Discovery-On-Chip: Integrated microfluidic system for antibody discovery

Proposers
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Introduction

The primary goal of this collaboration is to build a platform for discovery and early development of innovative technologies, therapies, and solutions for treatment, prevention and control of cancer. Targeting colon cancer (CC) stem cells (CCSCs), with intrinsic self-renewal and drug-resistance properties, are increasingly viewed as the only tumor cells capable of tumor initiation, growth, metastasis, recurrence and drug-resistance. The identification of CCSC-specific biomarkers and therapeutic strategies to tackle CCSCs is a major unmet need, carrying enormous potential of improving CC diagnostics and therapies. Use of microfluidic lab-on-chip systems in preclinical research has been acknowledged to have a high potential, but miniaturized systems complexity, as well as the very high level of interdisciplinarity required, have limited the number of demonstrations. This project joins technology experience on microdevices at INESC MN with experience developing antibodies against cellular proteins (iMed).

Partner 1

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

Partner 2

iMed is the research Institute of Medicines at Faculdade de Farmácia da Universidade de Lisboa with a mission to develop innovative medicines and benefit human health. The area of drug discovery focuses on integrating cell-based approaches with emerging –omic technologies and pathway modeling to identify new targets, and use of both small molecules and biopharmaceuticals targeting single molecules or complex interacting disease pathway components.

Project outline/goal

In this project we will innovate in early development by antibody discovery against colon cancer (CC) stem cells. Specifically cancer cell specific antibody fragments will be identified against specific cell surface antigens by phage display. To optimize discovery of antibody biopharmaceuticals, we will develop microfabricated lab-on-chip systems to support and complement the objectives of identification of stem cell-specific cell-surface antigens. Antibody libraries will be used to continuously flow on top of CCSCs present in a chip. During fluid traffic, these cells will be subjected to multiple selection conditions with antibody phages, and selected binders will be detected by FITC-conjugated anti-M13 antibody. The selected cells will be recovered and the antibody will be isolated. This method using mAb-CHIP has the advantage to select antibodies without further amplification, which will be crucial to identify rare binders. These chips involve a cell culture area, which can be a simple chamber or a more complex 3D construct that recapitulates a given tissue microenvironment.

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