**University of Leicester**

**BBSRC MIBTP Studentship Project 2025-6 entry.**

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**Section 2 – *Project Information***

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| **Project Title** | Development of a robust, validated, non-animal derived toolbox to study the ageing immune system  |
| **Project Summary**  |
| **Summary** Many developed and developing countries are experiencing a rapid demographic shift towards an ageing society. The immune system of older individuals is more susceptible to severe infections, poor vaccine responses, cancer, and inflammation. Understanding how the immune system ages is critical to overcoming these key challenges in our ageing populations. This project aims to develop a toolbox that enables the study of immune system changes as people age, and identifying ways of measuring the biological age of the immune system. These are called biomarkers of ageing – and the availability of reliable markers is a major barrier to discovery of interventions that can slow ageing. This project will address this challenge using a multidisciplinary approach with collaborators in bioinformatics, proteomics, molecular biology and industry. The assay systems developed will have scientific, commercial, and societal value. **Ageing immune system** The immune system is critical to the maintenance of health; the ageing of the immune system is associated with1: * Impaired immunity
* increased susceptibility to infections
* reactivation of chronic viral infections
* Reduced vaccine responses
* Weakened protection against the development of malignancies
* Predisposition to inflammatory diseases
* Weaker/dysregulated wound repair

Ageing results in shrinkage of the thymus - the source of T cells, which decline in number and function. The balance between adaptive and innate immunity changes, favouring the development of inflammation. Immunocytes display shortening of telomeres, dysregulation of redox balance, and accumulation of DNA damage. Immunocytes become senescent with age, meaning they continue to survive and secrete proinflammatory mediators, but no longer proliferate. Some animal models suggest that targeting immunosenescence has the potential to halt ageing. A challenge to our understanding, and towards developing interventions to slow ageing, is the availability of [robust biomarkers of ageing](https://www.agingconsortium.org/). These are molecules associated with biological age and predictive of lifespan. Without robust biomarkers, the study of ageing is dependent on expensive and slow longitudinal studies. **Ageing biomarkers** Towards robust biomarkers for ageing, a consortium of scientists is sharing open  [transcriptomic and proteomic data](https://bio-learn.github.io/data.html).  These contain putative markers of biological age, with some validation data. The scaling of these into robust reproducible commercial assays, for deployment in biotech R&D, has the potential to accelerate ageing research. Recombinant antibodies against key molecules represent scalable non-animal reagents, that can be deployed to characterise the expression of putative aging biomarkers in leukocytes and/or plasma. Such validated quantitative assays would hold high commercial and societal value. Unfortunately, a large portion of antibodies currently used in research (particularly animal derived) are not fit for purpose, thwarting the discovery of ageing mechanisms and biomarkers. We recently showed that out of 614 antibodies widely used in neuroscience, >50% had poor performance in 3 commonly used applications2. Our laboratory is the immunology lead for an international industry-academic [open science partnership](https://f1000research.com/gateways/ycharos/about-this-gateway) with 13 commercial antibody manufacturers (who contribute antibodies and KO cell lines in-kind). Together we have identified robust tools to accelerate research into neurodegeneration and immune ageing.  **Objectives and methods** 1. Utilise open datasets to prioritise key potential biomarkers of the ageing immune system

 1. Develop robustly validated recombinant flow cytometry and ELISA panels to study key age-associated molecules in the immune system
2. Telomere maintenance enzymes
3. DNA repair enzymes
4. Redox active enzymes (e.g. NADPH oxidases)
5. Markers identified in objective 1

 1. Obtain plasma and whole blood samples to produce preliminary validation data to confirm
2. Performance of assays relative to quantitative mass spectrometry benchmark and any competitor technologies (e.g. available commercial ELISA)
3. Age association of any markers in a preliminary study for future commercial exploration

**Student development opportunities** The student will receive excellent training in cutting edge bioinformatics, molecular biology, immunology techniques used across our international industry-academic partnership. They will become part of a community of scientists advancing innovative open science practices. The student will be well positioned to explore commercial and/or academic opportunities that follow on from this work, using our extensive network of collaborators in academia and industry. Techniques that will be undertaken during the project* Use of large datasets within UK Biobank and [Biolearn](https://www.agingconsortium.org/)
* Data visualisation tools
* R programming language
* CRISPR Cas 9 KO cell line generation utilising RNP transfection and screening approaches
* Lentiviral expression and knockdown vector production
* Flow cytometry and ELISA assay development and validation
* Multicolour flow cytometry on blood leukocytes
* ELISA with plasma samples
* Exploration of commercialisation opportunities
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| **References** |
| 1. [https://doi.org/10.1513%2FAnnalsATS.201602-095AW](https://doi.org/10.1513/AnnalsATS.201602-095AW) (*Annals of the American Thoracic Society, 2016)*
2. <https://doi.org/10.7554/eLife.91645.2> (*eLife, 2023*)
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