Project Details	
Project Code	MRC21IIRBa Di Lorenzo
Title	Automated T-cell expansion in an integrated bioelectronics microfluidic chip: paving the way for personalised T-cell therapies for blood cancer
Research Theme	Infection, Immunity & Repair
Summary	Advanced cell-based therapeutics will shift toward personalised solutions where patients are treated as individuals rather than receiving one-size-fits all treatment. To enable this, we propose a highly interdisciplinary project that will lead to an innovative real-time monitoring and control platform for automated stem cell culturing.
Description	Personalised and advanced therapeutics have the potential to transform the precision of healthcare interventions. For this potential to be realised, however, novel approaches to personalised therapeutic manufacture are required to overcome significant economic and technological challenges. Current manufacturing systems are designed with the 'one-size-fits-all' approach, which is not suitable for patient-specific healthcare applications. Our long-term vision is to redefine the manufacture of cell-based therapeutics through the development of a self-regulated on-body micro-manufacturing and processing facility. With this focus in mind, we propose a highly interdisciplinary PhD project, which, by combining engineering with life science, material chemistry mathematics and physics, will develop an innovative bioelectronic device for cell culturing with integrated sensing capability. We will employ the T lymphocyte cell (T-cell) immunotherapy application as an exemplar. This choice was made given the promising curative potential of T-cells for some of the most aggressive forms of cancer, including Acute Lymphoblastic Leukaemia. The following objectives have been designed: Objective 1: Electrochemical monitoring and control of T-cell growth and proliferation. The T-cells will grow onto gold electrodes functionalised with 3D macroporous scaffolds of a conducting polymer, such as poly(3,4-ethylenedioxythiophene (PEDOT), activated with collagen to help cell attachment and proliferation. The inclusion of cells within the porous architecture affects the impedance of the electrically conducting polymer network. Therefore, impedimetric measurements will be performed to monitor in situ cell growth. This methodology will be also used to investigate the effect of electrical stimulation (i.e. application of a fixed potential to the system) on cell proliferation and will be validated by time-lapse microscopy analyses. The 3D polymeric scaffold will be embedded in a microfluidic channel to allow media perfusion, homogenous cell spreading and long-term cell viability. Objective 2: Automatization of T-cells culturing. Closed-loop, control algorithm approaches will be used to optimise, automatically, T-cell growth (control output) while varying cell environmental conditions (control input); the information gained will be used to refine current protocols for T-Cell expansion. The existing personalised T-cell immunotherapies are time consuming (requiring up to 21 days), with poor levels of process control and limited yields. With this project we aim to develop an innovative engineering system to ensure robust, reproducible and consistent manufacture of T-cells, minimise the risk of failure and ultimately facilitate personalised therapeutics.
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