UNIVERSITY OF OXFORD

RADCLIFFE DEPARTMENT OF MEDICINE

Research Strategy

2025-2030

Using science to support a healthier, longer life for all

Foreword

I am delighted to launch our new Research Strategy, which responds to opportunities and challenges that are driving a need for change, building on the outstanding and impactful research delivered by the Radcliffe Department of Medicine (RDM) over the last 13 years.

Recent scientific advances have revealed greater common ground between our key areas of research: cardiovascular disease, diabetes and metabolism, immune diseases, blood diseases, and cancer.

There is also greater synergy among the new technologies we can use to make progress in each area, such as genomic regulation and manipulation, immune and stem cell biology, single cell techniques, tissue and clinical imaging, informatics and AI, and clinical studies involving human model systems, experimental medicine and trials.

Against this backdrop of exciting new opportunities, many sources of research funding have become more restricted, our buildings and facilities have not all kept pace with our research successes, and there are areas where we could be more efficient.

Our new Research Strategy sets out how we will build on the cross-disciplinary opportunities to maximise our research impact, and attract the necessary funding to ensure an academic environment that supports our exceptional people.

Professor Keith Channon, Head of the Radcliffe Department of Medicine

RDM at a glance

Research

100 Principal investigators

Impact

18 Spinout companies

People

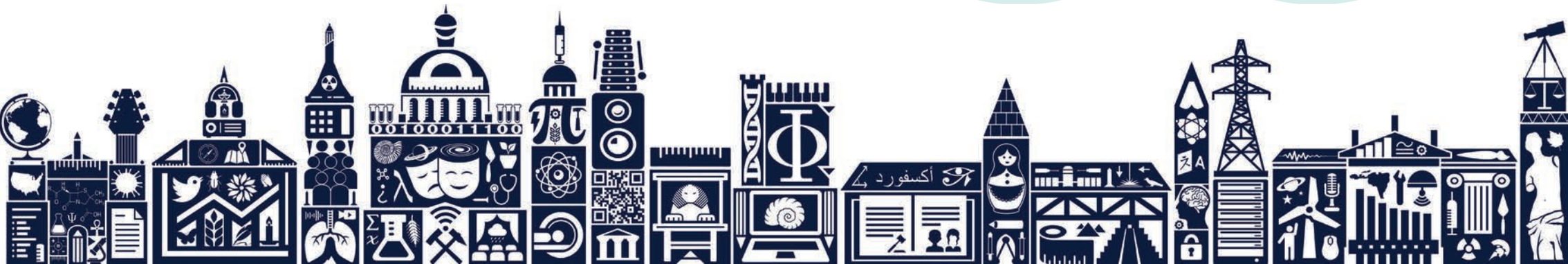
16 Academic staff
298 Research staff
140 DPhil students
120 Research support staff
98 Professional services staff

Finance

£47m Research income
£22m Non-research turnover
£69m turnover

Estate

3 sites in Headington
13,400m^2



Vision

To use science to support a healthier, longer life for all.

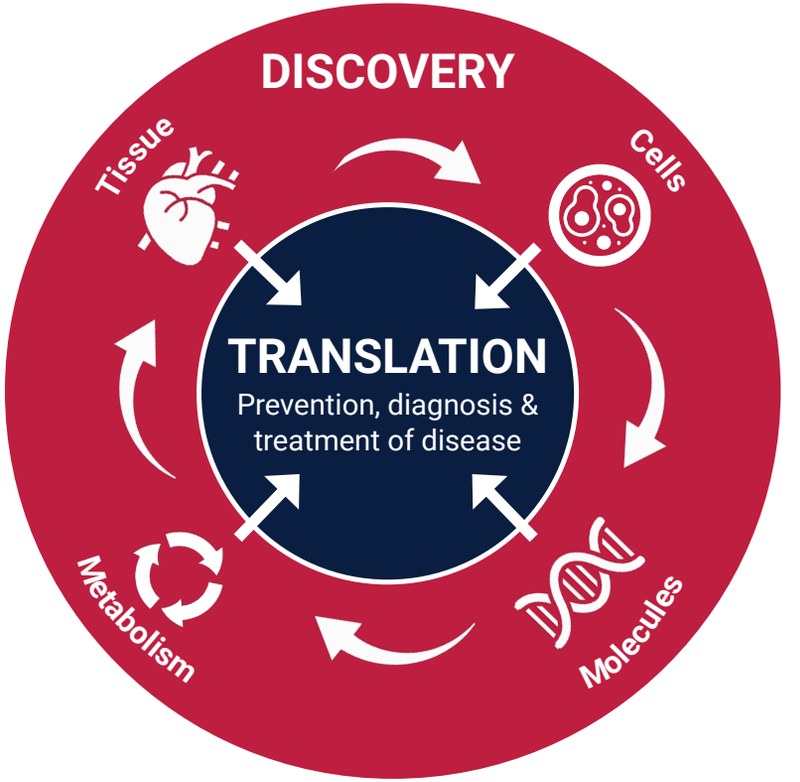
Mission

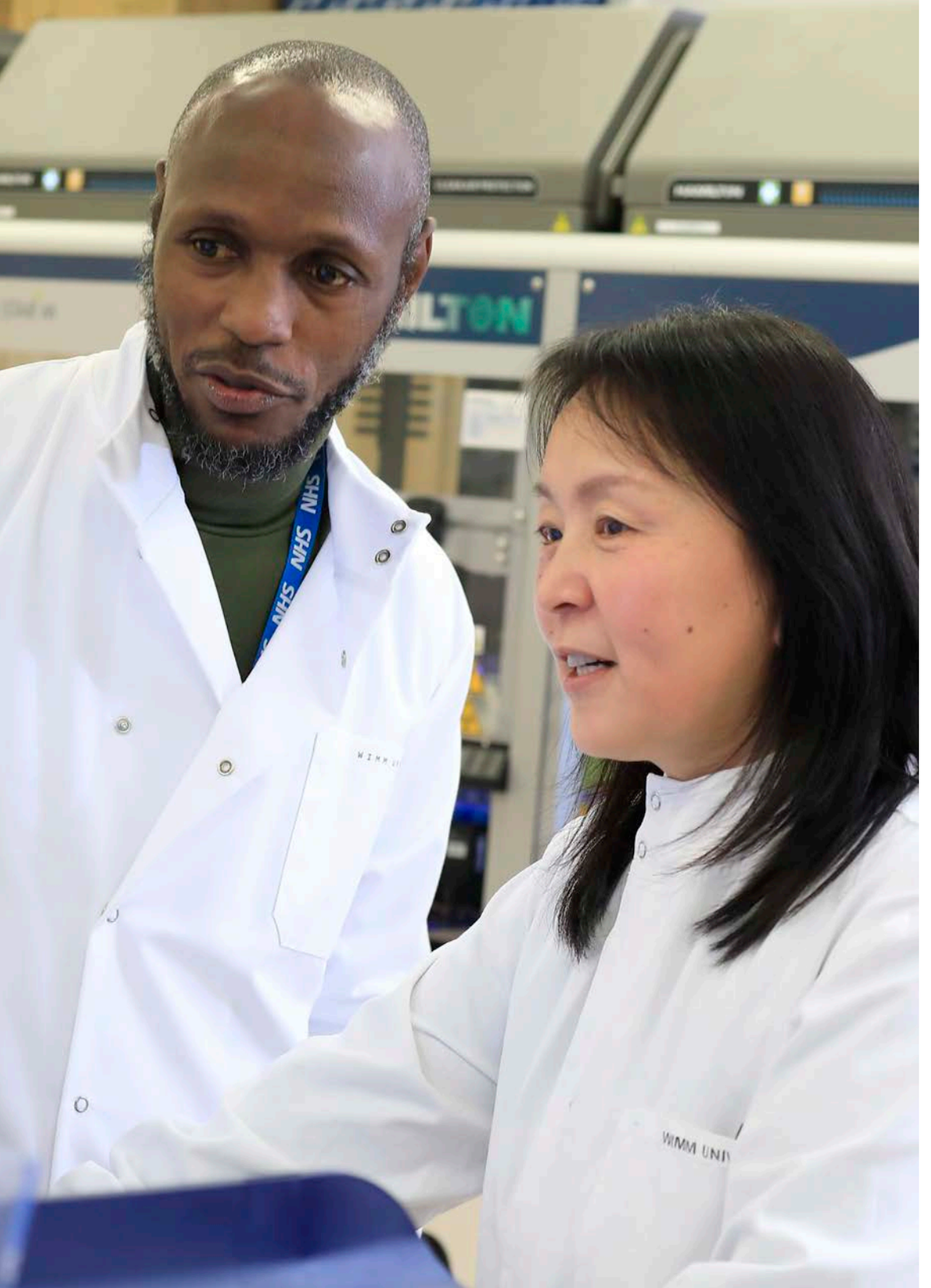
To improve health through world-leading cross-disciplinary research to understand shared mechanisms of disease and to accelerate the transition from scientific discovery to clinical care.

Strategy

Over the next five years we will:

- Deliver high impact research that generates new insights into the causes, prevention and treatment of diseases
- Drive interdisciplinary cross-cutting themes to foster collaboration, shared platforms and capabilities
- Lead clinical trials of new treatments that impact on diagnosis and patient care
- Develop new technologies in experimental and clinical imaging that enable new research insights and clinical translation
- Develop IP leading to new spinouts and licence deals





Objectives and Enablers

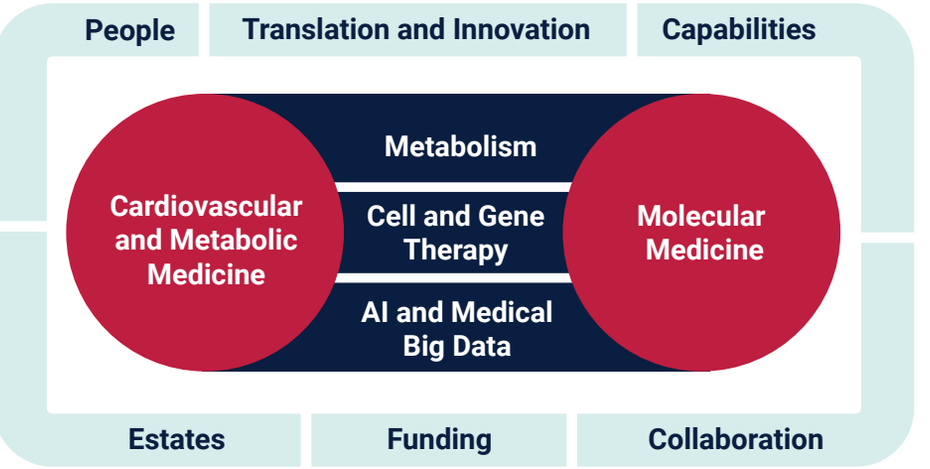
Our vision and mission will be delivered through transformative research in two Sections: Cardiovascular and Metabolic Medicine, and Molecular Medicine.

These two Sections share many approaches, capabilities and areas of linked research. To promote cross-disciplinary advances, more effective knowledge exchange and resource efficiencies, we will build cross-cutting research themes in areas that include:

- Metabolism
- Cell and Gene Therapy
- AI and Medical Big Data

The success of RDM's research strategy will require support in key areas. We will focus on six core enablers:

- People
- Collaboration
- Capabilities
- Translation and Innovation
- Funding
- Estates



Cardiovascular and Metabolic Medicine

RDM's Section of Cardiovascular and Metabolic Medicine will bring together our major research programmes in cardiovascular medicine, acute stroke, diabetes, endocrinology and metabolism, aiming to understand the shared mechanisms of disease and increasing cross-disciplinary synergies.

We will investigate the mechanisms involved in maintaining health across all cells and tissues relevant to cardiovascular, neurovascular and metabolic diseases, to advance diagnosis, prevention and treatment. The Section of Cardiovascular and Metabolic Medicine will capitalise on its strengths in discovery science and experimental models, -omics, translation and clinical trials, underpinned by capabilities in areas such as experimental medicine, clinical imaging and metabolism.

Key questions and approaches include:

What are the shared mechanisms that drive multi-morbid cardiovascular and metabolic disease?

1. Understand normal tissue function, homeostasis, and its dysregulation in the development of cardiovascular and metabolic disease.
2. Adopt a multi-system, multi-organ approach to identify unifying upstream mechanisms for multi-morbid cardiovascular and metabolic disease.
3. Understand the role of inflammation and circadian rhythm in the development of cardiovascular and metabolic disease.
4. Extend the focus on immune mechanisms in cardiovascular and metabolic medicine, particularly stem cell 'training' and cellular ageing, linking with blood, immune diseases and cellular ageing.

How can we harness innovative methods such as AI to improve scientific insight into disease and patient outcomes?

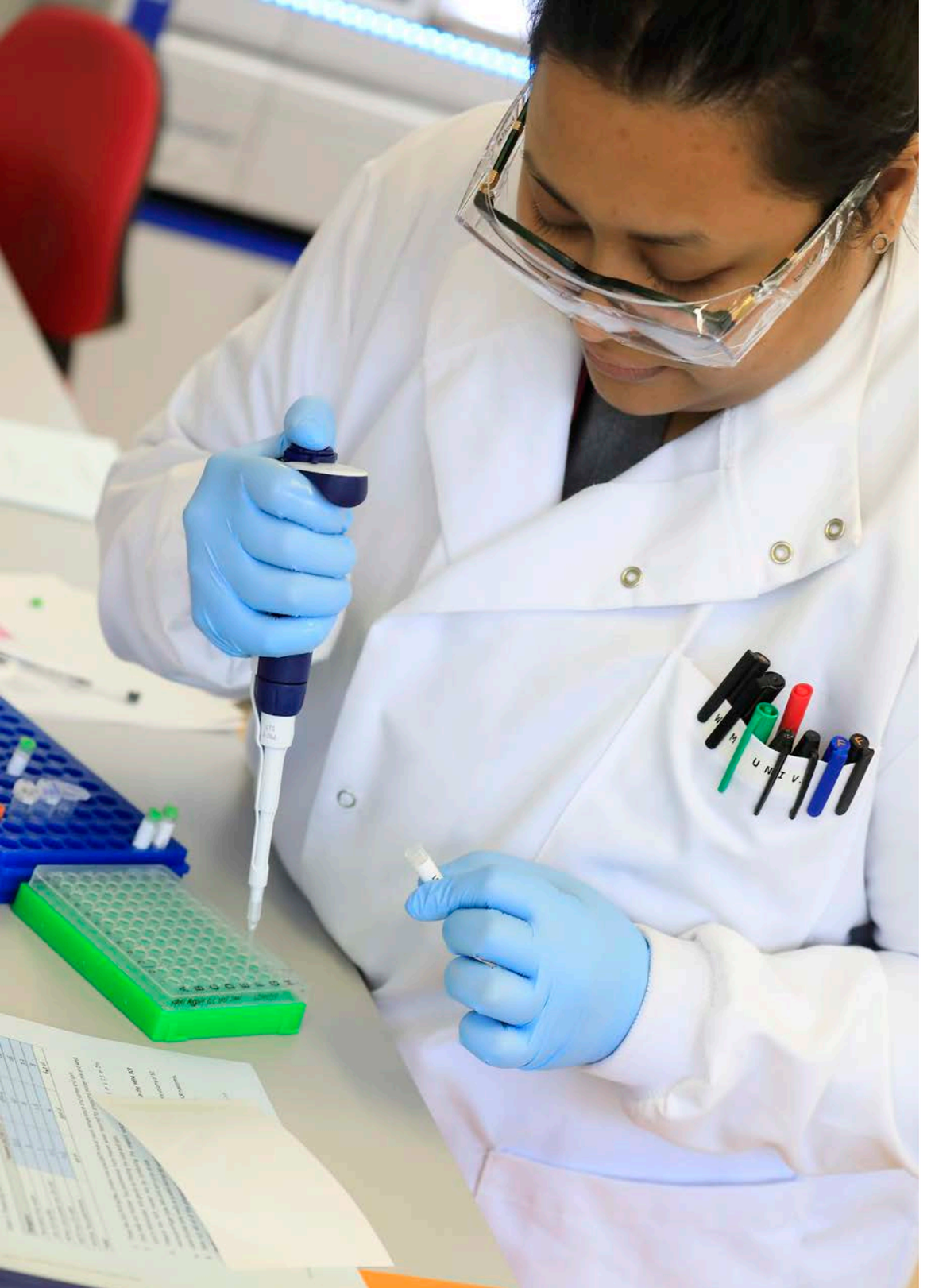
1. Use multi-modal imaging and advanced computational approaches at the tissue and multi-organ level to identify new mechanisms, targets, and biomarkers to support the development of new therapeutics, diagnostics and interventions.
2. Develop more integrated approaches for AI and core lab activity within all three cardiac imaging modalities (echo, CCT and CMR).
3. Strengthen data science capacity to exploit big data resources such as UK Biobank, Our Future Health, and RDM's clinical and molecular datasets.
4. Build and exploit RDM's data resources, using AI/ML/deep learning to interrogate new and existing data sets.

How do modifiable risk factors interact and contribute to cardiometabolic disease pathogenesis?

1. Understand the progression of cardiometabolic disease and the impact of factors including age, sex, body composition, genetics, and circadian rhythms, using big data, computational models, imaging, and omics to identify optimal time and methods to intervene or prevent the disease.
2. Improve understanding of the interrelationships among obesity, cardiovascular and metabolic disease to support the development and testing of novel drug therapies.

How can we improve the discovery and translation of innovative approaches to treat cardiometabolic disease?

1. Build cross-disciplinary capacity in cardiometabolic clinical research facilities and clinical trials infrastructure to support activity across cardiac, metabolic disease and stroke.
2. Develop better infrastructure for proof-of-principle clinical trials and continue to work with the Oxford University Hospitals NHS Foundation Trust to facilitate faster and smoother approval paths for clinical studies and trials.
3. Develop new diagnostic tools and treatments for genetic cardiometabolic disease. Investigate how genotype and phenotype impact prediction, presentation and treatment of disease.
4. Develop genetic therapies for inherited heart muscle diseases (via the CureHeart international collaborative).
5. Expand the use of human models (iPSC-derived systems, CRISPR-edited cells, adipose-derived models) and establish a dedicated CRISPR facility.
6. Identify novel metabolic treatments for heart disease and expand infrastructure for metabolic imaging.
7. Develop and trial strategies for prediction, prevention and treatment of multimorbid cardio-metabolic disease.



Molecular Medicine

RDM's Section of Molecular Medicine will combine our strengths in blood and bone marrow, immunology and pathology, exemplified by the Weatherall Institute for Molecular Medicine, applying these discoveries to improve diagnosis and treatment of blood diseases, cancers, infection, inflammatory conditions and ageing.

We will apply new discoveries in the mechanisms of immune-mediated and blood disorders in order to identify new tests, targets, technologies and therapies, across a wide range of diseases, including those in Cardiovascular and Metabolic Medicine, forming cross-cutting research themes. In Molecular Medicine we will support particular expertise in stem cell biology, gene and cell therapy, -omics, gene regulation, bioinformatics and cellular imaging. These programmes span fundamental discovery science, experimental model systems, translational research and experimental medicine, and clinical trials.

Key questions and approaches include:

How do stem cells produce mature blood cells, how is this process altered in disease, and how can we improve the prognosis of patients with both inherited and acquired forms of blood and immune disorders?

1. Foster world-class research on the origin and production of normal and diseased blood cells throughout life, to understand the biology of these cells and how to manipulate them for future cell therapies.
2. Deliver new insights into fundamental cell biology including, mechanisms of DNA damage and repair, epigenetic and niche regulation of haematopoietic cell differentiation, and single cell functional genetics linked to bone marrow ageing and cancer.
3. Understand how germline and somatic genetic mutations affect the behaviour of single cells within the bone marrow and tissues during aging and disease evolution. How human somatic mosaicism arises in bone marrow and barrier tissues and what the consequences of this are for tissue and organ integrity and ageing.
4. Understand normal and malignant haematopoiesis, the impact of cancer driver mutations, the impact of the tumour microenvironment, and develop mouse models to understand blood pathologies.

5. Define mechanistic causes of blood cancers to enable prevention and improved treatment.
6. Understand how cells respond to the environment and retain information in development and disease, including cell signalling, gene regulation, and cytokine production/reaction.

How does the immune system protect tissues and barrier surfaces throughout life, what role does inflammation play in tissue damage, and how can we harness immune mechanisms to develop precision medicine approaches?

1. Deliver transformative insights into fundamental molecular immunology via the development and application of the latest technical advances to key unknowns of the immune system.
2. Define new immune sensing mechanisms, how adaptive B and T cell immunity is regulated within tissues and the role of tissue immunity in barrier defence, injury and repair.
3. Reveal the immune contribution to barrier tissue health through life and at the extremes of age, and how barrier infections can become systemic and life threatening.
4. Shed light on the mechanisms of infection pathogenesis at tissue surfaces particularly with regard to anti-microbial resistant pathogens.
5. Understand how the immune system can be harnessed for tissue health and disease prevention, focusing on engineering immunity to prevent tissue inflammation, cancer, defective repair and invasive infections in vulnerable cohorts.
6. Provide a causal molecular understanding of immune mediated disease pathogenesis to enable precision medicine for these conditions.
7. Drive immune innovation and engineering based on our discovery science via our spinouts, licensing deals and early phase trials.

How can we develop new cell and gene therapies, including in vivo delivery strategies, improved methods of genome editing and cell specific targeting?

1. Develop gene therapy medicinal products (involving the insertion, removal, or alteration of the genetic material within a patient's cells to treat or prevent disease).
2. Create innovative technologies to support the development of new products to tackle disorders of the eye, blood and brain as part of the MRC CoRE in Therapeutic Genomics.
3. Accelerate patient access to somatic-cell medicinal products (where viable cells are modified to provide a treatment) through the Oxford Centre for Advanced Cellular Therapeutics and the creation of a cellular therapy trials unit and cell engineering laboratory.
4. Develop next generation gene transfer and gene editing vectors to minimise immune recognition and improve the safety and potency within in vivo applications.
5. Identify and utilise human genome encoded vectors and genome engineering components (with a focus on developing potential IP and spinouts).
6. Leverage RDM capabilities in cell processing to attract industry cell therapy partnerships.
7. Collaborate across RDM immunological cell biology teams to generate novel cell therapies.

How can we build capabilities across molecular medicine to catalyse research and translation?

1. Innovate with creation of spinouts, licensing deals and early phase trials.
2. Capitalise on our strengths in advanced/4D human tissue models across organs to model disease by securing funding for platforms able to scale and interrogate disease pathways in these models linking to trials based approaches undertaken by the Therapy Acceleration Lab.
3. Capitalise on our strengths in data science, computational methods development and AI based approaches as applied to immune, genetic and haematological diseases by significantly upscaling GPU capacity.
4. Recruit expertise/secure platform in chemistry/quantitation of metabolic flux to assist in our discovery science.
5. Ensure that our research facilities respond to needs and opportunities, to remain internationally leading and state-of-the-art.

Cross-Cutting Research Themes

Many disease mechanisms and scientific approaches are shared between RDM's two Sections of Cardiovascular and Metabolic Medicine and Molecular Medicine. This opens up opportunities to expand our research across historical disciplinary boundaries, with transformative potential.

We will promote cross-cutting research themes to drive this connectivity and collaboration, pump-priming new strategic funding bids and developing new platforms and areas of expertise. The themes will be flexible and responsive to need and opportunities. Current cross-cutting themes include:

Metabolism in Molecular Medicine

We will investigate how metabolism influences disease progression at molecular, cellular and tissue/organ levels, by:

- Generating new collaborations among researchers with a shared interest in metabolism to resolve key medical and scientific questions.
- Expanding and establishing capabilities in cardio-metabolism, immuno-metabolism and other metabolic-related disease.
- Developing partnerships with the Nuffield Department of Medicine in metabolomics, lipidomics, and proteomics research facilities.
- Leveraging clinical trials capabilities and routinely collected NHS data.
- Exploiting existing strengths such as metabolic imaging, single cell biology, microscopy and genome engineering to support translational metabolic research.

Cell and Gene Therapy

We will coalesce innovation and excellence in advanced therapeutics, catalysing the development of new treatments by:

- Generating new collaborations to share expertise and capabilities and accelerate the development of new tools, technologies and treatments.
- Expanding our portfolio of cell therapy processing – providing a rapid pathway from idea to patient for CAR-T and related advanced therapeutics.
- Growing our capabilities across state-of-the-art cell and gene therapy platforms and genome engineering, including Adeno-Associated Virus (AAV) capsid and vector manufacturing.
- Coupling our skills in gene transfer vector design, and adaptive and innate host reactions to create next-generation in vivo gene transfer/gene editing delivery systems.

AI and Medical Big Data

We will develop new capabilities and deploy advanced analytical tools to biological and clinical questions, utilising RDM's large/complex datasets, by:

- Establishing an AI working group to share best practice and strengthen the interface with other units across the University and externally.
- Building a support group for RDM researchers to discover how AI and other similar tools could be used within their research areas.
- Expanding capacity and capabilities in AI methods applied to clinical and research datasets.
- Building capacity in the Centre for Computational Biology, offering leading integrative and AI methodologies defining the molecular pathogenesis of immune mediated diseases and blood disorders.
- Expanding AI capabilities into epidemiology and public health in partnership with others.
- Developing capabilities in AI and digital pathology and linking digitised pathology images with clinical data sets, working with Oxford Cancer.

Core Enablers

RDM's research strategy will be underpinned by six core enablers that support and develop the key infrastructure that is necessary to deliver excellent research with clinical impact.

People

We will build an empowered community of researchers, students and staff, by:

- Delivering on our Athena Swan Silver Award action plan, ensuring a supportive culture for everyone.
- Supporting the development of all staff through training and mentoring.
- Helping early and mid-career PIs to apply for long-term funds.
- Increasing the transparency of application processes for Fellowships and Professorships.
- Increasing the structure and support around key career transition points.
- Offering all staff the opportunity to discuss their career aspirations and support to plan their development.
- Ensuring that everyone is informed about career paths, and development and funding opportunities.
- Identifying world-class future academic leaders, within Oxford and world-wide.

Collaboration

We will make connectivity and collaboration a cornerstone of our culture, by:

- Rolling out our cross-cutting research themes, capitalising on our existing strengths to boost collaborations and grow new areas of research expertise.
- Introducing a varied programme of events open to anyone in the Department.

- Supporting researcher and student initiatives (both academic and social).
- Developing a larger graduate programme with more focus on studentships shared by PIs in RDM and on increasing fully funded studentships.
- Building academic collaborations and partnerships internationally.
- Increasing collaboration with clinicians.

Capabilities

We will provide state-of-the-art facilities and capabilities to support world-leading research by:

- Promoting and simplifying access to research facilities internally and externally.
- Ensuring that SRFs are relevant to research needs and opportunities.
- Developing our existing state-of-the-art research facilities.
- Establishing new research facilities where there are urgent gaps in existing provision.
- Expanding the use of the Oxford Biobank to facilitate studies in cardiovascular, metabolic and immune disease.
- Building translational gastrointestinal and dermatology capabilities to deliver more clinical studies and trials.

Translation and Innovation

We will translate scientific research into life-changing solutions including therapeutics, diagnostics and processes, by:

- Creating new IP, licence deals and successful spinout companies.
- Training researchers to evaluate potential opportunities for innovation and entrepreneurship.
- Working with NHS colleagues to deliver clinical research, develop clinical evidence and support the rapid translation of research benefits into improved diagnostics and clinical care.
- Working with industry partners to support translational research, from clinical trials to new process and technology development.
- Developing human tissue models to expedite translation of discovery science to the clinic.
- Playing a leading role in clinical trials with biomarkers discovered within RDM.
- Involving public and patient viewpoints in research and translation activities.

Funding

We will support researchers to expand and diversify funding from research councils, charities, industry and philanthropy, by:

- Expanding our focus on raising philanthropic funding, maintaining an up-to-date portfolio of investment proposals that are ready to share with philanthropic leads.
- Developing a clear long-term funding strategy to support the development of new RDM space and/or buildings in locations suited to RDM's mission and objectives.
- Identifying strategic funding opportunities, bringing together cross-departmental teams to support applications.
- Building close relationships with industry to support translational research and clinical trials.
- Developing grant-writing workshops and maintaining a list of 'go to' staff who can advise on each major funder.
- Educating staff about research costs and how these are managed.
- Helping to improve research contract processes so that they can better facilitate research progress.

Estates

We will ensure our estate meets the needs of our staff and students, now and in the future, by:

- Setting out our immediate needs and ten-year vision in an RDM estates strategy, for sharing with the Medical Sciences Division, the University and other stakeholders.
- Seeking the best space and research adjacencies for our researchers.
- Using our space in an efficient and cost-effective manner, whilst allowing room for growth.
- Ensuring our estates needs and ambitions are captured in the University's capital planning processes (major, minor and small works) and funding is secured as possible.
- Working with the Oxford University Hospitals NHS Foundation Trust to maintain and improve the space we occupy which is embedded in their premises or sited on their land.

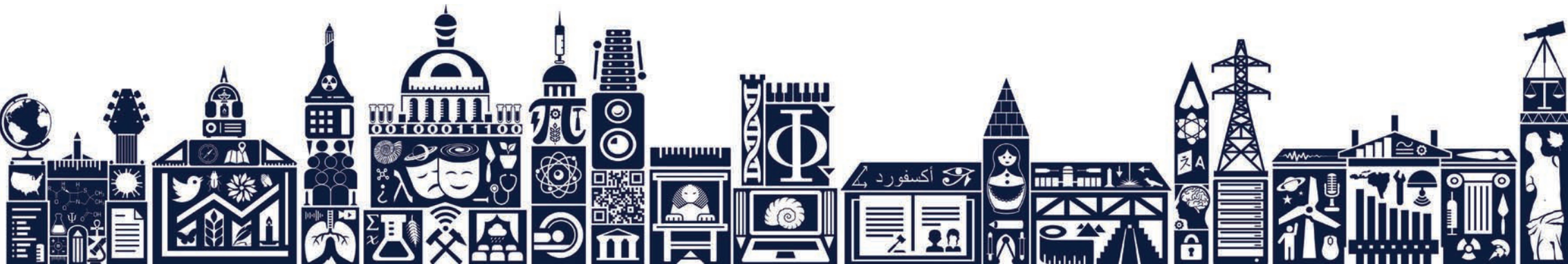
Afterword

I am delighted to see that the Radcliffe Department of Medicine (RDM) has invested time in the creation of this research strategy.

Academics and clinicians are operating in challenging times, and it is more important than ever to think about where we should focus our efforts.

This strategy sets out how RDM plans to broaden our knowledge in key scientific areas, which will ultimately bring benefits to patients.

Professor Gavin Screaton, Head of the Medical Sciences Division, University of Oxford



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