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Bioreactor and methods for organ-on-a-chip application in fibro-proliferative disorder modelling

Fibroproliferative disorders constitutes a group of medical conditions characterized by excessive tissue fibrosis, which is the overproduction and accumulation of fibrous connective tissue. These disorders often result from an abnormal wound healing process where fibroblast proliferation and overactivation, as well as extracellular matrix deposition exceed normal levels found in physiological wound healing. Despite advances, these disorders remain challenging to treat, necessitating ongoing research and development of new therapeutic strategies. Here, we present a biochip model that can generate a profibrotic environment in the absence of pro-fibrotic cytokines (i.e., TGF beta or PDGF) and demonstrate how to apply musculoskeletal organ-on-a-chip technologies to i) investigate the modulating effect of biomechanical stimuli (i.e., fluid shear and compressive loading) on pro-fibrotic mechanisms (i.e., myofibrotic differentiation of stromal fibroblasts) and ii) demonstrate how to apply fibrosis-on-a-chip systems modelling musculoskeletal fat pad fibrosis in a screening study on the attenuating effect of anti-fibrotic agents (i.e., human platelet lysate).

Technology

The innovative biomimetic biomechanical fibrosis-on-a-chip model was developed to promote a stimulative niche to model fibro-proliferative disorders under dynamic mechanobiological parameters including hypoxia, fluid perfusion as well as dynamic multi-axial loading.

Application

research tool screening tool

Options

R&D cooperation, License agreement

IPR

EP 24 170 834 priority filing: 17.04.2023

Advantages

- allows precise in situ formation and maturation of patient-derived stromal organoids using primary cells under varying actuation frequencies and loading intensities
- implementation of an in-situ oxygen sensing to develop a slightly hypoxic environment via stromal cell crowding that stimulates a natural pro-fibrotic environment of local tissue fibrosis
- the fibrosis model can be used to investigate pro- and anti-fibrotic treatments and stimulants under more relevant conditions
- high feasibility of the developed fibrosison-a-chip setup for **screening studies**

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Isometric and lateral views comprising two individual tissue units on an object slide format as design variant. Each unit comprises two medium reservoirs, one microchannel, a hydrogel compartment with a flexible membrane on top, and an overlaying pneumatic control layer with structured airfilled microchannel structures.

Reference

Vetmeduni EM174