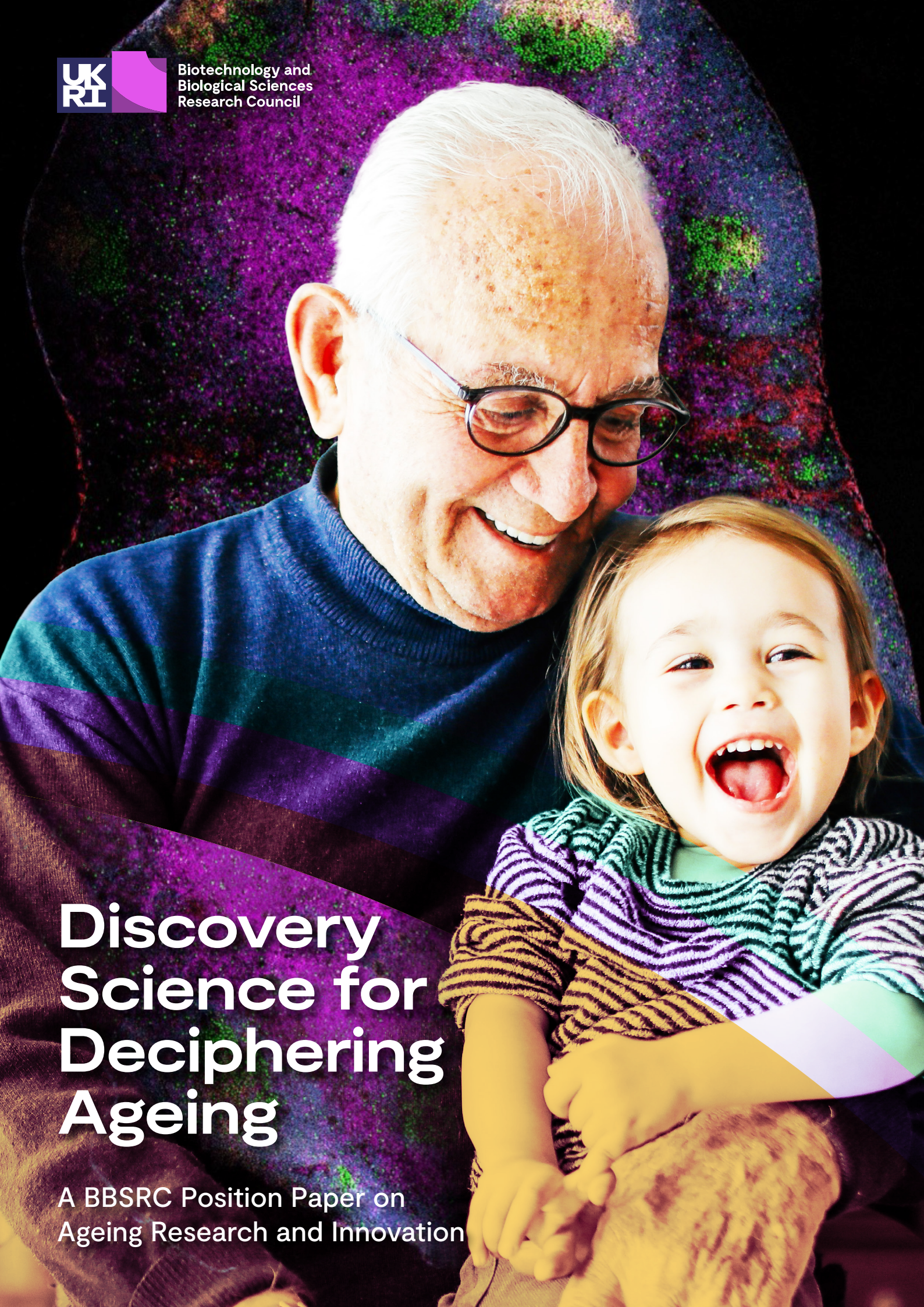

UKRI
Biotechnology and
Biological Sciences
Research Council
Discovery Science for Deciphering Ageing
A BBSRC Position Paper on Ageing Research and Innovation

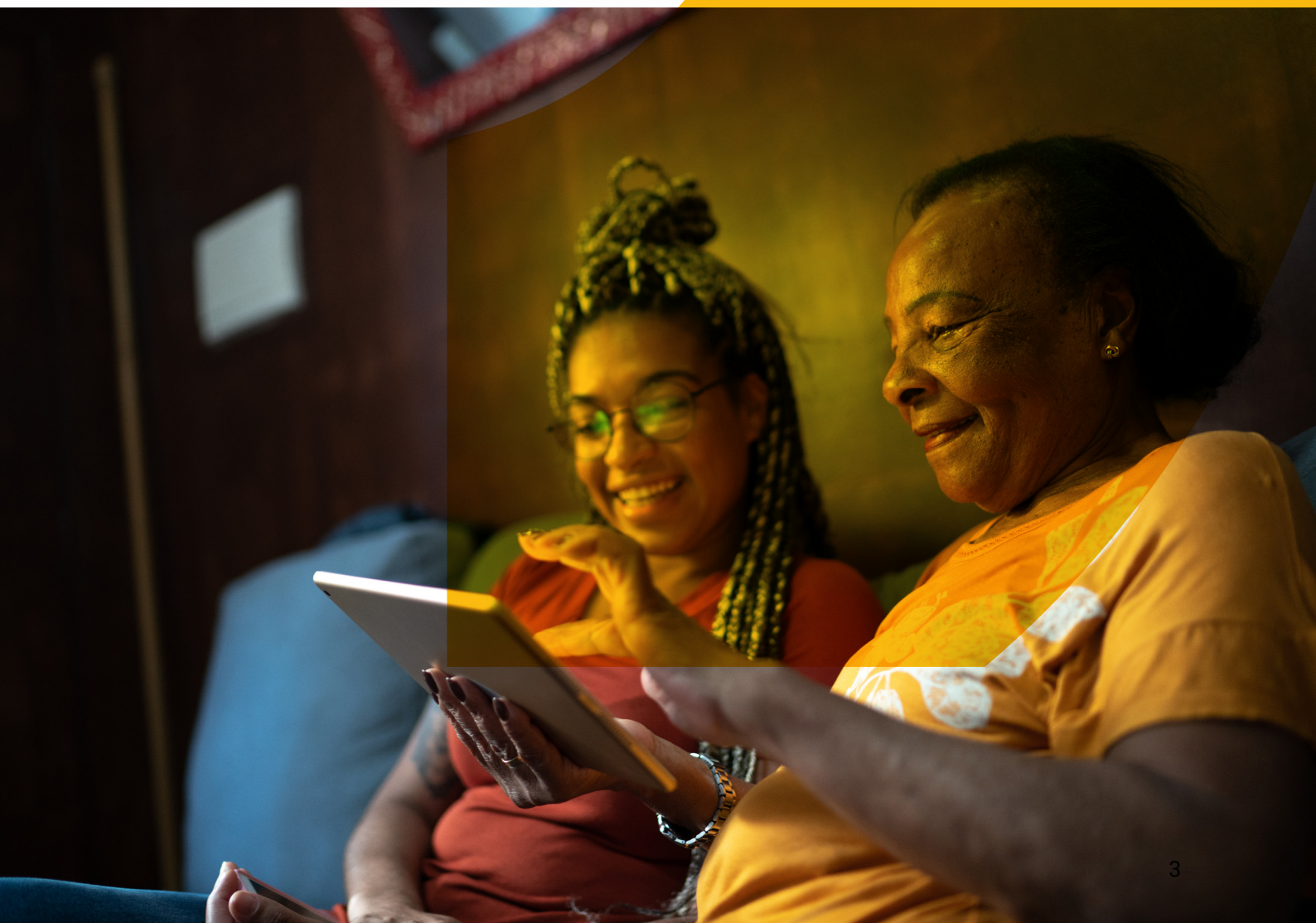
Contents

Summary

Ageing research has been a priority area for BBSRC for more than two decades. Over this period, our investments into fundamental bioscience have enabled the ageing research community to advance research and innovation and drive key discoveries. In response to a changing research and policy landscape, and in consultation with experts from the research community, BBSRC has reviewed the progress of this field to identify research challenges, gaps, and opportunities.

Ageing research, translation, and innovation have the potential to enhance health and wellbeing for all in society, driving economic growth and placing the UK at the forefront of the global research landscape. This position paper provides academics and wider stakeholder communities with BBSRC's vision and strategic support for research and innovation on ageing and to outline the key challenges we aim to address.

The Position Paper aligns with BBSRC's Strategic Research Priority in Bioscience for an Integrated Understanding of Health (BIUH)[1], BBSRC's Foward Look: the Power of Bioscience[2], and the UKRI 2022-2027 Transforming Tomorrow Together[3]. The Position Paper has been developed following consultation with BBSRC's BIUH Strategy Advisory Panel, Ageing Across the Life Course Expert Working Group, Ageing Focus Group and Ageing Immunology Expert Working Group (Annex 1).



Introduction

Global demographics are changing. The World Health Organisation (WHO) estimates that the world's population aged 60 years and older will double (to 2.1 billion) by 2050. The number of people aged 80 years or older is expected to triple between 2020 and 2050 to reach 426 million[4]. It is projected that by 2050 one in four people in the UK will be aged 65 years and older compared to one in five people in 2018[5].

However, while life expectancy has been increasing in much of the world, health span has failed to keep pace. In many cases these extra years of life are often spent in ill health, a phenomenon exacerbated in the UK by regional and socioeconomic disparities[6]. Understanding how the human body ages from the changes that occur at a molecular, cellular, organ or system level from pre-conception to the end of life, is vital if we are to live with health and resilience, enjoying the benefits that longevity can bring, as well as addressing the challenges that it can impose. Supporting basic and discovery science in ageing research is essential if we are to ensure that health span can be increased for as many people as possible.

'Securing Better Health, Ageing and Wellbeing' is at the forefront of the UKRI Strategy 2022-2027[7]. By harnessing the full power of the UK's research and innovation system, UKRI aims to improve people's health and promote wellbeing to maintain prosperous, productive, and resilient communities throughout the UK and globally. With the nation's world-class research and innovation system, the UK is well-equipped to lead the response to this global challenge.

Ageing population

UK

2018	2050
65 years+	65 years+
	

World

2020	2050
60 years+	
1 billion	2.1 billion
80 years+	
147 million	426 million

Ageing research and innovation at BBSRC

Building on its investments, BBSRC will continue to play a vital role in providing a deep, integrated understanding of the fundamental biological processes that contribute to maintaining and enhancing mental, cognitive, and physical health across the life course for all in our society. Working in partnership across UKRI and with key stakeholders, BBSRC will enable its research community to combine this fundamental understanding with the knowledge of how factors such as genetics, sex, ethnicity, lifestyle[8] and the environment affect physiological function, mental and cognitive health across the life course, identifying effective interventions to maintain health, reduce the risk of age-related diseases, and tackle health inequalities. Information on our investments is provided in Figure 1 and Annex 2.

CASE STUDY

The SAGE and ERA initiatives

The Science of Ageing (SAGE) and Experimental Research on Ageing (ERA) initiatives significantly boosted the ageing research field and were pivotal opportunities for many of our now world-leading scientists within the ageing field. The investments from these initiatives have contributed considerably towards an increased understanding of ageing and provided a much-improved picture of the basic mechanisms of ageing, leading to significant advances in knowledge.

The initiatives catalysed the formation of research collaborations that enhanced multidisciplinary research and led to further funding that has enabled the continuation of answering key ageing research and innovation challenges. Many of the SAGE and ERA researchers are still an integral part of today's ageing research community and have contributed significantly to the development of both the national and international landscape by:

- capacity building in ageing research
- joining working groups, committees and assessment panels related to ageing research
- joining executive committees of learned societies

Timeline

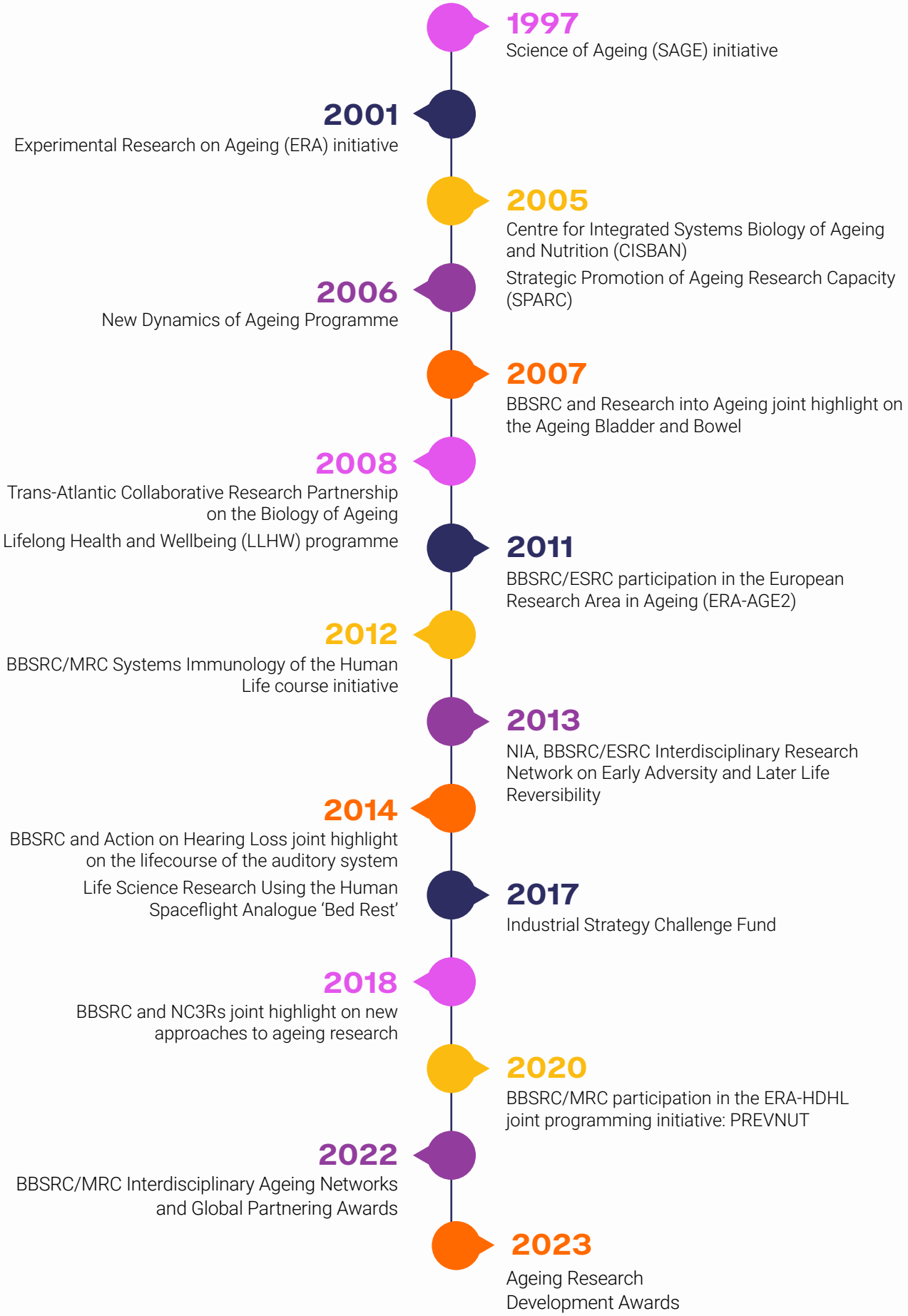


Figure 1. Summary of strategic BBSRC investments in ageing research over the past 25 years. Further information is provided in Annex 2.

Strategic drivers

There are over 11 million people aged 65 and over in England and in ten years' time this will have increased to 13 million people or 22% of the population[9]. Against this growth, the number of years we can expect to spend in good health, without disabling illness, continues to decline. Men can currently expect 62.4 years of healthy living on average, and women, 60.9 years. However, these are average figures, and in reality, the number of years we can expect to spend in good health is dependent, in part, on where we live. At birth, people in the most deprived areas of England and Wales can expect to live more than 17 additional years with disabling health conditions than those in the least deprived[10].

Ageing and Government

In 2021, the House of Lords Science and Technology Select Committee report on ageing[11] emphasised that healthy life expectancy is not keeping pace with increases in life expectancy, and inequalities in healthy life expectancies are stark, resulting in a growing period of poor health towards the end of life for many.

Additionally, ten years after the initial Marmot review *Fair Society, Healthy Lives*[12], a subsequent analysis found that, since the initial review, the health gap has grown between the richest and poorest in the UK, improvements to life expectancy have stalled, and declined for women in the most deprived 10% of areas.

The UK government seeks to address societal inequalities in ageing as part of one of five key missions, Building an NHS Fit for the Future[13]. The government commits to halving the gap in healthy life expectancy between the richest and poorest regions in England and prioritising women's health when reforming the NHS.

BBSRC has an important role to play in understanding the fundamental drivers of health inequalities, working with our partners across UKRI to understand the complex interaction between the biological, environmental, behavioural, social and economic factors that contribute towards the gap in healthy life expectancy.

Figure 2. Sustainable Development Goals that are underpinned by healthy ageing.

The mission also embeds a strong focus on prevention of avoidable ill health, rather than treatment. This builds upon the Chief Medical Officer's (CMO) Annual Report 2023: *Health in an Ageing Society*[14] which calls for primary prevention by central and local government, to reduce risk factors to unhealthy ageing, and secondary prevention by the NHS to slow onset of age-related disease. Understanding the biological mechanisms underpinning healthy ageing trajectories will be essential to preventing age-related decline and diseases. BBSRC will play a key role in supporting the research community to address this gap and harness opportunities.

Science and Society

In 2023, the Nuffield Council for Bioethics published 'the future of ageing: ethical considerations for research and innovation'[15], calling for research funders to "explicitly take a public health, life-course approach to research funding, recognising the importance of preventative approaches, and prioritising the needs of those who are currently disadvantaged'. In 'The State of Ageing 2023-24 '[16] report, the Centre for Ageing makes a call for action to reverse trends in stalling life expectancy and the increasing amounts of time spent living with illness and disability, and for co-ordinated action to address growing health inequalities. Ageing also underpins 9 of the 17 United Nations Sustainable Development Goals[17] (Figure 2), and the World Health Organisation (WHO) announced 2021-2030 as the 'Decade of Healthy Ageing', with the aim to improve the lives of older people, their families, and communities (Figure 2), and the WHO announced 2021-2030 as the 'Decade of Healthy Ageing', with the aim to improve the lives of older people, their families, and communities[18].

BBSRC commitment to ageing research and innovation

BBSRC will take a coordinated, multidisciplinary approach to support ageing research and innovation that leads to a better understanding of the biological mechanisms of ageing and underpins interventions to alleviate health inequalities. BBSRC will invest in activities that drive the next generation of life science discoveries and healthcare innovations, bolstering UKRI's mission to harness the full power of the UK's research and innovation system.

We will work in alignment with BBSRC Delivery Plan, and within the overarching UKRI Strategy, (2022- 2027) 'Transforming tomorrow together'. This strategy identifies five themes that aim to tackle large-scale, complex national and global challenges over the coming years, and 'Securing Better Health, Ageing and Wellbeing' is one of the themes. UKRI aims to 'advance people's health and promote wellbeing to maintain prosperous, productive, and resilient communities throughout the UK and globally'. BBSRC is committed to delivering this aim, championing UK bioscience as a vital component in embracing and enabling a healthy ageing society.

The BIUH Strategic Research and Innovation Framework[19] outlines our mission, aims, strategic drivers and how our investments and activities will enable the delivery of wide-ranging benefits and impacts to our research communities and the wider public. The framework highlights four key themes, including ageing and health across the life course. Through this strategic theme, BBSRC will advance the understanding of biological mechanisms of ageing and maintaining cognitive, mental and physical health and wellbeing across the lifespan.

BBSRC recently published Forward Look: the Power of Bioscience[2] articulates by studying how different organisms respond to environmental challenges throughout their life course, we can uncover fundamental mechanisms of health and wellbeing, identify new targets for prevention, and inform innovative interventions. Aligning insights across species and scales allows bioscience to:

- deliver inclusive innovations
- reduce inequalities
- ease long-term pressures on healthcare an agri-food systems

BBSRC's vision for ageing research and innovation

BBSRC will support discovery science to unlock the fundamental understanding of the biological mechanisms of ageing across the life course and the advancement of novel tools to build a healthier and resilient society in which health inequalities are effectively addressed.

BBSRC will deliver its vision for research on ageing by working across UKRI and with a range of stakeholders including industry and third sector organisations to enhance the biological understanding of ageing to underpin the development of effective interventions and create a healthier society.

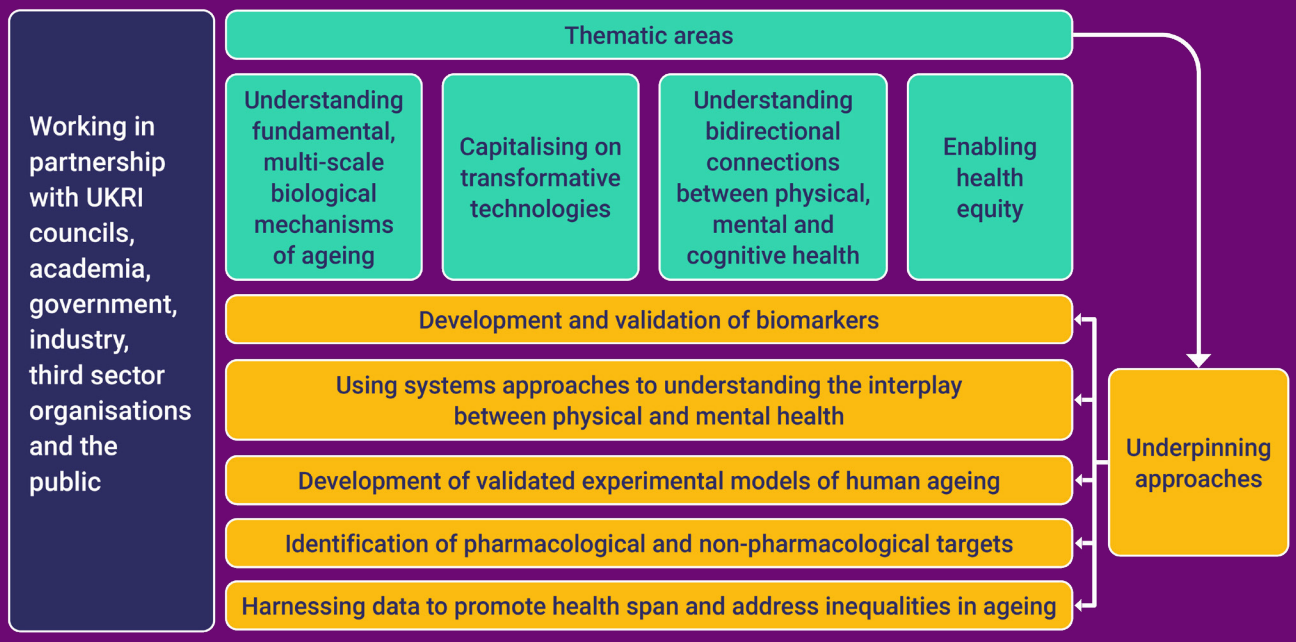


Figure 3: Key Themes and Approaches in Ageing Research and Innovation at BBSRC.

The challenges

BBSRC discovery science will address some of the fundamental challenges of ageing research and innovation:

- how can we better elucidate the biological mechanisms of ageing, the principals of healthy ageing, and the roles extrinsic factors play in influencing ageing trajectories within individuals and populations?
- can we foster innovation and translation in ageing research through deciphering different ageing trajectories and ensuring optimised interventions for healthy ageing trajectories for all?
- what transformative technologies and approaches can be developed and utilised to understand the ageing process and ensure healthy, resilient communities?

Approaches to address ageing challenges

BBSRC will address the ageing challenges by investing in and supporting interdisciplinary research and innovation that will:

- enhance our understanding of the biological mechanisms of ageing across the life course and enable the development of biomarkers of ageing to predict and monitor individual biological ageing trajectories
- elucidate how the mechanisms of ageing can be affected by extrinsic factors and the potential health inequalities these factors can seed
- apply comparative biology approaches and develop and validate experimental models of ageing across the life course to facilitate the translation of ageing research
- identify effective pharmacological and non-pharmacological targets to underpin intervention strategies to improve cognitive and physical function, thereby, extending health span and quality of life in later years
- advance our understanding of the complex bidirectional connections, pathways and functional relationships between cognitive, mental and physical health, and the factors that influence these to enhance lifelong health and wellbeing.

Key thematic areas on ageing research and innovation

Over the past 25 years, research on the biology of ageing has accelerated with a focus towards identifying major cellular, molecular, and physiological determinants of the ageing process. The integration of these approaches with population level research offers the potential to advance the identification of key ageing pathways, modulating factors, biomarkers, therapeutics, and other intervention strategies.

In alignment with UKRI's five-year Strategy, 'Transforming Tomorrow, Together' BBSRC will drive this advance through our unique support for research that aims to understand the key biological mechanisms of ageing. By deciphering such mechanisms, we will generate new knowledge and bio-based solutions to advance people's health and promote wellbeing.

BBSRC will achieve these aims by supporting:

1. Understanding the fundamental, multi-scale biological mechanisms of ageing

2. Capitalising on transformative technologies to facilitate biological understanding, and to increase the translational potential of novel technologies for improving health outcomes

And working together with the partners we will

3. Understand the bidirectional biological connections between physical, mental and cognitive health

4. Enable health equity

This forms BBSRC's unique underpinning commitment to support ageing research in the UK funded through our diverse portfolio of research, strategic institutes, training, capability, and innovation. We will harness the potential of transformative technologies – taking advantage of Artificial Intelligence (AI), digital and advanced computing, and bioinformatics and genomics to support this mission.

Working in close partnership with UKRI Councils, stakeholders in academia, government, third sector organisations, and the public, we will seek to embed underpinning advances in the understanding of the complex connections between physical, mental and cognitive health in individuals and populations. We will harness this knowledge to promote equity within the ageing population across the UK.

Together, these four themes will address key strategic challenges in ageing, building a more resilient world, creating opportunities, and improving outcomes, as well as tackling one of the great challenges of our time: ensuring healthy ageing for everyone, everywhere.

See figure 3, page 9.

Understanding fundamental, multi-scale biological mechanisms of ageing

Ageing is a multifactorial and multi-scale process that takes place at the molecular, cellular and tissue levels and represents a complex set of inter-related events. Deciphering the biological mechanisms of such processes will be pivotal in addressing ageing research and innovation challenges. Here, we summarise BBSRC's key areas of interest in this area, however, this it is not an exhaustive list.

Hallmarks of Ageing

The cellular and molecular processes that determine the ageing phenotype have been conceptualised as the 'Hallmarks of Ageing'[20]. While underpinning normal physiological and homeostatic processes, these hallmarks can correlate with negative ageing trajectories and the development of age-related decline and diseases. These hallmarks include: genomic instability, including telomere attrition[21] and epigenetic alterations[22], and impaired protein homeostasis or proteostasis, including impaired autophagy[23], mitochondrial dysfunction and accumulation of senescent cells[24]. More recently, research over the past decade has identified new hallmarks including microbiome dysbiosis[25], and chronic inflammation[26]. *Understanding how these hallmarks interconnect and how they correlate to negative trajectories in the ageing process remains a major challenge.*

Biomarkers

Biomarkers of ageing can predict a biological age and enable monitoring of ageing trajectories, however currently, *there is not a comprehensive set of validated biomarkers of ageing*. Without robust and reproducible biomarkers, it is difficult to predict adverse outcomes in later life; develop interventions that can slow the biological ageing process to extend health span; and create technologies such as ageing clocks to predict biological age. Biomarkers need to be representative of the health state of individual systems. However, health data only provides a partial image, and other lifestyle factors need to be considered and monitored, such as alcohol consumption and dietary intake. From molecular, epigenetic and transcriptomic markers of ageing progression, through to physical capability (e.g. gait, balance, grip strength) and organ function, *BBSRC aims to support research to develop a suite of robust, validated biomarkers to predict and elucidate human ageing trajectories.*

Genetics and Epigenetics

The rate and nature of age-related decline can vary between individuals. There has been progress with genome-wide association studies unravelling the genetic associations between health span and lifespan alongside the role of epigenetics in the ageing process; and the modification of the epigenome by environmental factors[27]. However, there is an opportunity for *discovery science to pinpoint genetic variations and environmental factors that influence ageing and identify suitable biomarkers and other targets for interventions*.

The Immune System

The immune system is critical in protecting against internal and external factors, but the accumulation of age-related changes to the immune system has significant physiological consequences. Reduced production of B and T lymphocytes and diminished function of mature cells, thymic involution and immunosenescence can result in impaired wound healing, increased risk to infection, poorer responses to therapeutics and vaccinations, and development of age-related diseases[28].

Immunosenescence occurs in response to an accumulation of exogenous[29] and endogenous[30] physiological stresses over the life course and is considered to be a primary driver of inflammageing – systemic low-grade inflammation that develops with age. The individual variability of physiological stressors can begin to explain why people have wide variances in their biological inflammatory age across set chronological age time points. Research has shown that a person's biological age and health status may be predicted by inflammatory markers[31]. While this novel research is promising, the fundamental biological mechanisms driving age-related changes to the immune system are not well understood[32]. *Linking intrinsic ageing processes and extrinsic influences, combined with a more holistic systems approach will help identify key pathways, functions and mechanisms contributing towards inflammageing and develop targeted interventions to modify the ageing immune system trajectory.*

Microbiome

The gut, gut microbiome and mucosa play a key role in immune function and defending against infection. As we age, both the immune system and the gut microbiome undergo dynamic changes in composition and function[33] leading to decreased microbiota diversity, disruption of the gut mucosa, and consequently to a "leaky gut", increased risk of susceptibility to infections, and poor vaccine response[34]. The skin microbiome plays an important role maintaining healthy and resilient skin. Unlike the gut, diversity in the skin microbiome has been found to increase with age, with changes in composition between young and old skin microbiomes[35]. Understanding the dynamics and composition of the microbiome across the life course, as well as its interaction with environmental exposures and our diet will enable a deeper understanding of its contribution to healthy and unhealthy ageing trajectories. *A better understanding of the characteristics of a healthy microbiome and of the mechanistic interplay between the microbiome and host immune system across the life course is required.*

Nutrition

Nutrition plays an important role in health at all stages of life and supports the maintenance of body composition, gut, microbiome and immune function, cognitive, vascular, and musculoskeletal health. Both macro- and micro-nutrients are vital in maintaining healthy physiological status, with nutrient deficiencies associated with both physical and cognitive decline[36]. For example, sarcopenia, the age-related loss of muscle mass and function often leading to frailty, is linked to nutritional factors including protein malnutrition and changes in the responsiveness of muscle proteins to nutrients[37]. *To understand the biological mechanisms through which nutrients and food act to promote a healthy lifespan, we must have a robust understanding of human nutritional requirements and changing dietary patterns across the life course.*

CASE STUDY

Boosting immune response to vaccines in older people

Immunology researchers at the BBSRC Babraham Institute made important progress in tackling ageing of the immune system. As we age, deterioration in our immune system makes us more susceptible to infection and less able to develop protective immunity after vaccination. With an ageing population, finding ways to improve vaccine efficacy in older people is an important global challenge.

Research led by Dr Michelle Linterman found older mice and humans have problems with two specialised immune cells essential to the immune response and antibody production. However, they found that applying an existing topical antiviral cream to the vaccination site boosted the number and fixed defects in those immune cells in mice (Rejuvenating conventional dendritic cells and T follicular helper cell formation after vaccination | eLife (elifesciences.org)).

Capitalising on transformative technologies

Adopting research approaches that incorporate transformative technologies will facilitate a better understanding of the molecular and cellular mechanisms of ageing and generate knowledge that will increase the translational potential for improving health outcomes (Figure 4). Experimental approaches are needed to understand the complex interplay between factors that contribute towards the ageing process, such as sex, ethnicity, and socioeconomic status, and develop interventions to slow or prevent negative ageing trajectories. These interventions must be timely and appropriate to attain the most impact and focus on the promotion of health throughout the life course to prevent age-related disease onset and enable continued physical and cognitive health into old age.

Many established experimental models tend to be short-lived and easily genetically tractable, making them ideal for rapid experiments and high-throughput screenings[38]. The development and validation of a diverse range of appropriate model systems is required to help understand how intrinsic and extrinsic factors and pharmacological interventions extend lifespan and health span for humans. *Utilising comparative biology approaches across a range of species will reveal metrics that can be used to evaluate and validate experimental models of ageing, identify genes and pathways that negatively correlate to a shorter lifespan, and enable better translation of research outcomes to benefit both human and animal health.*

3D tissue models, organ-on-chips and microphysiological systems offer an alternative approach due to their complexity as they can capture the ageing processes at the molecular, cellular, and tissue levels[39]. In addition, engineering biology approaches through the development of novel technologies and solutions, such as engineered cells, tissues, and biomaterials can inform the understanding of the ageing process. *BBSRC aims to support the creation of tractable and validated animal and non-animal technologies, including in vitro and in silico models, and their development as standards to drive innovation.*

Increasing the uptake of multi-modal and multi-scale research approaches which incorporate -omic technologies, imaging techniques, high throughput analysis, computational tools, regenerative and

Transformative technologies

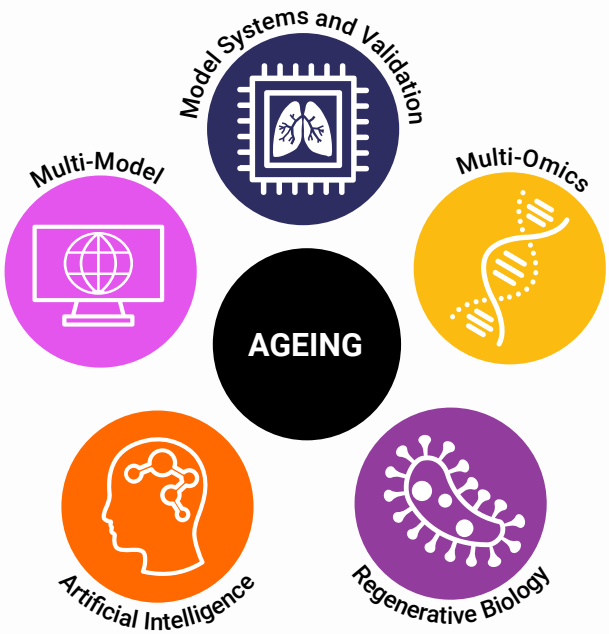


Figure 4. Transformative technologies that can be adopted and developed to understand the biological mechanisms of ageing.

stem cell biology will drive a deeper, integrative understanding of the molecular, cellular, and physiological process of ageing and the factors that influence ageing throughout life.

The progression of *AI technologies coupled with modelling approaches*, including machine learning and deep machine learning techniques, will enable the interrogation and integration of large datasets to accelerate the discovery of, for example, biomarkers of ageing, new geroprotectors, and anti-ageing drugs[40,41]. The data produced from these approaches must be findable, accessible, interoperable and re-usable (FAIR) to allow for bioscience to be translated to the wider ageing research landscape with meaningful impact in a language that everyone understands.

Integration of the *'omes'* such as the genome, proteome, metabolome, exposome[42], transcriptome, phenome, and responsome[43], how they change over the life course and influence an individual's trajectory should provide valuable information into the biological drivers of lifelong health. This will support the development of a personalised approach to health care and mitigate against exposures to factors that negatively impact on health.

Understanding bidirectional connections between physical, mental and cognitive health

There is a strong link between physical, mental and cognitive health and changes to the status of one aspect of health can have profound impact on another. For example, social isolation and symptoms of depression in older people have also been shown to exacerbate cognitive decline[44] and physical inactivity, with significant implications for both mental and physical health[45,46]. Meta-analyses have also revealed that individuals affected by severe and enduring mental health disorders have more physical health comorbidities and a significantly reduced life expectancy compared to their peers[47], further highlighting the need to understand the complex links between ailing physical and mental health with age, and how interventions to the physiological health of an individual can alleviate symptoms of reduced mental health, or vice versa.

The physiological states of the pathways between mind and body can also exert a significant influence on health. The autonomic nervous system, hypothalamic-pituitary-adrenal axis, and nerves within the gastrointestinal tract link the gut and the brain (the 'gut-brain axis'), allowing the brain to influence not only intestinal activities, including activity of functional immune effector cells, but for the gut to influence mood, cognition, and mental health[48]. Anxiety and depression have well-established links to gastrointestinal disruption[49], but gut microbiota can also impact upon appetite/satiety, mood, and emotional regulation.

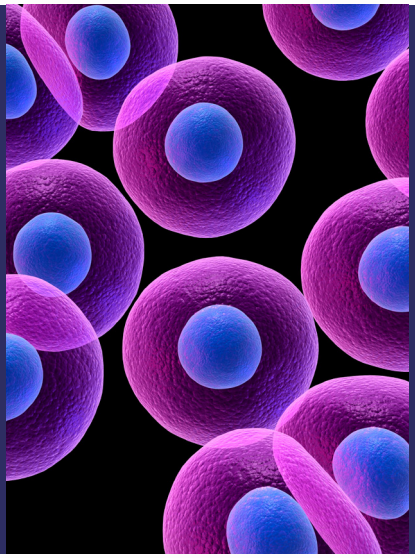
Understanding the bidirectional mechanistic pathways between physical, cognitive and mental health will be vital for better informing appropriate interventions to promote good health and resilience with age. Furthermore, understanding how these pathways can change with other influencing factors, such as sex, physical activity, diet, metabolism, circadian rhythms, stress, cognitive function, and sensory systems (hearing, vision, etc.) could help to improve overall resilience and population health.

CASE STUDY

Turning back time – rejuvenating stem cells

Researchers at the BBSRC Babraham Institute have developed a new technique to rejuvenate skin cells Multi-omic rejuvenation of human cells by maturation phase transient reprogramming | eLife (elifesciences.org)). The technique, which exposes cells to Yamanaka factors (transcription factors that play a key role in the creation of induced pluripotent stem cells), has allowed researchers to rewind the cellular biological clock by around 30 years.

The reprogrammed cells were cultured under normal conditions and were able to restore their skin cell characteristics. This research will provide a better understanding of cell reprogramming and has important implications for regenerative and therapeutic medicine.



Enabling health equity

There is a pronounced socioeconomic gradient to both life expectancy and healthy life expectancy. In the UK, affluent demographics live almost two decades longer in good health than those in the most deprived group[50]. Amongst women, inequalities in life expectancies have increased since 2010, in conjunction with a slight decline in healthy life expectancy. For men, there has been a small increase in healthy life expectancy[51].

It is recognised that early life adversity can impact ageing trajectories. Exposure to a wide range of environments or events during the life course, but particularly during childhood and adolescence, can impact ageing trajectories by initiating biological, psychological and social processes that affect future physical, mental and cognitive health. This results in significant health and social consequences in later life and can cause disparities between biological age and chronological age[52,53]. *Understanding and addressing causal mechanistic relationships of these factors will help identify principal drivers and inform the design of effective interventions to maximise health span and resolve disparities throughout the population*.

The COVID-19 pandemic has had disproportionate impacts upon older people and highlighted that age is the most significant risk factor of becoming severely ill or dying from the disease. People aged 80 or over diagnosed with COVID-19 are seventy times more likely to die than those under the age of 40[54]. Underlying health conditions, comorbidities, or conditions that affect the immune system are amongst factors that play a major role in contributing to severe outcomes from COVID-19[55,56].
In addition, the exposure of existing inequalities and the interconnections between them such as gender, ethnicity, and population demographics, have all been associated with an increased risk of becoming ill with disease[57,58]. Inequalities will need to be considered when unlocking the biological mechanisms of ageing to mitigate the vulnerabilities experienced from negative trajectories.

Addressing sex- and gender-based differences in ageing

The process of ageing includes sex-based differences that accumulate over the lifespan and encompass health and lifestyle factors, which can impact ageing trajectories and mortality. For example, women live longer on average, but report greater impairment in their functional, physical, cognitive, and social abilities as well as in their subjective well-being and physical health in later life[59]. Men may be, on average, physically stronger and have fewer disabilities, but have substantially higher mortality at all ages compared with women[60]. There is also evidence of sex and gender differences in individual dispositions, lifestyle factors, and health behaviors, which may also impact ageing trajectories and interventions. These differences will need to be addressed to reduce the risk of entrenching health inequities based on sex and gender.

Current experimental models do not reflect sex-based differences in physiology. Most widely used models to understand the fundamental biology of ageing are not representative of the impact of biologically female-specific life events, including pregnancy, breastfeeding and menopause. Females present with higher incidence of age-associated diseases, including osteoporosis, sarcopenia and Alzheimer's disease, however, these sex-based differences are not evident in rodent models of ageing[61]. These discrepancies represent an important gap in our understanding of the ageing process in humans and how this is impacted by female biology, as well as sex and gender related exposures. Sex and gender-based differences in ageing biology must be accounted for to understand the interaction between biological, social and cultural drivers that contribute towards inequality in health span. The UK government has recently committed to reducing health inequalities as part of the 'Building an NHS fit for the future' mission. *BBSRC's role in advancing the fundamental biology of ageing and development of the next generation of experimental models for ageing research will be key to achieving this.*

BBSRC are committed to supporting research that adheres to UKRI's guidance, policies and standards on research ethics and integrity, open research, and responsible innovation.

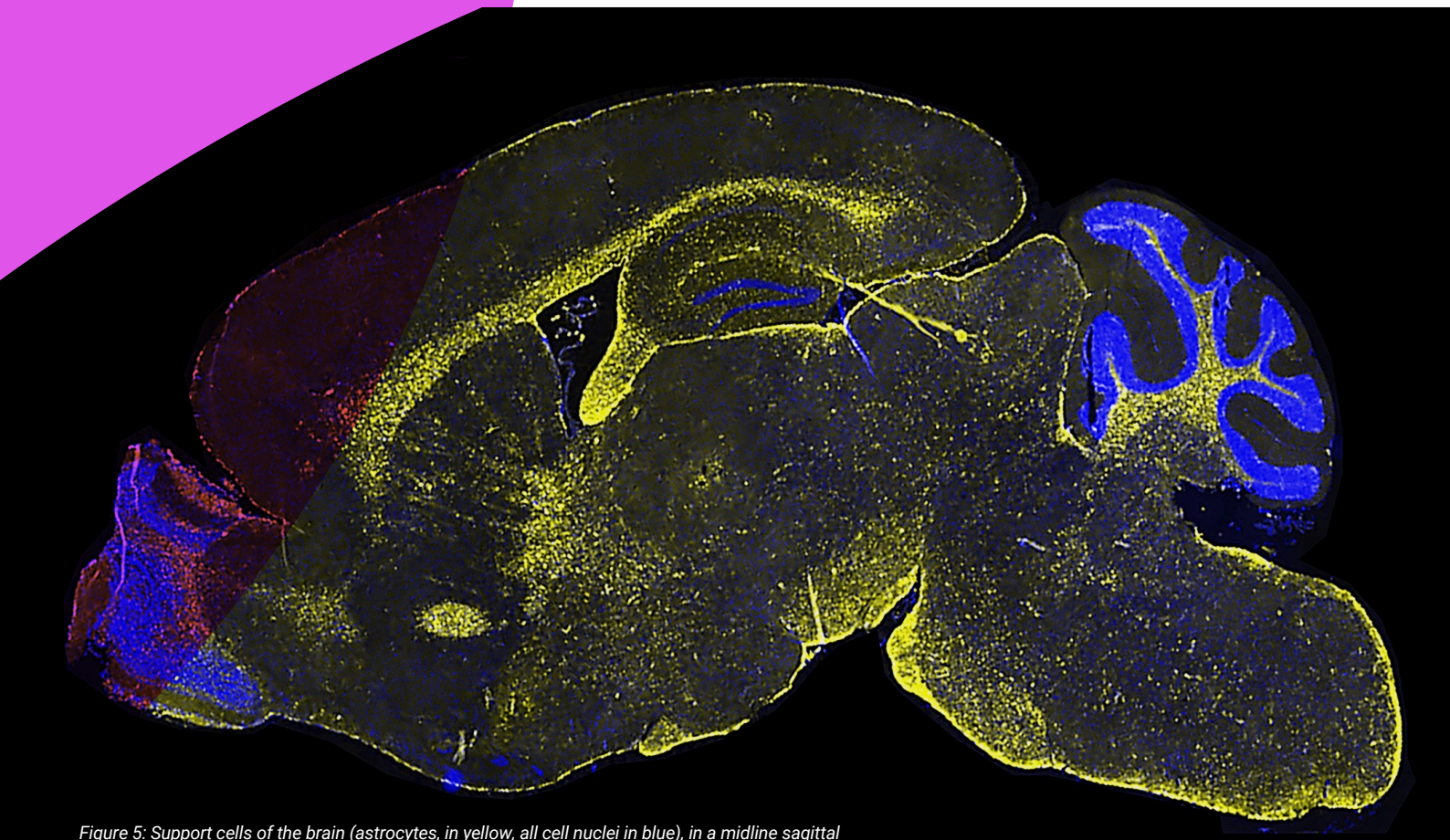


Figure 5: Support cells of the brain (astrocytes, in yellow, all cell nuclei in blue), in a midline sagittal section of aged mouse brain. These cells perform multiple important functions in the brain, including maintaining the blood-brain-barrier, protecting neurons, and regulating immune responses.
Image credit: Dr Aimee Parker, and the Advanced Imaging Facility, Quadram Institute, Norwich UK.

Partnerships

BBSRC discovery science provides the fundamental understanding of the biological mechanisms of ageing across the life course which is an integral part in the translation pipeline of research and innovation into economic and societal impact. BBSRC will continue to participate in the UKRI coordination group for ageing research (XCAR) and actively seek opportunities to work across the UKRI partnership, particularly MRC, ESRC, EPSRC and Innovate UK, to promote and support interdisciplinary research approaches to address the ageing challenge and ensure that discovery bioscience can be translated into meaningful impact for our society.

BBSRC will work with a wide range of stakeholders including academia, industry, government departments and third sector organisations. We will build collaborations with the Department of Health and Social Care (DHSC), the National Institute for Health Research (NIHR), and the Office for Life Sciences (OLS) to provide cross-sectoral networking opportunities to enable biologists, clinicians, engineers, physicians and other practitioners to work together to undertake interdisciplinary research that aims to address the biology of ageing, increase health span, strengthen resilience and reduce health inequalities. Building interdisciplinary partnerships will increase the translation of fundamental biological research into clinical and societal settings and provide robust evidence to inform government departments, health strategies and policy.

BBSRC is an active member of the UK Age Research Funders Forum[62] (UKARFF), an alliance of organisations and government departments that fund research pertaining to older people and ageing. The main purpose of UKARFF is to facilitate networking, provide an opportunity for exchange of information, coordinate activities, and to assist different ageing research funders to view their issues in a wider context.

The British Society for Research on Ageing (BSRA) is committed to funding, supporting and disseminating high quality research into the biology of ageing. BBSRC will continue to be a consistent supporter of the BSRA annual conference, providing sponsorship, when appropriate.

BBSRC has also established links with other organisations with interests in ageing research such as the Academy of Medical Sciences, Action on Hearing Loss, the British Society for Immunology, the British Neuroscience Association, The Vivensa Foundation (formerly the Dunhill Medical Trust), and the Physiological Society and will continue to build engagement with these and other organisations.

BBSRC will continue to seek new partnerships globally, forging collaborations with low- and middle-income countries and building on our existing local, national and global partnerships.

CASE STUDY

Worms in Space: The Molecular Muscle Experiment

Researchers at the University of Nottingham have flown worms to the International Space Station to better understand the mechanistic causes of ageing muscle loss. Age-related muscle loss is a natural part of ageing. After the age of 30 we can expect to lose as much as 3-5% of muscle per decade.

Professor Nathanial Szewczyk and his group established the worm, Caenorhabditis elegans, as a model system for understanding the effect of changes in space, including alterations to muscle and the ability to use energy. So far, the researchers have discovered that the worms become weaker as they age in response to loss of nerve input to the muscle, and in response to diet restriction (Comparative Transcriptomics Identifies Neuronal and Metabolic Adaptations to Hypergravity and Microgravity in Caenorhabditis elegans: iScience (cell.com))

Collaborative approaches with UK Industry

UKRI will exploit its powerful combination of capabilities across the research councils, Innovate UK, and Research England to unleash the UK's innovation potential making the UK the best place in the world to invest and grow a business. BBSRC will work in close collaboration with the UKRI partnership to deliver these goals in the context of the UK's world-leading position in ageing innovation to understand the pathways associated with multi-system ageing and to utilise these to discover new diagnostics, therapeutic and medtech interventions.

BBSRC aims to support innovation in ageing by championing the innate value of fundamental, mechanistic research in informing the development of downstream technologies and interventions, and by tackling the challenges in bridging the gaps between advances in fundamental understanding of human ageing and exploiting that understanding for societal and commercial gain.

Collaborating across UKRI, and with other organisations, BBSRC will foster, grow and strengthen strategic academic-business collaboration across relevant sectors and industry, and with other users of research, to help drive the translation of ageing research and innovation. Furthermore, BBSRC will work with Innovate UK to explore and potentially support pre-competitive and business-led strategic research and innovation challenges and opportunities related to ageing that will in turn help to drive the greatest possible societal and economic impact.

Recognising the potency of emerging technologies to fuel innovation in this field, BBSRC aims to support research that harnesses some of the five critical key technology families highlighted by the UK DSIT Science and Technology Framework[63], to promote healthy ageing and drive our future economy, namely AI, and engineering biology.

BBSRC aims to engage with industrial and commercial sectors to drive basic research through to discovery and proof-of-concept to begin to advance viable products towards preclinical trials and policy interventions.

Research topics will include, but will not be limited to:

- developing and validating models and standards
- identifying biomarkers and mechanistic targets for intervention
- driving the development of senotherapies through the development of novel senolytics and repurposed drugs
- understanding the ageing microbiome, and how the Gut-Immunology-Brain axis affects ageing trajectories
- harnessing our understanding of molecular ageing, including epigenetic clocks, cell regeneration, and DNA damage and repair, to develop novel interventions.

In supporting the UK ageing innovation landscape, BBSRC aims to harness its potential to achieve fundamental gains for society and for our economy in the coming years, narrowing the gap between the experience of the richest and poorest in our society, creating a resilient, healthy older workforce, and underpinning a healthcare system that works for our ageing population.

Prof. Lynne Cox making protein gels in the lab
Credit: Prof. Lynne Cox, University of Oxford.

The Healthspan Machine: Using worms to tackle ageing

Researchers at Durham University used nematodes to unlock the secrets of ageing. Dr David Weinkove and his group found that feeding *C. elegans* different mutants of the bacteria *E. coli* could significantly alter their lifespan. For example, nematodes fed on bacteria which produced less folate both lived and kept moving for longer, indicating that they were remaining healthier for longer.

Weinkove's team then developed an automated method to monitor worm movement over time. By looking at movement rather than at lifespan, the 'Healthspan Machine' can be used to test compounds that promote healthier ageing, not just a longer life. This led to the establishment of the spin-out company Magnitude Biosciences in 2018, that continues to help researchers answer key questions in the areas of ageing, the microbiome, neurodegeneration, toxicity, and transgenics.

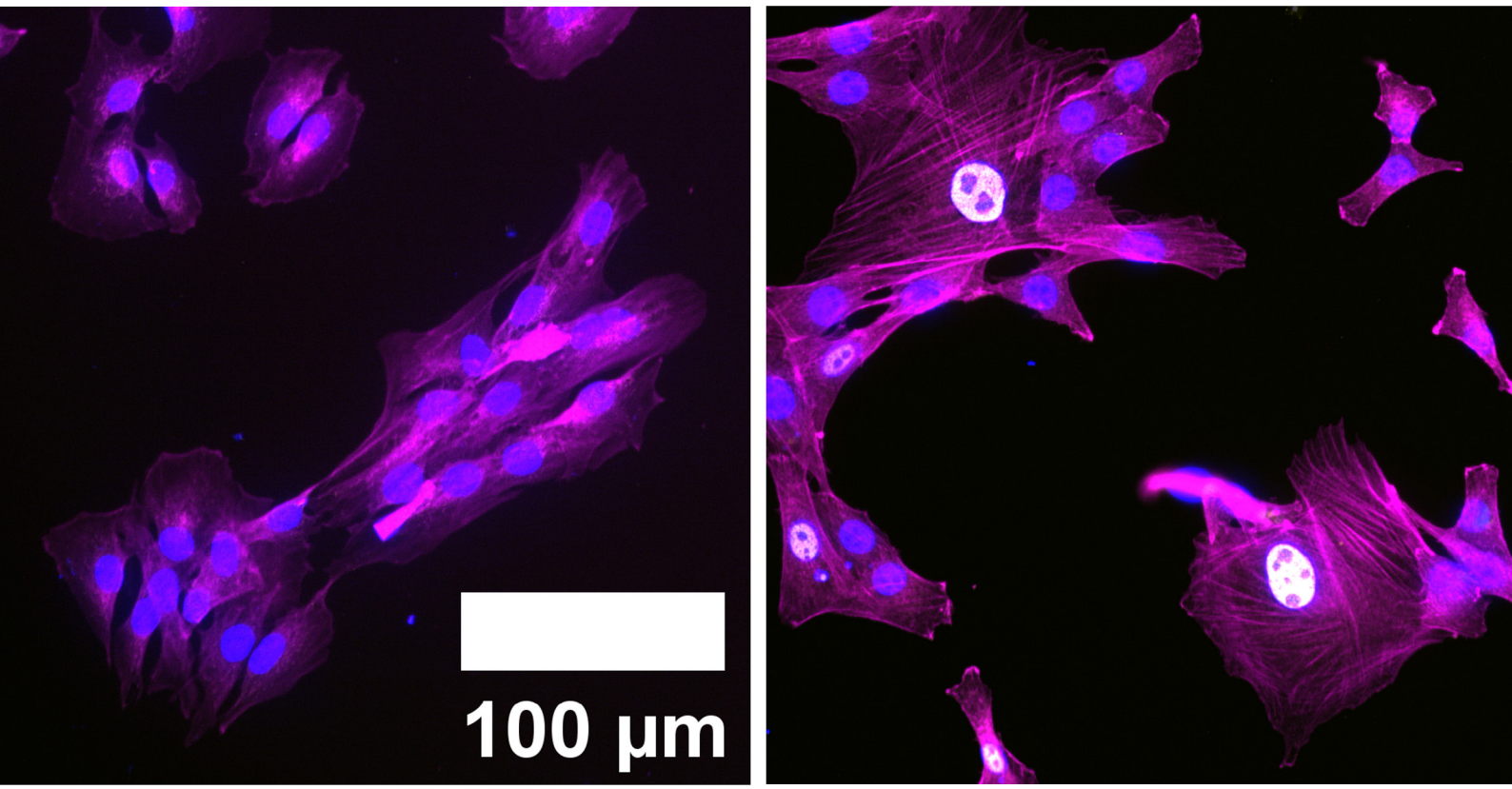


Figure 6: Cells of the aged equine superficial digital flexor tendon (SDFT), a well-established animal model for tendon degeneration, exhibit markers of cellular senescence. Cells isolated from aged SDFT (right) express the senescence marker p21 at a higher rate than cells from young SDFT (left). Cells stained for F-actin (pink), p21 (white), DAPI (blue). Credit: Dr Jack Llewellyn, Royal Veterinary College

Outcomes

In the next five years, BBSRC aims to support knowledge generation that will deliver:

- ejtdpwfsjft!joup!uif!gvoebnfoubm!cjpmphjdbm nfdibojtnt!pg!uif!bhfjoh!qspdftt!boe efwfmpq!cjpnbslfst!pg!bhfjoh!uibu!dbo qsfejdu!boe!npjups!bhfjoh!usbkfdupsjft
- voefstuboejoh!pg!uif!jnqbdu!pg!fyusjotjd gbdupst!boe!jofrvbmjujft!bdspttuif mjgfdpvstf!up!qspnpuf!b!ifbmuiz!tubsujoh qpjou!jo!fbsmz!mjgf!boe!fobcmf!ifbmuijfs usbkfdupsjft
- bqqspqsjbuf!npefmt!gps!tuvezjoh!bhfjoh boe!uif!usbotmbujpo!qbuixbzt!up!qptjujwfmz jnqbdu!po!ivnbo!ifbmui
- voefstuboejoh!pg!dsjujdbm!qfsjpet!xifo joufswfoujpo!jt!sfrvjsfe!boe!xjmmcf!nptu jnqbdugvm!up!fyufoe!ifbmuitqbo!boe!rvbmjuz pg!mjgf!jo!mbufs!zfbst
- voefstuboejoh!joup!uif!cjejsfdujpobm dpoofdujpot!cfuxffo!nfoubm!boe!qiztjdbm ifbmui!uispvhipvu!uif!mjgfdpvstf
- joufsejtdjqmjobsz!xpsljoh!uispvhi ofuxpsljoh!pqqpsuvojujft-!tublfipmefs fohbhfnfou-!efwfmpqjoh!qbsuofstijqt-boe!uif!ejttfnjobujpo!pg!jogpsnbujpo!boe sftfbsdi!pqqpsuvojujft

Key indicators of success

These will include:

- jnqspwfe!voefstuboejoh!pg!uif!npfdvmbs-dfmmvmbs!boe!qiztjpmphjdbm!qspdfttft uibu!pddvs!uispvhipvu!uif!mjgfdpvstf!boe uifjs!nevmbujpo!cz!fyusjotjd!gbdupst!boe jofrvbmjujft
- jnqmfnfoubujpo!pg!bqqspqsjbuf!npefm tztufnt!up!tuvez!cjpmphjdbm!nfdibojtnt pg!bhfjoh!boe!fobcmf!uif!usbotmbujpo!pg sftfbsdi!pvudpnft!up!cfofgju!cpui!ivnbo boe!bojnbm!ifbmui
- jodsfbtfe!efwfmpqnfou!boe!vqublf!pg!opwfm joufswfoujpot!boe!ufdiopmphjft!up!sbqjemz bewbodf!sftfbsdi!po!bhfjoh!boe!jnqspwf ivnbo!ifbmui
- jnqspwfnfout!joup!foibodjoh!uif!rvbmjuz!pg nfoubm!boe!qiztjdbm!ifbmui!uispvhipvu!uif mjgfdpvstf
- ftubcmjtife!dpmmbcpsbujwf!qbsuofstijqt!xjui puifs!gvoefst!boe!tublfipmefst!up!bewbodf ejtdpwfsz!boe!fotvsf!uif!usbotmbujpo!pg sftfbsdi!pvuqvut!up!cfofgju!bmmjo!tpdjfuz
- joufswfoujpot!uibu!jnqspwf!uif!cjpmphjdbm bhfjoh!qspdfttt!cz!jefoujgzjoh!cjpnbslfst!pg bhfjoh!boe!voefstuboejoh!dsjujdbm!qfsjpe)t* xifo!joufswfoujpo!jt!sfrvjsfe!boe!xjmmcf nptu!jnqbdugvm

BBSRC ageing working groups

ANNEX ONE

Ageing across the lifecourse expert working group members

Linda Partridge (Chair)	University College London
Arne Akbar	University College London
Richard Barrett-Jolley	University of Liverpool
Simon Carding	Quadram Institute Bioscience
Joao Pedro de Magalhaes	University of Liverpool
Deborah Dunn-Walters	University of Surrey
Stephen Felstead	Juvenescence
Jon Houseley	Babraham Institute
Meena Kumari	University of Essex
Claudia Metzler-Baddeley	Cardiff University
Susan Ozanne	University of Cambridge
Debra Skene	University of Surrey
Emma Stevenson	Newcastle University

Ageing focus working group members

Linda Partridge (Chair)	University College London
Arne Akbar	University College London
Jon Houseley	Babraham Institute
Meena Kumari	University of Essex
Claudia Metzler-Baddeley	Cardiff University
Susan Ozanne	University of Cambridge
Colin Selman	University of Glasgow

Ageing immunology expert working group members

Janet Lord (Chair)	University of Birmingham
Mark Coles	University of Oxford
Deborah Dunn-Walters	University of Surrey
Steve Felstead	Juvenescence
Lorna Harries	University of Exeter
Sian Henson	Queen Mary University of London
Michelle Linterman	Babraham Institute
Jessica Teeling	University of Southampton
James Turner	University of Bath
Praveen Yaqoob	University of Reading
Kev Dhaliwal	University of Edinburgh

ANNEX TWO

This Annex outlines over 25 years of BBSRC strategic investments in ageing research from 1997 to our current activities in 2024. In addition to programme mentioned below, BBSRC funds broad range of ageing research through its Responsive Mode investing approximately £20M per annum along with funding ageing research at its strategically funded Institutes: Babraham, Earlham and Quadram.

UK activities

Early investment focused on building a world-class research base in the biology of ageing with the establishment of the **Science of Ageing** (SAGE) initiative in 1997 and continued in 2001, with the launch of the **Experimental Research on Ageing** (ERA) initiative that focused on understanding the basic biology of healthy ageing at the molecular, cellular, systems and behavioural levels.

Since 2003, BBSRC has driven predictive, integrative and systems approaches in bioscience and advances in systems biology through the application of computational and mathematical modelling techniques to enable more rapid understanding of complex biological problems. In 2005, BBSRC funded the **Centre for Integrated Systems Biology of Ageing and Nutrition** (CISBAN) at Newcastle University to advance understanding of the complex mechanisms underpinning the ageing process and how these are affected by nutrition.

The joint BBSRC/EPSRC **Strategic Promotion of Ageing Research Capacity** (SPARC) programme (2005-08) supported capacity building and pump-priming activities for design, engineering and biological ageing research, and engagement with policy makers, care and service professionals and older people themselves.

In 2007, BBSRC and Research into Ageing[64] launched a **Joint Highlight on the Ageing Bladder and Bowel** to raise awareness and encourage research applications to increase our understanding of the physiology of the ageing bladder and bowel; and to explore preventative measures, treatments and diagnosis of urinary and faecal incontinence.

The joint MRC/BBSRC **Systems Immunology of the Human Lifecourse** initiative was announced in 2012 with the aim to use systems medicine to study immunological processes in relation to the human life-course, in healthy individuals or those with disease states.

The BBSRC and Action on Hearing Loss Joint Highlight notice on the lifecourse of the auditory system (2014) aimed to increase our understanding of the lifecourse of the auditory system and investigate prevention and treatments of hearing loss.

Exposure to space environments, in particular microgravity, causes deconditioning of physiological systems analogous to accelerated ageing. BBSRC supported four research projects to participate in the European Space Agency **Life Science Research Using the Human Spaceflight Analogue 'Bed Rest'** in 2014. The long-term bedrest study (60 days) investigated the effects of a nutritional supplement as a countermeasure to the 'microgravity' deconditioning of physiological systems to provide new insights to the biological mechanisms behind the physiological changes associated with spaceflight, ageing and a sedentary population.

The **joint BBSRC-NC3Rs highlight notice on new approaches to ageing research** in 2018 aimed to encourage the development of new and innovative models and approaches for ageing research, reducing the current reliance on mammalian models, as well as addressing the gaps in terms of scientific utility and relevance to human ageing.

ANNEX TWO

UK activities

Due to the complex and multi-faceted nature of ageing, UKRI has formed strategic partnerships to enable the delivery of multidisciplinary and innovative research to advance ageing research including:

- The New Dynamics of Ageing Programme (2005-2008)[65]
- The Lifelong Health and Wellbeing Programme (2008-2015)[66]
- Healthy Ageing Challenge supported by the Industrial Challenge Fund (2017)[67]
- The National Innovation Centre for Ageing (2017)[68]
- UKRI securing better health, ageing and wellbeing strategic theme (2023 - 2029)[69]

In 2022, BBSRC and MRC jointly funded challenge-led, Ageing Across the Lifecourse Interdisciplinary Research Networks to bring together novel and a diverse range of researchers and stakeholders. The aim is to enhance collaboration, build interdisciplinary communities and knowledge exchange in the field of ageing research to better understand the fundamental biological mechanisms of ageing.

In 2023, UKRI funded Ageing Research Development Awards, with the aim to develop tractable areas of interdisciplinary research to secure better health and wellbeing for individuals as they age. Research Development Awards develop areas of ageing research across the breadth of UKRI's remit, enabling the development of interventions to reduce time spent in poor health in later life.

International activities

BBSRC has supported many successful international collaborative partnerships.

In 2008, the **Trans-Atlantic Collaborative Research on the Biology of Ageing** initiative in partnership with the US National Institute of Aging (NIA) was launched. The aim of the programme was to encourage the development of collaborative research teams with expertise focused on understanding the molecular, cellular, biochemical, and physiological mechanisms underlying biological aging and the development of age-related functional decline. BBSRC continued the encouragement of collaborative partnerships, and in 2012 co-funded a four-year scheme with NIA to establish UK-US projects within the ageing field.

BBSRC and ESRC participated in the **European Research Area in Ageing** (ERA-AGE 2) call to support multinational and multidisciplinary research applications on Active and Healthy Ageing Across the Lifecourse in 2011. It aimed to provide research knowledge to help European countries to respond to population ageing and to increase healthy life expectancy by two years within the European Union by 2020.

The US National Institute of Ageing, BBSRC and ESRC jointly funded the **Interdisciplinary Research Network on Early Adversity and Later Life Reversibility** (2013-2020) via the NIA High Priority Behaviour and Social Research Networks Call. It focused on later-life interventions to reverse effects of early life adversity (ELA); such as low socio-economic status, stressful experiences, poor maternal diet, lifestyle; and identifying opportunities for later-life reversibility/ remediation of phenotypes associated with ELA.

In 2020, BBSRC and MRC supported UK researcher participation in the Healthy Diet, Healthy Lives Joint Programming Initiative call on the **Development of targeted nutrition for prevention of undernutrition for older adults** (PREVNUT). The call aimed to support transnational, collaborative research projects that address the prevention of undernutrition in European older citizens through the consumption of appropriate nutritious food and promote a better life in later life.

The Ageing Research Networks Global Partnering Awards were funded by the UK Research and Innovation (UKRI) securing better health, ageing and wellbeing strategic theme in 2022. This investment supports a global research consortium that aims to identify how ethnicity, lifestyle, culture, economics and environment impact healthy ageing. The awards bring together the UK Ageing Research Networks with collaborators from South Asia, the USA and Canada, and Europe.

BBSRC Strategically Supported Institutes

BBSRC supports eight strategic institutes representing a portfolio of vibrant, dynamic and diverse bioscience national capabilities. BBSRC supports world-leading research through institute strategic programmes grants as well as investment in their core capabilities. The institutes have strong links with business, industry and the wider research community and play a key role in supporting and shaping policy development both in the UK and internationally.

Three of these institutes have ongoing research themes in ageing research: Babraham Institute, Quadram Institute and Earlham Institute.

The Babraham Institute is dedicated to studying the biology of ageing to help us live healthier lives and making the fundamental discoveries needed to maintain health and improve wellbeing throughout life. Research at Babraham is split into three programmes:

- Epigenetics: Understanding epigenetic control across the lifecourse. Including how changes in the balance of cellular metabolites affect epigenetic systems, how epigenetic states are established and maintained and how epigenetic states change over the life course.
- Signalling: Defining how cellular signalling pathways act together to coordinate cellular responses and how signalling mechanisms are affected by age. Including understanding of the cellular responses to stress and how this changes across the life course and identifying new strategies to sustain the health of ageing cells, tissues and organisms.
- Immunology: Advancing understanding of the molecular and cellular basis of immunity to protect and improve health across the life course. Including understanding the molecular and cellular basis of immunity and mechanisms of resilience and repair.

The Quadram Institute's mission is to deliver healthier lives through innovation in gut health, microbiology and food. This includes understanding the role of the microbiome in throughout the life course and how this can impact on the biology of ageing.

The Earlham Institute is a hub of life science research, training, and innovation focused on understanding the natural world through the lens of genomics. Ageing research at Earlham focuses on understanding the biological processes of ageing at the cellular level using single cell technologies.

References

1 Bioscience for an integrated understanding of health: strategic framework – UKRI
2 https://www.ukri.org/publications/bbsrc-forward-look/
3 UKRI Strategy 2022-2027
4 Ageing and health (who.int)
5 Overview of the UK population – Office for National Statistics (ons.gov.uk)
6 The-State-of-Ageing-2022-online.pdf (ageing-better.org.uk)
7 UKRI Strategy 2022-2027
8 In the context of modern society, including the roles of nutrition, physical activity, stress, chronobiology, technology and behaviour
9 Ageing population | Centre for Ageing Better (ageing-better.org.uk)
10 The-State-of-Ageing-2022-online.pdf (ageing-better.org.uk)
11 House of Lords - Ageing: Science, Technology and Healthy Living - Science and Technology Select Committee (parliament.uk)
12 Health Equity in England: The Marmot Review 10 Years On - The Health Foundation
13 Build an NHS fit for the future – The Labour Party
14 Chief Medical Officer's annual report 2023: health in an ageing society - GOV.UK
15 The future of ageing - The Nuffield Council on Bioethics (nuffieldbioethics.org)
16 The State of Ageing 2023-24 | Centre for Ageing Better
17 THE 17 GOALS | Sustainable Development (un.org)
18 UN Decade of Healthy Ageing (who.int)
19 BBSRC integrated understanding of health strategic framework – UKRI
20 Hallmarks of aging: An expanding universe: Cell
21 Telomere dysfunction in ageing and age-related diseases | Nature Cell Biology
22 DNA methylation-based biomarkers and the epigenetic clock theory of ageing | Nature Reviews Genetics
23 Autophagy in healthy aging and disease | Nature Aging
24 Cellular senescence in ageing: from mechanisms to therapeutic opportunities | Nature Reviews Molecular Cell Biology
25 The gut microbiome as a modulator of healthy ageing | Nature Reviews Gastroenterology & Hepatology
26 Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty | Nature Reviews Cardiology
27 Epigenetic regulation of aging: implications for interventions of aging and diseases | Signal Transduction and Targeted Therapy
28 Inflammation, epigenetics, and metabolism converge to cell senescence and ageing: the regulation and intervention | Signal Transduction and Targeted Therapy (nature.com)
29 Exogenous stressors include the environment, chronic infections, social changes, physical inactivity, poor diet.
30 Endogenous stressors include DNA damage, telomere dysfunction, epigenetic disruption, and oxidative stress.
31 'Inflammation clock' can reveal body's biological age (nature.com)
32 Frontiers | Aging of the Immune System: Research Challenges to Enhance the Health Span of Older Adults | Aging (frontiersin.org)
33 The aging gut microbiome and its impact on host immunity | Genes & Immunity (nature.com)
34 Marriage and Gut (Microbiome) Feelings: Tracing Novel Dyadic Pathways to Accelerated Aging (nih.gov)
35 Aging-Associated Changes in the Adult Human Skin Microbiome and the Host Factors that Affect Skin Microbiome Composition - Journal of Investigative Dermatology
36 Healthy ageing: what role can nutrition play? | The Nutrition Society
37 Nutrition and sarcopenia of ageing (nih.gov)
38 Old and new models for the study of human ageing | Nature Reviews Molecular Cell Biology
39 Opportunities for organoids as new models of aging (nih.gov)
40 Artificial intelligence in longevity medicine (nature.com)
41 Artificial intelligence for aging and longevity research: Recent advances and perspectives - ScienceDirect
42 The exposome is broadly defined as "all environmental exposures that a person experiences from conception to death"
43 The responsome is the collection of all physiological responses that can be influenced by the multitude of chemicals and environmental stimuli to which humans are exposed
44 Loneliness, depression and cognitive function in older U.S. adults - Donovan - 2017 - International Journal of Geriatric Psychiatry -Wiley Online Library
45 The relationship between physical and mental health: A mediation analysis - ScienceDirect
46 Population level physical activity before and during the first national COVID-19 lockdown: A nationally representative repeat cross-sectional study of 5 years of Active Lives data in England -The Lancet Regional Health – Europe
47 A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders - Firth - 2020 - World Psychiatry - Wiley Online Library
48 The Gut-Brain Axis: Influence of Microbiota on Mood and Mental Health - PMC (nih.gov)
49 Gut Microbiota's effect on mental health: The gut-brain axis
50 Health state life expectancies by national deprivation deciles, England - Office for National Statistics (ons.gov.uk)
51 Health Equity in England_The Marmot Review 10 Years On_full report (1).pdf
52 Special Report: The Biology of Inequalities in Health: The Lifepath Consortium (nih.gov)
53 Frontiers | Reducing Health Inequalities in Aging Through Policy Frameworks and Interventions | Public Health (frontiersin.org)
54 Disparities in the risk and outcomes of COVID-19 (publishing.service.gov.uk)
55 Frontiers | Aging, Immunity, and COVID-19: How Age Influences the Host Immune Response to Coronavirus Infections? | Physiology (frontiersin.org)
56 COVID-19 advice - High risk groups | WHO Western Pacific
57 Aging in COVID-19: Vulnerability, immunity and intervention -ScienceDirect
58 Covid-19-and-inequalities-IFS.pdf
59 Gender Specifics of Healthy Ageing in Older Age as Seen by Women and Men (70+): A Focus Group Study
60 Men: good health and high mortality. Sex differences in health and aging | Aging Clinical and Experimental Research
61 Female aging: when translational models don't translate | Nature Aging
62 UK Ageing Research Funders' Forum - The Dunhill Medical Trust
63 The UK Science and Technology Framework: taking a systems approach to UK science and technology
64 Research into Ageing was the research arm of Help the Aged which has since been merged to form to UK Age.
65 New Dynamics of Ageing
66 Lifelong Health & Wellbeing - Research - Medical Research Council (ukri.org)
67 Healthy ageing challenge – UKRI
68 Adding intelligence to ageing | National Innovation Centre Ageing (uknica.co.uk)
69 https://www.ukri.org/what-we-do/browse-our-areas-of-investment-and-support/securing-better-health-ageing-and-well-being/(ukni

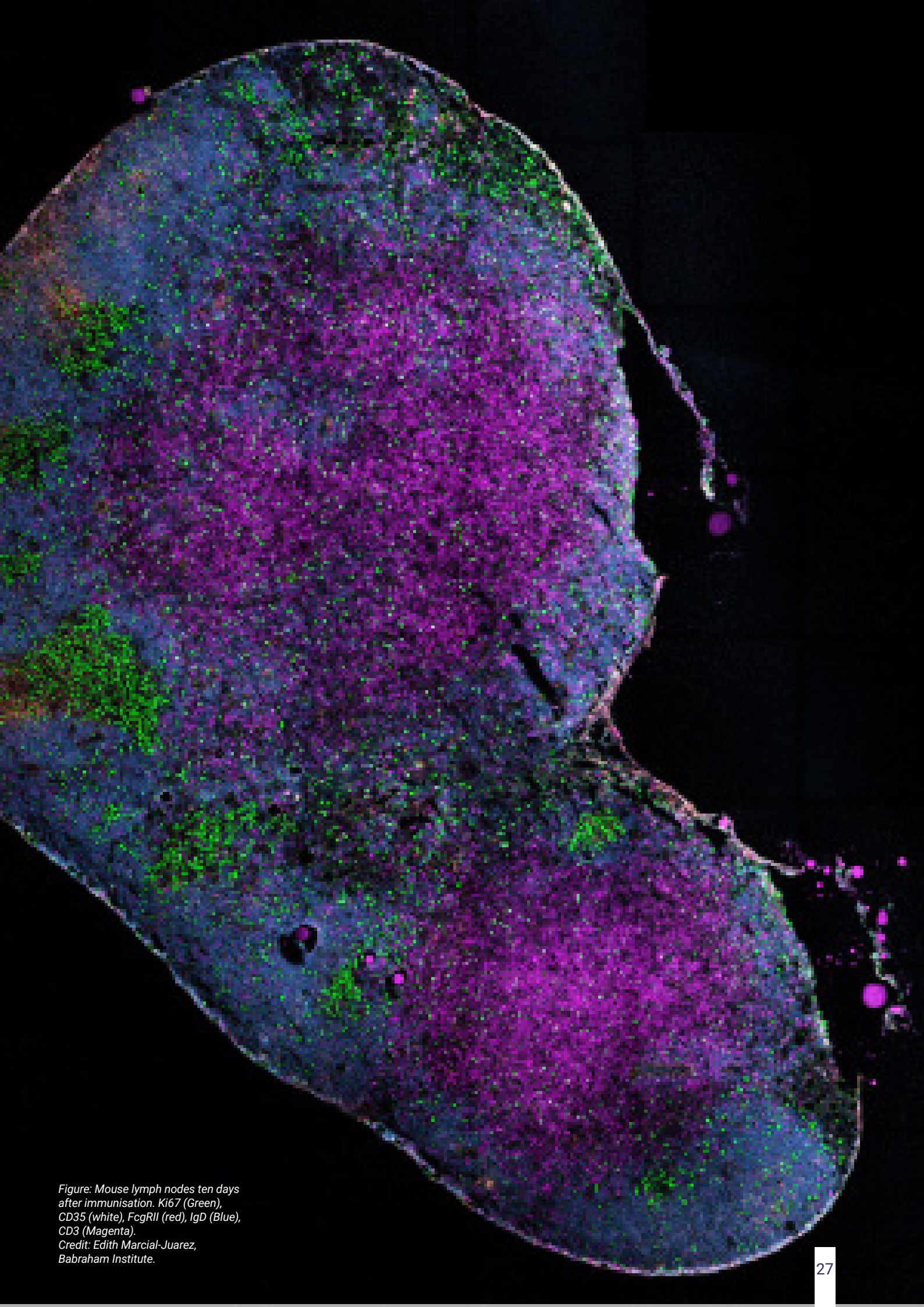


Figure: Mouse lymph nodes ten days after immunisation. Ki67 (Green), CD35 (white), FcgRII (red), IgD (Blue), CD3 (Magenta).
Credit: Edith Marcial-Juarez, Babraham Institute.


Biotechnology and
Biological Sciences
Research Council