring treatment options

References

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https://www.mayoclinic.org/diseases conditions/preeclampsia/symptoms-causes/syc-20355745

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