

Microfluidic biosensor for antibody therapy management

Proposers

Joao Goncalves – iMed-Research Institute for Medicines, Faculdade de Farmacia da Universidade de Lisboa

Joao Pedro Conde – INESC MN e Técnico, Universidade de Lisboa

Immune responses leading to the generation of anti-drug antibodies (ADA) can cause adverse events, but the most common problem is loss of efficacy, when ADAs bind the drug and neutralize its activity or speed up its biological elimination. To assess immunogenicity of biotherapeutics, a variety of methods for detection, quantitation and characterization of antibody responses have been developed, the results of which can provide intelligence for patient safety and treatment as well as increased knowledge about the immune response to the drug. However, assays for antibodies in biological fluids are susceptible to a wide range of technical difficulties in addition to scientific challenges in their interpretation. Bioanalytical methods for pharmacokinetic assays and for detecting and monitoring ADAs require rigorous optimization and validation to detect and characterize antibodies, and demand reagents and controls with high specificity and sensitivity, particularly when the drug is a monoclonal antibody.

To overcome these issues, this research project aims to develop a microfluidic biosensor to detect and quantify ADAs in plasma. Microfluidic chips will be fabricated using top-down clean room microfabrication and soft-lithography processes. Three main technical challenges will be addressed in the biochip design, fabrication and test: (i) processing the plasma to avoid matrix interference and possibly pre-concentrate the ADA of interest; (ii) achieve clinical sensitivity in assay times below 15 min; and (iii) produce a chip with integrated detection that can allow for multiplexing of the detection of several analytes of interest.

We will aim to utilize a multi-tiered approach to measure ADAs, NAb and antibody concentration in plasma. The sensor will be used in the development and validation of qualitative and quasi-quantitative immunoassays capable to detect at the same time multiple variables of antibody treatment. The first tiers are focused on detecting anti-drug antibodies (ADAs) that bind to the biologic drug. Samples are screened for the presence of antibodies, and antibody titer assessment followed by confirmation of the specificity of binding. At the end the integration of pharmacokinetic (PK) and immunogenicity data will provide the physician with better options patient treatment.