The ImunoAgeing project

Changes occurring in the immune system of ageing humans -broadly referred to as 'immunosenescence'- have huge consequences on health, but the exact nature of these modifications and the underlying mechanisms are still largely unknown.

ImmunoAgeing project aims to define the extent to which immunosenescence comprises changes in levels of specific immune cell types or molecules, or functional competence of cells, and to detect genetic and non genetic factors that drive these changes. The studies are designed to better understand the mechanisms and pathways of immunosenescence as the basis to prevent or alleviate imbalances and resulting immune-mediated pathological effects in the immune system of the elderly.

The project is designed to fill the existing gap in information by elucidating key determinants, **both inherited and environmental,** as well as **pathways and mechanisms** governing this process and its clinical hallmarks.

Toward this aim the **existing longitudinal and cross-sectional collections of data and samples** from the general population and from patients with a variety of autoimmune diseases across a broad spectrum of ages will be exploited.

The project builds on two population studies in the founder population of SardiNIA and in the more cosmopolitan population of the UK to study features of immunosenescence across immune cell types and molecules, including changes in levels and in functional capacity.

ImmunoAgeing

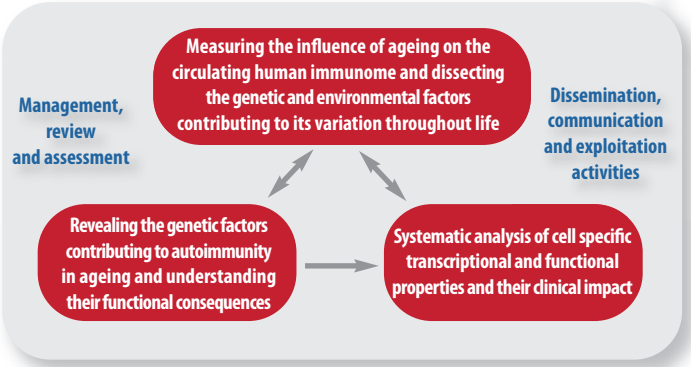
Aims

1. To assess the role of quantitative variation of ~140 circulating immune cell subtypes and ~ 25 soluble factors (cytokines and antibodies) in immunosenescence, and identify genetic and modifiable environmental exposures (including smoking, diet, alcohol intake and physical activity) contributing to this variation in a large population cohort of volunteers over a broad spectrum of ages (CNR).

2. To assess the extent and genetic bases of 'subclinical' autoreactivity during ageing and its correlation with chronic viral infections, contractions in the B & T cell repertoire and the other cellular and humoral immune traits assessed in AIM 1 (UCAM and CNR).

3. To elucidate the functional and transcriptional properties of those cell types that show the strongest age-related changes, and whose circulating levels are affected by known genetic variants, and combine all available data to reveal pathways, biomarkers for early diagnosis and therapeutic targets to prevent or minimize the negative features of immunosenescence (UIBK, CNR and UCAM).

The Aims **capitalize on and add value to existing sample and data collections** from large general-population cohorts, and are **synergistic:** the results of each Aim and participating centre further informing analyses of the others.



Positioning of the project

In its entirety, the project will create the bases to identify those persons most likely to manifest clinical consequences of immunosenescence, and will reveal molecules and pathways prone to therapeutic modulation. Hence, our **basic research** will provide the **knowledge-based foundation for future biomedical commercial developments,** by revealing biomarkers and therapeutic targets, and by providing the rationale for generating robust assays to assess compounds to prevent or alleviate the pathological signs of immunosenescence.

National and international research and innovation activities feeding into the Project

The project is firmly grounded in preliminary results that are innovative and have already shown the potential to fulfil our Aims, for each of the partnering organizations.

- CNR with the ProgeNIA/SardiNIA (afterwards referred to as ProgeNIA) project has a 13 year experience in both cross-sectional and longitudinal studies of genetics and epidemiology for ageing-related traits and diseases in a Sardinian cohort of ~7,000 volunteers, including an elderly group of ~300 > 90 years old.

- The Cambridge BioResource (CBR), of which UCAM are founder and major users, was set up in 2005 and now exceeds 13,000 healthy genotyped volunteers (aged 16-80 years), and more recently patients.

- UIBK will be contributing based on its strong record in the analysis of age-related changes and their functional consequences in immune cells, like CD8+ and CD4+ T cells, Tregs, B cells and dendritic cells.

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ImmunoAgeing

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ImmunoAgeing

An integrated approach to dissect determinants, risk factors and pathways of ageing of the immune system