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Introduction

Because of their effectiveness in regenerating large muscle defects *in vivo,* we investigate the use of satellite cells derived from muscle biopsies as a cell source for muscle tissue engineering. Despite their *in vivo* potency, however, their proliferative and myogenic capacity *in vitro* has been disappointing.[1]

We therefore concentrate on optimizing culture conditions by mimicking the natural niche environment of these cells. The elasticity of the environment is an important aspect of this niche and has been shown to influence differentiation pathways of stem cells[2]. We hope to improve the *in vitro* capacities of satellite cells by varying substrate elasticity. The potential for myogenesis is evaluated from morphological and functional parameters.

The model system used in these experiments provides for high-throughput and well-controlled measurements and can ultimately be expanded to 3D tissue culture conditions using biomaterials and/or different cell types.

Material and methods

Tibialis Anterior (TA) muscles from Swiss White mice are digested in collagenase and triturated to release single fibres from which satellite cells are liberated with a 19G needle. The satellite cells are plated on Matrigel™-coated polyacrylamide (PA) gels (Figure 1) with elastic moduli (E) ranging from 1.4 to 72 kPa on top of 13 mm ø coverslips and cultured in plating medium (DMEM advanced, 10% HS, 20% FBS, 0.5% CEE, 1% pen/strep, 1% L-glut.).

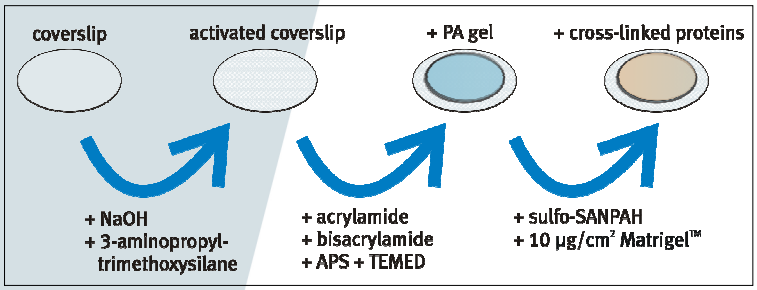

Figure 1: Creation of coated PA gels on top of coverslips

Results

- Satellite cells proliferate on all substrates
- Fusion first takes place on 17 kPa, which mimics physiological elasticity of striated muscle.
- Subsequently, satellite cells fuse on 8.1 and 35 kPa
- Eventually fusion takes place on all E-moduli

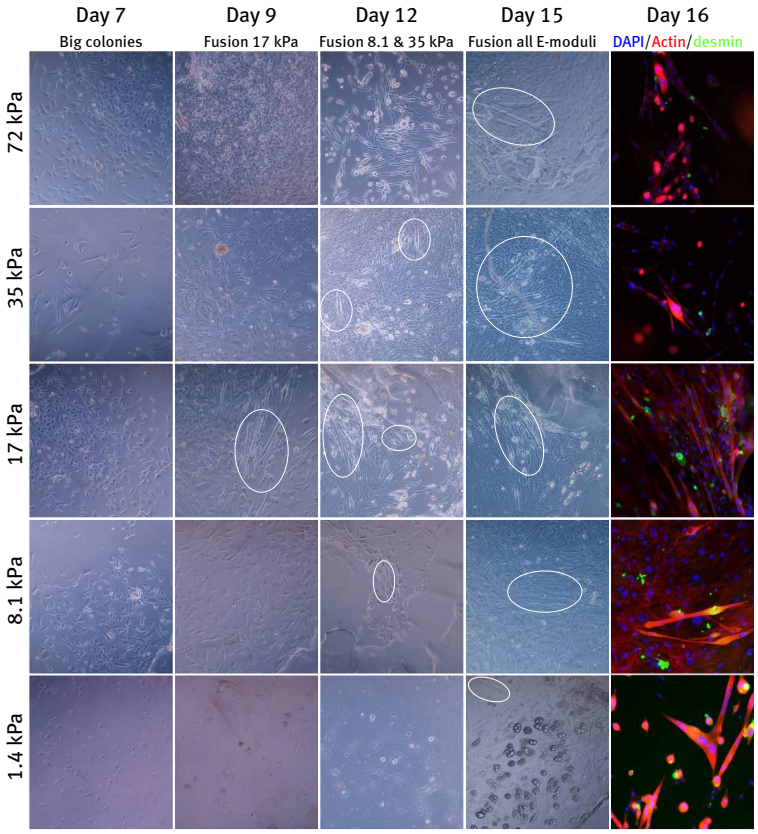

Figure 2: Proliferation and differentiation of satellite cells on substrates with varying elasticity

Conclusions

Timing of differentiation of satellite cells seems to be dependent on the elasticity of their environment. Fusion first takes place on physiological elasticity of striated muscle, subsequently at the elastic moduli closest to this physiological value and lastly at the outer values.

Overall, we have developed a robust tissue culture system, that gives us the possibility to pursue long term proliferation of satellite cell derived progenitor cells and evaluate their proliferative and differentiative capacities.

In the future, different biochemical and biophysical cues will be used to influence and optimize these processes.

References:

[1] *Collins, C. A., I. Olsen, et al. (2005). "Stem Cell Function, Self-Renewal, and Behavioral Heterogeneity of Cells from the Adult Muscle Satellite Cell Niche." Cell 122(2): 289-301.*

[2] *Engler, A. J., S. Sen, et al. (2006). "Matrix elasticity directs stem cell lineage specification." Cell 126(4): 677-89.*