iCASE Project / AY 2025 -2026

In vitro and in silico development of nanobodies for lateral-flow point-of-care diagnostics

Project Reference: ICS-CHE-PS

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Industrial Partner: 52 North Health

BBSRC DTP main strategic theme: Transformative technologies

BBSRC DTP secondary strategic theme: Bioscience for an integrated understanding of health

Project outline:

This project aims to advance point-of-care diagnostics through the identification of novel biomarkers and the deployment of novel technologies to develop nanobodies targeting epitopes that are unique within them, to achieve the highest specificity. Relevant biomarkers will be identified by analysing available 'omics data, and a preliminary shortlist has already been compiled. Nanobodies targeting them will be obtained in the academic lab using a combination of pioneering in silico and in vitro approaches of antibody discover and optimisation. This project will develop, explore and employ artificial intelligence (AI) strategies available in the Sormanni lab to obtain nanobodies targeting pre-determined epitope that are unique on the surface of the identified biomarker [1,2]. Then, the affinity of such nanobodies will be optimised with a combination of in vitro directed evolution approaches, such as yeast or ribosome display, which are both already up and running in the lab, and machine learning approaches to predict out-of-library sequences with increased affinity. Moreover, stability and solubility will be further optimised computationally with an established pipeline [3], as these molecular properties are essential to enable the development of lateral-flow devices of suitable shelf life.

The obtained nanobodies will be deployed in state-of-the-art lateral-flow devices (the "ASTER" platform) developed by the industrial partner, to enable the rapid and cost-effective detection of both cell- and non-cell-based biomarkers [4]. Once established, this platform will enable the quantification of such biomarkers without requiring expensive laboratory tests or visits into the clinic, thus facilitating timely clinical interventions.

The primary focus will be on identifying and raising nanobodies for biomarkers within blood lymphocytes. These biomarkers will serve as crucial indicators for monitoring drug- or disease-related immunosuppression at the point of care, addressing a critical need in healthcare. By integrating highly specific nanobodies with advanced detection technologies, ASTER will enable quantitative, rapid, and reliable point-of-care diagnosis, improving patient outcomes and healthcare efficiency. Furthermore, this research will provide a unique opportunity to explore and discover novel biomarkers associated with the response to anticancer immunotherapy, possibly leading to novel insights for cancer treatment strategies.

This strongly multidisciplinary project bridges computational structural biology, biophysics, immunology, and diagnostics. It offers an exceptional opportunity for a PhD candidate to make a

significant impact on both fundamental research methodologies and life-sciences diagnostic industries. The proposed research will contribute a step-change in technology capabilities, with the potential to advancing precision medicine, improving patients' healthcare journeys, and reducing healthcare costs.

[1] Aguilar Rangel et al. Science Advances 2022

[2] Ramon et al. Nature Machine Intelligence 2024

[3] Rosace et al. Nature Communication 2023

[4] https://nhscep.com/2024/03/12/new-finger-prick-test-detects-sepsis-in-cancer-patients-at-home/