The Future of Immunology

Shaping the future of immunological research in the UK together

#futureofimmunology
AbbVie
AbbVie is a global, research and development-based biopharmaceutical company committed to developing innovative advanced therapies for some of the world’s most complex and critical conditions. The company’s mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world.

BioIndustry Association
Established over 25 years ago at the infancy of biotechnology, the BIA is the trade association for innovative enterprises involved in UK bioscience. Members include emerging and more established bioscience companies; pharmaceutical companies; academic, research and philanthropic organisations; and service providers to the bioscience sector. The BIA represents the interests of its members to a broad section of stakeholders, from government and regulators to patient groups and the media. Our goal is to secure the UK’s position as a global hub and as the best location for innovative research and commercialisation, enabling our world-leading research base to deliver healthcare solutions that can truly make a difference to people’s lives.
British Society for Immunology
The British Society for Immunology is the leading UK membership organisation working with scientists and clinicians from academia, industry and healthcare to forward immunology research and application around the world. Our friendly, accessible community of over 3,500 immunologists gives us a powerful voice to advocate for immunological science and health for the benefit of society. We achieve our mission to promote excellence in immunological research, scholarship and clinical practice to improve human and animal health by:
• Working with our members to support current and future generations of immunologists
• Sharing our passion for immunology through meetings, publications and the media
• Engaging with the public and those working in the research and health environments
• Working with partners to build on common interests

National Rheumatoid Arthritis Society
NRAS aims to provide a voice to people affected by Rheumatoid Arthritis (RA) and juvenile idiopathic arthritis (JIA) across the UK. Founded in 2001, NRAS is the only UK charity devoted specifically to RA, and launched a service for families, children, young people and adults affected by JIA in 2014.
The charity’s mission includes:
• Support everyone living with the impact of RA and JIA at the start and at every stage of their journey
• Inform – be their first choice for reliable information
• Empower all to have a voice and take control of their RA or JIA
Foreword

The therapeutic dividend of many decades of fundamental immunological research is now being realised at an astonishing pace, touching every aspect of health and wellbeing.

The past 70 years have witnessed an accelerating journey of discovery into the workings of the immune system, revolutionising our understanding of the detection of cellular stress and the presence of foreign invaders, the diversity of the antigen receptors on T and B cells, and the elegant molecular anatomy of MHC-restricted peptide recognition. At the same time, the advent of multiple molecular, biochemical and cell imaging techniques have created the possibility of more targeted interventions to direct immune responses in different directions.

Investigations into the brain-body interface and the influence of the microbiome are yielding new insights and will continue to do so over the next decade. When I was a PhD student, neuro-immuno-psychiatry was regarded as a dead-end of research. Now, immune-psychiatry is developing into a mature field: we are continuously discovering more around systemic inflammation’s association with depression and the relationship between the mind and vascular inflammation. Elsewhere, we have learned that the microbiome, and the host’s response to it, appear to influence significantly immune and inflammatory responses.

This remarkable accumulation of insights and discoveries has paved the way for a whole new wave of “advanced therapeutics” - antibodies, recombinant proteins, cells or gene-modified cells that either inhibit unwanted immune responses to self, allergens, or transplant antigens, or amplify immunity against cancer cells that the immune system is otherwise inclined to ignore.

In light of all this progress, and the opportunities that the future holds for patient benefit across a wide spectrum of diseases, it is essential that the UK continues to invest in the people and platforms that drive translation into the clinic and that we take all possible steps to strengthen the biotech sector that has such an important role to play in commercialising novel therapies.

We have developed the infrastructure for experimental medicine that is arguably the best in the world. Much of this has been made possible by the National Institute of Health Research, along with the major charities such as the British Society for Immunology, the Wellcome Trust and the Medical Research Council. Now is the moment to capitalise on this era of unprecedented opportunity to secure our position as a world leader in advanced therapeutics. This ambition is now within our grasp.

Professor Sir Robert Lechler PMedSci
President, The Academy of Medical Sciences
Vice Principal (Health), King’s College London
Lupus is a chronic, often severe autoimmune rheumatic disease, which leads to inflammation, and which may result from, or be triggered by, a dysregulation of the normal immune response.

This means that the immune systems that usually attack only unwelcome invaders – like bacteria or viruses – for reasons not yet fully understood, attack healthy tissue, causing inflammation, pain and damage in different parts of the body, including an person’s eyes, joints, gut, and skin.

Over the past 70 years the UK’s outstanding academic institutions and dynamic life sciences industry have led the field in immunological research. Not only has the UK provided its brightest minds with the support and funding they need to push the boundaries of medical knowledge, it has also consistently ensured that the fruits of their work reach and improve the lives of patients.

This has led to scientific breakthroughs in the treatment of immune-mediated inflammatory diseases, helping the thousands of people in the UK and millions worldwide affected by these conditions to lead healthier and more active lives.

Immune-mediated inflammatory diseases in the UK

Psoriasis

- An estimated 1.8 million people in the UK live with psoriasis – that is between 2% and 3% of the population
- It is more than just a skin condition, and can affect people physically and psychologically
- It can start at any age but most often develops in adults under 35 years old, and affects men and women equally

Lupus

- Lupus is a chronic, often severe autoimmune rheumatic disease
- It is considered a relatively rare disease – diagnosed nearly 9 times more in women than in men (128 versus 15 per 100,000)
- People are usually diagnosed under the age of 50 and it is considered to have a genetic predisposition with cases of lupus clustering in families
Rheumatoid Arthritis (RA)

- Over 400,000 people across the UK live with RA³
- It is not associated with aging and can affect people at any age³
- 31,000 new cases are diagnosed each year – that’s more than three people every hour³
- Women are three times as likely as men to have RA³
- £560 million annual cost to the NHS and £4.8bn total cost to the UK economy, including cost of treatment, care and lost productivity³

Inflammatory Bowel Disease (IBD)

- IBD, which includes Crohn’s disease and Ulcerative Colitis, affects approximately 300,000 people in the UK¹
- Up to a third of Crohn’s diagnoses are in teenagers and young adults and the median age for diagnosis of Ulcerative Colitis is 11.7 years⁴
- Symptoms can be managed to deliver periods of remission but flare ups can require admission⁴
- The nature of the condition means that it can have a significant social and psychological impact⁴

3 NRAS, What is RA?, https://www.naras.org.uk/what-is-ra-
4 Crohn’s & Colitis UK, About Inflammatory Bowel Disease, https://www.crohnsandcolitis.org.uk/about-inflammatory-bowel-disease
Campaigning for those affected by inflammatory conditions

As Chair of the APPG on Inflammatory Bowel Disease (IBD), it has been a privilege to support and witness the work of many dedicated campaigners who have achieved significant improvements for people living with IBD and other immune-mediated inflammatory diseases.

I’m proud to say the IBD care standards which have been jointly developed by the clinical and patient communities, have been largely adopted as NICE guidance and are helping to set a benchmark for evidence-led, patient-centred practice.

Thanks to the work of patient groups, campaigners and parliamentary colleagues, we are seeing a drive to improve services and reduce variation for IBD patients across the NHS.

Many patients now have better access to diagnostic tests in primary care and timely referral to specialist support for the right treatment and care.

The UK has a unique opportunity to build on these achievements. Thanks to the world class research conducted here, we know more about the common mechanisms across immune-mediated inflammatory diseases and how these can be treated more effectively. Services and practice within the NHS now need to reflect this knowledge and use it to deliver real benefits for patients. But there is still work to be done to address unmet need. The NHS’s 10-year plan and the Life Sciences Industrial Strategy provide the opportunity for the Government, NHS, and the wider community to work together to achieve this.

The call to action set out in this booklet provides a blueprint for how we can achieve this joint vision, highlighting the need for maintained research funding, enhanced access to innovation, and responsive service reform. Having observed the impact the community has when it works together, I hope today’s event will mark the start of ongoing collaboration to benefit patients today and in the future.

Melanie Onn MP
Chair of the All-Party Parliamentary Group on Inflammatory Bowel Disease
1948
Astrid Fagraeus published PhD thesis describing antibody production by B plasma cells

1948
1956
Gell and Coombs publish their classification of hypersensitivity

1950
Hench/Kendall/Reichstein win Nobel Prize in Physiology or Medicine for discovery of cortisone and its use in rheumatoid arthritis

1956
British Society for Immunology formed

1960
Nobel Prize in Physiology or Medicine awarded to Peter Medawar & Frank Macfarlane Burnet for the discovery of acquired immunological tolerance

1963
Gell and Coombs publish their classification of hypersensitivity

1959
Ciclosporin, the world’s first immunosuppressant drug, used for organ transplant

1968
Human leukocyte antigen (HLA) term first coined

1975
First monoclonal antibodies produced

1980

1970
1980
70 years of immunology
2018
Stem cell transplant is used – with success – to treat MS patients

2011
IL-17 is associated with a range of autoimmune conditions defining it as a new therapeutic target

2017
Stem cell transplant is used – with success – to treat MS patients

2007
National Institutes of Health launch Human Microbiome Project to understand role of microbiome in diseases, such as IBD

2004
Psoriasis first described as an autoimmune disease

2003
Human genome project completed – scientists use this to map specific gene mutations to inflammatory disorders

2001
Mutations in the NOD2 gene first associated with autoinflammatory disease

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1989
Charles Janeway describes pattern recognition theory, outlining how immune cells detect self from non-self

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Intravenous immunoglobulin first used to treat autoimmune-like disorder

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2017
Stem cell transplant is used – with success – to treat MS patients

2018
Creation of the world’s largest IMID Biobank contacting in excess of 40,000 patients’ data

1987
Intravenous immunoglobulin first used to treat autoimmune-like disorder

1989
Charles Janeway describes pattern recognition theory, outlining how immune cells detect self from non-self

1993
First successful clinical use of anti-TNF to treat rheumatoid arthritis

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Psoriasis first described as an autoimmune disease

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Living with an immune-mediated inflammatory condition

As a patient, it’s incredibly reassuring to know that the UK is currently amongst the best places in the world for pharmaceutical innovation, in which immunology is key. We also have a world class academic and clinical research base spanning discovery and translational science so the UK is spawning some of the leading research collaborations in autoimmune inflammatory disease in the world.

In spite of the significant progress that has been made in treating RA with the advent of the biologics at the end of the ‘90s, there remains significant unmet need both in RA and other autoimmune inflammatory conditions. If, as a patient, you listen to sessions at EULAR and the BSR congresses, you could be forgiven for believing everyone is now in remission. This is far from the case. 6% of patients on the BSR Biologics Register are refractory to treatment. By comparison to other diseases we don’t know which drugs to use in which patients to get the best result and outcomes. Even the best units can generally only claim about a third of their patients are in remission and that doesn’t necessarily mean that the patient is pain and symptom free. We still have a long way to go.

There is no doubt that significant challenges will confront the UK’s research environment in coming years, so it is important that the priorities of the immunology sector are appropriately considered. Immune mediated inflammatory diseases have a major impact on quality of life not only of the individual affected but also on their immediate and wider family, employers and wider society.

Ailsa Bosworth
Chief Executive and Founder
National Rheumatoid Arthritis Society (NRAS)
Scientific progress in the treatment of psoriasis

Since the inception of the NHS in 1948 the UK can point to world leadership in psoriasis research and its translation into patient management. We have come a long way.

Ingram in 1953 developed his eponymous regime of coal tar and ultraviolet radiation which is still used in day-treatment centres around the country. For many years psoriasis was thought of solely as a disease of keratinocyte proliferation with little dependence on the immune system and treatments, such as retinoids, were developed accordingly.

The paradigm shift in understanding occurred in the early 1980’s when dermatologist Lionel Fry and his team at St Mary’s Hospital, London showed that T cells were key drivers of the epidermal proliferation characteristic of the disease. This ushered in the immune-mediated hypothesis for psoriasis confirmed by the efficacy of ciclosporin. In many ways this was the beginning of the biologic era as pharma and academics strove to identify druggable targets in the immune pathways of psoriasis.

Incremental gains were achieved with initial targeting of T-cells eventuating in the first biologic to be approved for psoriasis in the UK: efalizumab in 2006. Approvals for cytokine targeted biologics, initially anti-tumour necrosis factor-α, were followed by anti-interleukin(IL)-12/23, anti-interleukin-17 and most recently anti-IL-23, producing unprecedented levels of skin clearance, in 2018. Some of the pivotal licensing trials for these biologics were led from the UK and they have all trialled in the NHS often with help from the National Institute for Health Research (NIHR) Clinical Research Network.

The UK is leading the way both in essential high quality real world pharmacovigilance of biologic therapies for psoriasis namely the British Association of Dermatologists Biologic Interventions Register and in determining how patients can be matched to the right biologic first time as part of the Government (Medical Research Council) funded academic-industrial stratified medicine consortium – Psoriasis stratification to Optimise Relevant Therapy. Management of psoriasis is not only about drugs or the skin; UK led, NIHR funded initiatives on lifestyle management and tackling comorbidities such as cardiovascular disease and depression will bring a holistic, systems approach to management of this life-ruining and common disease.

Christopher Griffiths OBE FMedSci
Foundation Professor of Dermatology
University of Manchester
Translating immunological research into patient benefit

Providing timely diagnosis to people affected by an immune-mediated condition is crucial in ensuring that they receive the information, care and support they need. Born out of the pioneering immunological research at the University of Oxford, Oxford Immunotec develops leading diagnostic tests that provide accurate ways to identify and diagnose immunological and infectious diseases including tuberculosis.

The T-SPOT.TB test is an example of how the fruits of research can make a real change for patients. For the first time we can accurately diagnose people carrying a TB infection, enabling us to treat them before they ever develop the disease. Today the test benefits people in over 50 countries worldwide and due to its accuracy, it was recently included in the WHO’s list of the most essential diagnostics.

Oxford Immunotec’s team has grown quickly from one employee to over 500 employees and it continues its research in supporting the accurate diagnosis of immunological diseases. This includes the development of new diagnostic tools to better diagnose autoimmune and inflammatory conditions, through classifying patients into subgroups to add specificity to diagnosis and to better inform clinical understanding of disease progression.

As our knowledge of the human immune system continues to grow, we hope to remain at the forefront of converting those discoveries into cutting edge tests that improve human health.

Peter Wrighton-Smith PhD
Chief Executive Officer and Director
Oxford Immunotec
The UK has a proud record of scientific progress in immunology and we are on the cusp of achieving further medical breakthroughs in the years to come, providing hope for those affected by immune-mediated inflammatory conditions and their families.

Over the past 70 years the UK’s outstanding academic institutions and its dynamic life sciences industry have proudly led the field in immunological research. Not only has the UK provided its brightest minds with the support they need to push the boundaries of medical knowledge, it has also consistently ensured that the fruits of their work reach and improve the lives of patients.

This has led to scientific breakthroughs in the treatment of immune-mediated inflammatory diseases such as rheumatoid arthritis, Crohn’s disease, ulcerative colitis, psoriasis and uveitis, helping the thousands of people in the UK and millions worldwide affected by these conditions to lead healthier and more active lives.

For many people living with inflammatory diseases, these breakthrough treatments have been life-changing. There are those, however, for whom current treatment options have not been effective enough and who still suffer from inadequate control of their condition. They remind us that there is no room for complacency and that it is critical that we continue advancing our research efforts.

With the UK forging a new relationship with the EU, further challenges will confront the UK’s research environment in coming years. It is critical that the priorities of the immunology sector and the economic and societal benefits that can be gained from research and development activities in the UK are fully understood and recognised.

Continued investment in immunological research will not only benefit patients in the UK but will also be critical for the Government to meet the ambitions it has set out in its Industrial Strategy for the UK to become a top-tier global hub for biomedical and clinical research and medical innovation. However, we can only realise this scientific promise if the UK continues to lead the field in immunological research and in the adoption of this research.

The British Society for Immunology, the UK BioIndustry Association, the National Rheumatoid Arthritis Society and AbbVie have come together to jointly outline our recommendations for the actions that need to be taken to achieve our vision of the future of immunology in the UK. These can be found overleaf.
A call to action
Shaping the future of immunological research in the UK together

Research investment

• **Increase** funding for immunology research, especially in areas of immune-mediated inflammatory diseases, in line with the Government’s 2.4% GDP research investment target to ensure the UK remains a competitive and leading destination for research and clinical application in this area

• **Recognise** that without access to high level researchers and clinicians, the UK’s position as a world leader in immunological research will be under threat. Ensuring that the new immigration system will support our ability to recruit and retain talent is vital

• **Maximise** the research potential of our unique NHS. Encourage a research strategy that embeds research and innovation at the heart of the health system

• **Strengthen** relationships between academia and industry – target and encourage partnerships at the early stages of the R&D pipeline through to scaling and clinical application

Patient experience

• **Raise** awareness of immune-related inflammatory diseases to enhance understanding of the symptoms with the general public and clinicians

• **Expand** the use of shared-decision making between patients and clinicians on care and treatment for inflammatory conditions
**Timely diagnosis**

- **Invest** in the clinical and nursing workforce to ensure that it is equipped to provide patients affected by an immune-mediated inflammatory disease and their families with timely access to the services and support they need.

- **Develop** appropriate training tools for clinicians and healthcare professionals to recognise the early signs of immune-related inflammatory diseases to enable early diagnosis and enhance the understanding of the interconnected nature of this group of conditions.

- **Ensure** that clinicians and healthcare professionals understand the need for rapid referral to specialist care following diagnosis.

- **Implement** improved measurement of early diagnosis rates with commissioners to enable action to be targeted to those areas most in need.

**Patient access to innovation**

- **Accelerate** the introduction of new advances in treatment for immune-mediated inflammatory diseases so that patients are able to benefit at the earliest opportunity, including through the establishment of accelerated medicines pathways.

- **Introduce** adaptable health technology assessment processes that allow patients to access promising treatments whilst the data is still maturing and ensure a value-based approach to treatment assessment that fully recognises the voice of the patient and clinical community.

- **Adopt** new approaches to pricing and reimbursement that support as many patients as possible to benefit from advances in treatment while delivering value for the NHS.