Development of a human skeletal micro muscle platform with pacing capabilities

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Organoid systems are powerful tools to rapidly expand our knowledge of human biology and identify novel therapeutic targets for disease. Three dimensional bioengineered skeletal muscle has been recently shown to recapitulate many features of native muscle biology. However, current skeletal muscle bioengineering approaches require large numbers of cells, reagents and labour, limiting their potential for large scale studies. Herein, we use a miniaturized 96-well micro-muscle platform to facilitate semi-automated tissue formation, culture and analysis of human skeletal micro muscles (hμMs). Utilising an iterative screening approach we define a serum-free differentiation protocol that drives rapid, directed differentiation of human myoblast to skeletal myofibres. The resulting hμMs comprised organised bundles of striated and functional myofibres, which respond appropriately to electrical stimulation. Additionally, we developed an optogenetic approach to chronically stimulate hμM to recapitulate known features of exercise training including myofibre hypertrophy and increased expression of metabolic proteins. Taken together, our miniaturized approach provides a new platform to enable high-throughput studies of human skeletal muscle biology and exercise physiology.