Mechanical Strain Effects MDA-MB-231 Breast Cancer Cell Protein Expression

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Introduction

Biomechanical forces on cancer cells can cause morphological and chemical changes. One such change is epithelial-mesenchymal transition (EMT) of cancer cells in which localized epithelial cells transform into mesenchymal, invasive cells. The reverse process of mesenchymal-epithelial transition (MET) can also occur, in which the migratory, invasive mesenchymal cells regain their epithelial features such as polarity and cell-cell junctions.

The protein expressions of markers of the epithelial and mesenchymal states will be used to observe whether mechanical strain will affect protein expressions and EMT in breast cancer cells.

Materials and Methods

MDA-MB-231 breast cancer cells were mechanically strained by stretching silicone membrane bottom 6-well plates with Teflon pistons driven by a linear motor.

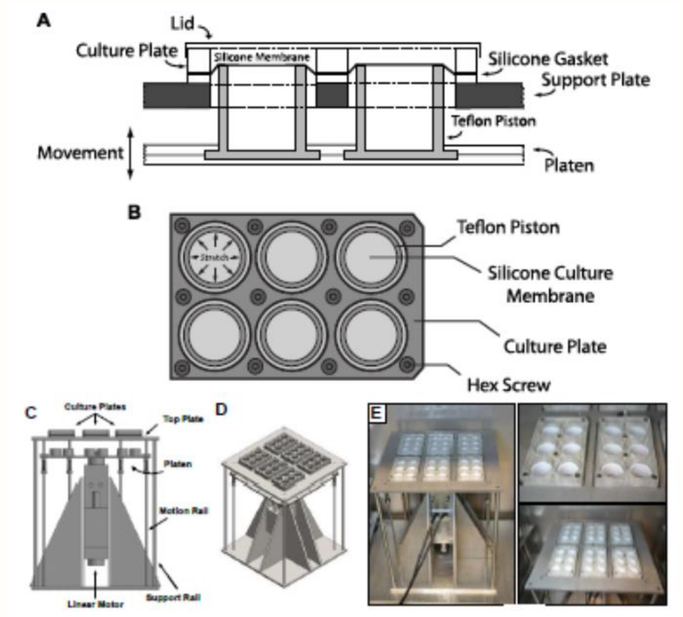
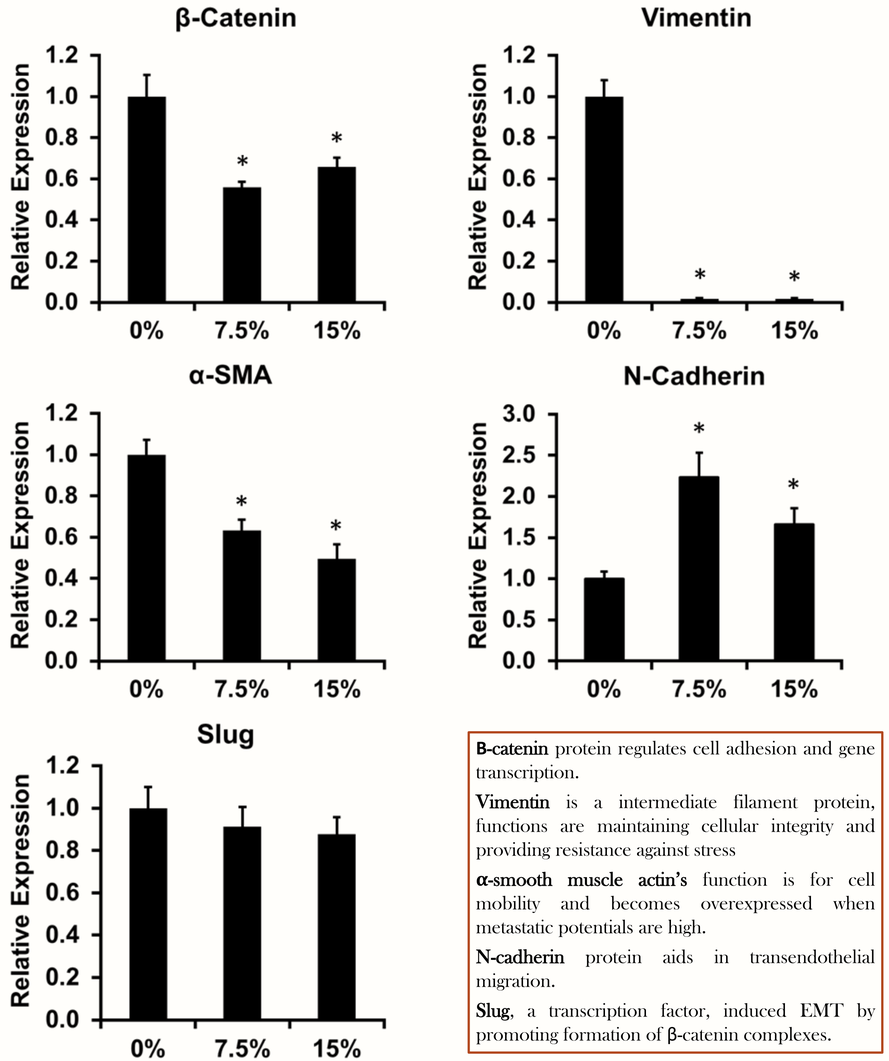


Figure 1. Depiction of the 6-well stretch plate that was used to apply cyclic mechanical strain to the breast cancer cells.

Materials and Methods

Experiments were conducted with one control (0% stretched) and two experimental (7.5% and 15% strain) groups. Mechanical strain was applied for 24 hours. Then breast cancer cells were lysed with a lysis buffer. Relative protein expression was examined with western blot. The relative expression was determined by the measuring the light intensity using ImageJ.

Results



B-catenin protein regulates cell adhesion and gene transcription.

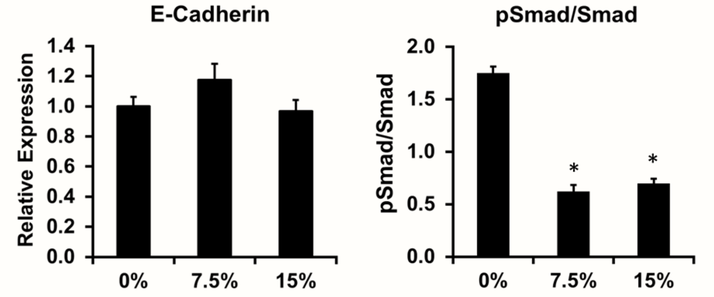
Vimentin is a intermediate filament protein, functions are maintaining cellular integrity and providing resistance against stress

α-smooth muscle actin's function is for cell mobility and becomes overexpressed when metastatic potentials are high.

N-cadherin protein aids in transendothelial migration.

Slug, a transcription factor, induced EMT by promoting formation of β-catenin complexes.

Results



E-cadherin protein aids in cellular adhesion to tissues.

SMAD is a intracellular protein that transduced signal to activate downstream gene transcriptions in the nucleus.

Conclusions

Increasing mechanical strain decreased the expressions of α-SMA, slug, and drastically decreased expression of vimentin. SMAD, β-catenin, and E-cadherin, exhibited a differential response to mechanical strain. There was a decrease in expression for SMAD and β-catenin at 7.5% strain compared to 0% and 15% strain. However, there was an unexpected increase in expression for N-cadherin at 7.5% strain and a mild, negligible increase for E-cadherin.

These results showed that the increase in mechanical strain decreases protein expression indicative of a mesenchymal cells phenotype. Additionally, it also increases E-cadherin expression which is an epithelial cell marker.

Future Work

Additional sources of mechanical force may be tested using a high-throughput shear stress device to simulate *in vivo* shear conditions. We will assess expression of proteins of interest and metastatic potential in response to fluid shear stress.

References

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R. Kalluri, R. Weinberg. Journal of Clinical Investigation. 2010.