**Enhancing drug assessment for Duchenne muscular dystrophy using organ-on-a-chip technology and nanoplasmonic biosensing of myotube integrity**

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Duchenne muscular dystrophy (DMD) poses significant challenges for drug development, given its complex and degenerative pathology. While extensive research has explored potential treatment molecules, the success rate remains limited, partially due to the limitations of standard preclinical research tools. To accelerate the evaluation of anti-DMD treatment candidates, we introduce an innovative Organ-on-a-Chip (OOC) platform. This technology offers a novel and promising approach to DMD drug development. The OOC platform comprises a microfluidic device capable of sustaining the culture and electrical stimulation of six patient-derived 3D contractile skeletal muscle tissues. The device is interconnected to a nanoplasmonic sensing device that enables the individual monitoring of myotube integrity for each muscle tissue as a key indicator of anti-DMD drug efficacy. The DMD *in vitro* model is constructed by encapsulating myogenic precursors in a fibrin-composite matrix using a PDMS casting mold. Following a regimen of electrical pulse stimulation based on continuous contractile stimuli, our model faithfully recapitulates the membrane fragility observed in DMD, as evidenced by reduced myotube integrity and elevated Creatine Kinase (CK) levels in the culture medium. The nanoplasmonic biosensor is integrated, offering fast, direct, and label-free measurement of CK levels, thereby enhancing the assessment of sarcolemmal damage. This technology takes advantage of surface plasmon resonance phenomena to detect biomarkers in the order of picograms, and its integration with the microfluidic device allows an independent, online monitoring of myotube integrity after electrical stimulation and drug administration. Following this approach, we used this OOC platform to assess the ability of drug candidates for DMD to reduce membrane fragility, such as utrophin upregulators. This innovative fusion of OOC and plasmonic sensing technologies represents a transformative approach to DMD drug evaluation. By combining microfluidics, contractile 3D muscle models, and nanoplasmonic CK monitoring, our platform provides a powerful tool for assessing the efficacy of anti-DMD treatments. This work underscores the potential of OOC technology in advancing the development of therapies not only for DMD but also for other neuromuscular disorders.