Cellect-Ab: Build a synthetic immune response in droplet microfluidics

Proposers
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Introduction

The primary goal of this collaboration is to build a platform for engineering and identifying an immune response against specific antigens. Due to the enormous success of antibody therapeutics, the interest of pharmaceutical companies in this field has increased. Considerable efforts have been made to optimize the antibody response and to improve the time spent to select a good candidate lead. These efforts aim to decrease the number of drugs that fail in the clinics, as well as the financial costs associated. The limitations of current antibody discovery platforms are: a) The constrained diversity of antibody libraries; b) The selection methods based on antibody display technologies and never in its native IgG format; c) The need to improve selection by discovery of mAb against membrane proteins expressed in native conformational conditions. To integrate the proposed solutions in a high-throughput manner, we will build this synthetic immune system in a droplet-based microfluidic strategy. This system is capable of performing a variety of "digital fluidic" operations that can be rendered programmable and reconfigurable. This project joins technology experience on microdevices at INESC MN with experience developing humoral immune responses.

Partner 1

iMed, is the research Institute of Medicines at Faculdade de Farmacia Da Universidade de Lisboa with a mission to develop innovative medicines and benefit human health through top class multidisciplinary research, technology and innovation. Capabilities are built around the drug discovery and development spectrum. The area of drug discovery focuses on integrating cell-based approaches with emerging high-throughput systems aiming the discovery of new biopharmaceutical drugs.

Partner 2

The Thin-Film MEMS and BioMEMS group at INESC MN has extensive experience developing integrated microfluidic systems for biosensing. Particular recent focus has been on integrated sample preparation modules, optical detection, and the use of nanoporous microbeads.

Project outline/goal

Since no current synthetic technology integrates all steps of humoral immune responses, CELLectAb answers to these weaknesses with a complete platform of mAb discovery that uses engineered human T-cells to perform simultaneously: a) Antibody diversification on CDR regions using a unique technology of randomization; b) Cellular expression of stable and fully human IgG; c) Discovery of IgG against native conformational targets present in the same cell. In CELLectAb we aim to apply cutting edge knowledge of antibody discovery, engineering, and evolution technologies to generate fully human therapeutic antibodies. This inventive platform technology provides a means for innovative genetic diversification of the binding molecule and its selection following binding to a therapeutic target within the environment of a single cell. To ensure the highest probability of success we will build a droplet system where each cell expressing an antibody is encapsulated with a specific antigen. The selection of antibodies, and corresponding cells, will enable the rapid identification of specific binders against cancer or inflammatory cells.

Student profile

Profile sought: preference, but not limited, to students with a background in Biomedical Engineering, Biological Engineering or Biotechnology with an interest in exploring complex microfluidic systems for practical applications.