Sarcopenic muscle extracellular matrix dictates muscle adaptation in a 3D-engineered muscle model of COPD

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Introduction: We investigated whether training-induced extracellular matrix (ECM) protein expression from sarcopenic COPD can replicate muscle wasting and loss of muscle strength in a 3D-engineered muscle.

Methods: Differences in ECM composition in COPD with muscle sarcopenia (FFMI; 15.6 Kg.cm^2, n=10) and without sarcopenia (FFMI; 19.0Kg.cm^2, n=19) were replicated in a xeno-free human 3D-engineered muscle tissue organoid. Human myoblasts (Lonza Biotechnology) embedded in specific ECM composition from sarcopenic and non-sarcopenic COPD were used to construct 3D-muscle. Muscle fibre width, and protein expression was analysed using immune fluorescence (IF) images. Gene expression was quantified using RT-PCR.

Results: Increasing concentration of ECM from sarcopenic COPD induced muscle fibre wasting and failure in myoblast cell attachment and differentiation (Figure 1). Sarcopenic compared to non-sarcopeni ECM produced myofibers with shorter length and smaller width evidenced by IF analyses of anti-sarcomeric α-actinin and anti-desmin staining (Figure 1). Myogenic and growth factors were also affected by ECM from sarcopenic COPD.

Conclusion: Muscle from sarcopenic COPD present a particular ECM composition that does not favour increase in muscle mass.

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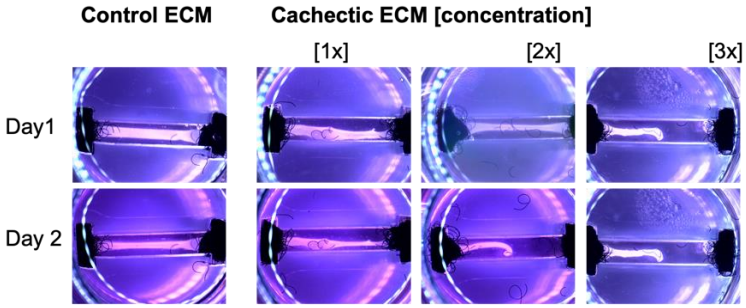

Figure 1: Muscle fibre from COPD across increasing concentration of ECM