Bio-sketch:

Prof. John Connelly is a Professor of Bioengineering in the Blizard Institute at Queen Mary University of London. He received his B.S. in Biological and Environmental Engineering from Cornell University and his Ph.D. in Bioengineering from the Georgia Institute of Technology. He then completed his postdoctoral training in Prof. Fiona Watt's laboratory at the University of Cambridge where he investigated the roles of cell shape and the actin cytoskeleton in keratinocyte terminal differentiation. He established his research group in the Blizard Institute in 2010, and leads a multi-disciplinary team of scientists and engineers. Research in the Connelly lab focuses on the role of mechanical and biophysical forces in the regulation of skin homeostasis and repair. In addition, the Connelly lab has developed a range of bioengineering tools for modelling the cellular microenvironment within the skin. On-going areas of investigation include understanding the role of impaired mechano-sensing in blistering skin diseases and scar formation and the development of next-generation human skin models, integrating immune cells, vascularisation, and appendages within 3D microfluidic platforms. He is the academic lead for the CREATE Lab core facility and the Research and Innovation Lead for the Centre for Predictive In Vitro Models (CPM), and he founded QMUL's Postgraduate Programmes in Regenerative Medicine.

Abstract:

Human skin is a highly intricate organ system that provides essential barrier, immunologic, sensory, and thermo-regulatory functions. As these complex processes involve dynamic interplay between multiple different cell types, they are extremely challenging to replicate in vitro. To address this challenge, our laboratory has recently leveraged advanced biofabrication methods to establish a suite of complex human skin models that capture key aspects of skin immunology and sweat gland function. We developed a microfluidic human skin equivalent (HSE) that supports the delivery of circulating immune cells via a vascular microchannel embedded within the dermis of a full-thickness construct. We demonstrated that specific stimulation of keratinocytes in the epidermis promotes rapid monocyte trafficking from the vascular channel into the skin. Single-cell transcriptomic analysis of the tissue-resident and recruited cell populations revealed dynamic and cell-specific patterns of gene expression that were characteristic of acute activation and resolution of an inflammatory immune response. Moreover, comparison of the gene signatures of the monocyte-derived cells to in vivo populations provided molecular level validation of the model and indicated a differentiation trajectory of the monocytes through to mature dermal macrophages. We also extended this model to replicate age-associated immune dysfunction by the inclusion of senescent fibroblasts, which promoted increased monocyte recruitment into the HSE. In addition to immune-responsive models, we also established a functional eccrine sweat gland (ESG) model using a microfluidic organ-on-chip platform. We implemented live imaging assays to assess ion channel signalling, and we demonstrated that the ESG-on-chip model accurately retains ion channel activation in response to cholinergic stimuli, a key function of the ESG. Together, the advanced human skin models presented here replicate key aspects of complex skin functions not previously possible in vitro, and they represent tractable experimental tools for interrogating mechanisms of human skin physiology and testing novel therapeutics.