Immunology:

An international, life-saving science

British Society for immunology
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60

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Scientific knowledge, like air, water or even disease, does not respect borders drawn on a map. Science is inherently an international endeavour, and this is particularly true for immunology. Researchers have always discovered more working together than in isolation, and have worked hard to build a strong, global scientific community. That the UK is a world-leader, ranking first amongst the G7 countries for the quality of our research in infection and immunology,[1] is a cause of celebration. The strength of our immunological science is an asset we are able to project to attract the best and the brightest minds from around the world – minds that contribute to the success of our institutions and, ultimately, to the innovations and knowledge that keep the UK at the forefront of immunological science.

Our researchers have access to some of the world's best scientific and technical facilities, and are pioneers in emerging areas such as genomics and other disciplines that use 'big data' to generate knowledge in new ways. Advanced technologies have transformed immunology, giving rise to innovations that enable pioneering applications that serve the global public good, from novel vaccines against tropical infections to advances in the treatment of cancers, diabetes and arthritis. The smallest breakthrough in immunology in the UK can have profound effects around the world.

This British Society for Immunology report sets out some of the international links, relationships and influences that fundamentally shape how immunology in the UK interacts with the global environment. This includes our relationship with the European Union (EU), which not only entitles immunologists to access funding schemes through its Framework Programmes, but also facilitates an unimpeded flow of students, researchers and highly skilled workers (and with them a cross-fertilisation of knowledge and ideas) that has allowed us to build a community of world-class immunological talent.

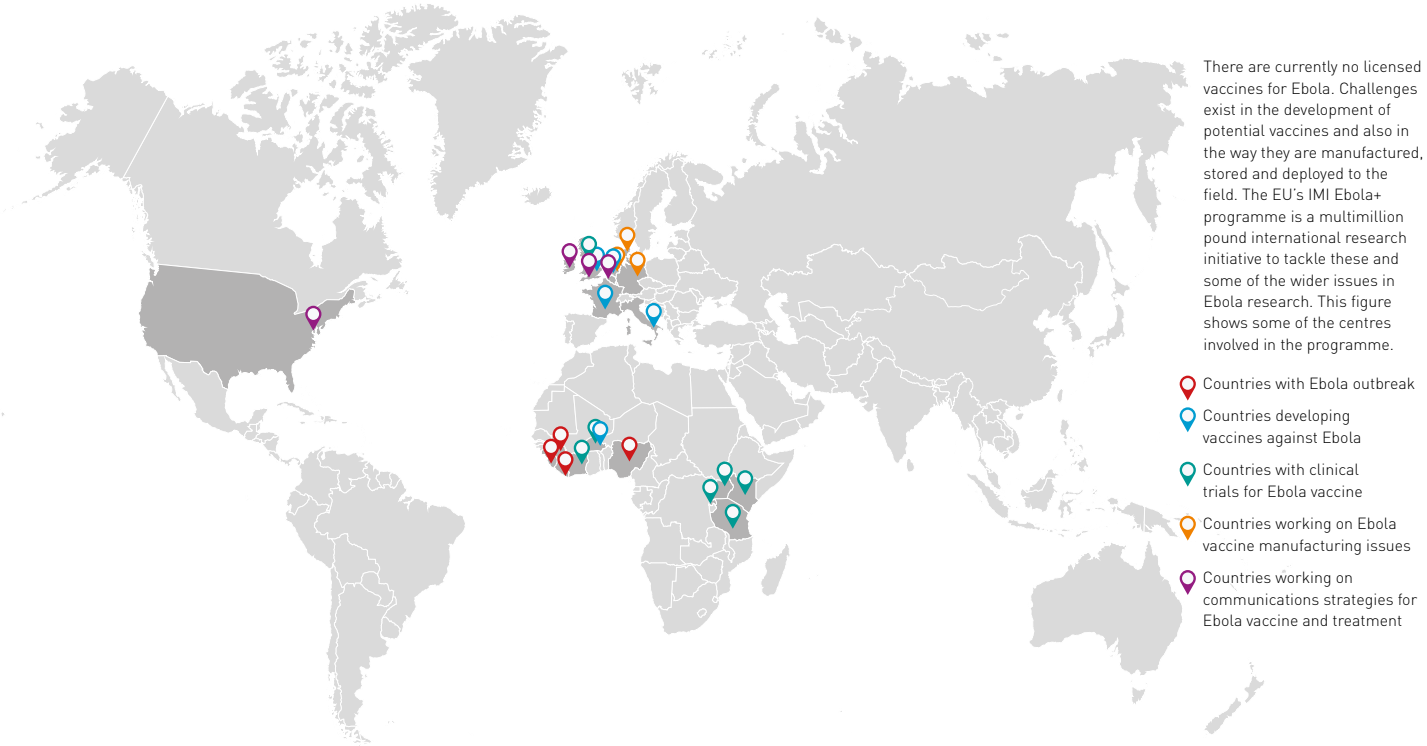
The success of the UK immunology community extends well beyond Europe however, and is bolstered by long-standing links with the United States and Canada. As the rapidly emerging knowledge economies in Asia begin to challenge the traditional scientific powerhouses of Europe and the United States, our scientists are increasingly looking to capitalise on opportunities for collaboration with their peers in China, Japan, Korea and other countries. Indeed, China is expected to become the world's biggest spender on research and development by 2022, opening up new opportunities for cooperation that can help safeguard our position at the forefront of science, pushing the boundless frontiers of knowledge.

The international nature of immunology means that we can only realise our full potential if the UK is able to attract and employ the most qualified and talented personnel; funding is joined up to support collaborative research; and data on health and outcomes are responsibly shared. In this report, we profile case studies that bring to life why these issues matter and make recommendations that, if implemented, will help ensure the pre-conditions for success are in place.

Innovation and knowledge arising from immunological research improves health and generates economic growth, both of which have profound impacts on society. It is vital that we ensure this international, intricately-linked community can continue to flourish now and in the future. Immunology is a global science, and with the right support, has global, life-saving impacts.

1. All Party Parliamentary Group on Global Health 2015 *The UK's contribution to health globally: benefitting the country and the world*

Developing vaccines against Ebola – a global effort



Recommendations:

1. Our strength in immunology is intrinsically linked with the quality of the workforce we can employ in the UK. The Government should do all it can to ensure that UK scientific institutions are the most attractive in the world to work for, and that they are able to employ the best and the brightest, irrespective of their nationality. **Steps should include ensuring visas for scientists are given priority, removing artificial barriers to securing visas, and making clear to the international scientific community that the UK welcomes overseas talent and is very much open for business.**

2. Funding from international sources, including European Framework Programmes, are a valuable component of the overall funding matrix available for immunological research. Access to these bespoke streams, which not only fund high quality science but also bring different partners together in multilateral collaboration, should be maintained and expanded. **The 2017 UK Presidency of the EU should seek to unlock further resources to expand and accelerate funding for immunological research**, with a view to unlocking new treatments for infectious diseases, autoimmune conditions like diabetes and rheumatic diseases, and cancer.

3. International collaboration underpins growth in our research base and supports high quality science. Scientists seek partnership where they recognise research excellence and the unique conditions of the EU have supported the emergence of collaborative networks between scientists here and the continent. **Beyond European shores, the research councils and government agencies (such as UK Trade and Investment) should continue to support the export of multinational partnerships in immunology** to emerging knowledge powerhouses, such as China. **Showcasing existing research partnerships and seeking to forge new ones should be a key focus of future UK trade missions.**

4. The UK is playing a leading role in the 'big data revolution', which presents immunologists with new, more precise ways to explore the biomedical and life sciences. **Nurturing the next generation of immunologists is key to ensuring the UK remains at the forefront of data-driven science. Our scientists must be equipped with the skills required to exploit new technologies**. This is absolutely crucial if the UK wishes to remain a global leader in ensuring the responsible usage – supported by appropriate confidentiality safeguards – of healthcare information in the interests of research.

5. Research conducted in the UK has benefits that extend far beyond our own shores. The Government should **capitalise on our status as a world leader in immunological research and take the lead in mobilising international action on global health issues** where immunology can make a real and lasting difference. These issues should be **a priority item for discussion at international political summits**, such that we can harness world-class clinical and research talent to engender lasting change for communities across the globe.

Immigration:

UK immunology benefits from being able to attract the best and the brightest from across the world

In 1958, a young biochemist called César Milstein came to Britain from Argentina to work in the same institution where another immigrant, Nobel Prize winner James Watson, had earlier helped decipher the structure of DNA. Nearly 20 years later, Milstein would be awarded the Nobel Prize for his work on monoclonal antibodies. His story is by no means unusual, and British scientific heritage is littered with examples of foreign nationals whose research has brought huge scientific and economic benefit to the UK only because they have chosen to adopt this country as their own.

Just as in the late 50s, today's global community of scientists are motivated to go wherever they recognise research excellence. Immigration is therefore key in maintaining our scientific competitiveness on the international stage. The BSI membership, and the experience of our members in working with colleagues day-to-day, tells its own story of the UK's success in attracting the best and the brightest to work here. The UK has a proud history of welcoming and benefitting from the contribution of foreign scientists. This open and welcoming reputation has contributed to an internationally fluid workforce, with 72% of the UK's scientists between 1996 and 2012 having spent time with a non-UK institution.[2] Today, non-UK academics make up more than a quarter (26%) of staff in our universities, with 16% of these (22,000) coming from within the EU.[3]

> *"Today's global community of scientists are motivated to go wherever they recognise research excellence. Immigration is therefore key in maintaining our scientific competitiveness on the international stage."*

2. Elsevier 2013 *International comparative performance of the UK Research Base – 2013*
3. CaSE 2016 *Immigration: Keeping the UK at the heart of global science and engineering*
4. Dame Julia Goodfellow speaking at Universities for Europe launch, 2015

> *Immigration facilitates not only the easy flow of students, researchers and highly skilled workers across borders (some of whom can plug key skills gaps for the UK), but also the fluid transmission of ideas, innovations and knowledge that drives modern day research.*

Our national science base benefits hugely from its international mix. There are well-established economic benefits, with £2.27 billion generated from EU nationals alone studying in our universities.[4] There are advantages to our research impact too, with analysis of the 2014 Research Excellence Framework establishing a link between high scoring institutions and the number of staff they have with international experience.[5] Moreover, internationalism has also been linked with increased scientific productivity, with a report for the Department for Business, Innovation & Skills highlighting that migratory scientists publish more articles per year on average than those with no previous non-UK affiliations.[1]

Immigration facilitates not only the easy flow of students, researchers and highly skilled workers across borders (some of whom can plug key skills gaps for the UK),[6] but also the fluid transmission of ideas, innovations and knowledge that drives modern day research. This demands an immigration system that supports the UK in maintaining its status as a global hub for the highest quality science. A major factor underpinning this is our adherence, as a member of the EU, to its requirements on freedom of movement. It is imperative that this principle, which has supported the UK in becoming host to a diverse community of international scientific talent, be maintained if we are to continue to enjoy the benefits that researcher mobility brings to our domestic science base.

Immunologists from outside of the EU who wish to study or work here must apply for a visa. The Government has been clear that it is committed to reducing net migration down to the "tens of thousands a year".[7] This commitment not only communicates the wrong message globally, compromising the UK's reputation as a welcoming country, but also sets a policy trajectory with worrying implications for science. Thankfully, PhD level roles are exempt from some of the new restrictions, including an increase in the minimum salary threshold (up from £20,800 to £30,000) for Tier 2 workers and the imposition of a levy on employers hiring non-EU workers. However, the fact remains that our science base – and the work of immunologists up and down the country – relies not only on skilled postgraduate researchers but also the technicians, teachers and administrative staff that are critical in supporting their work. Moreover, the annual cap on the number of available Tier 2 (general) visas – the most popular

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route for scientists wishing to enter the UK – continues to cause concern. This artificial barrier restricts employers from recruiting the best possible candidates and only serves to hold the UK back from achieving its full potential.

Perhaps more worryingly, however, are the effects of continued anti-immigration rhetoric, which may discourage scientists from choosing to come here and instead drive them into the open arms of our international competitors. The damage this is doing to our reputation is perhaps best articulated through the findings of a House of Lords inquiry on international science students in the UK. Its report found a collapse in the number of STEM students from India choosing to study here (down 38% in 2011/12 and a further 28% in 2012/13), a consequence, they suggested, perhaps not necessarily down to changes in the immigration rules themselves, but the way these rules are perceived abroad, with overblown rhetoric and inflammatory media coverage highlighted as potential contributing factors.[8] We urge the Government to take every opportunity to reverse this perception and to promote the UK as a world-class destination for work and study.

5. Manville C *et al.* 2015. *Characteristics of high-performing research units.* Prepared for the Higher Education Funding Council for England
6. UK Government 2015 *Tier 2 Shortage Occupation List.*
7. UK Government 2015 *PM speech on immigration, 21 May 2015.*
8. House of Lords Science and Technology Select Committee 2014 *International Science, Technology, Engineering and Mathematics (STEM) students.*

Case Study

Matthias Eberl is a German national who completed his PhD at the University of Giessen in Germany in 1998. He then spent the next eight years working across Europe in Giessen, York and Bern in Switzerland, before settling in the UK to set up his own lab at Cardiff University. Matthias' research focuses on the function of particular immune cells and their role in the immune response. His work has direct consequences for the diagnosis and treatment of infections and the development of new approaches in cancer immunotherapy.

Any successful research depends on the ability to recruit the best possible candidate for a specific position, regardless of their nationality. I co-lead, with a Swiss colleague, a laboratory that has hosted students and postdocs from France, Germany, Greece, Italy, the Netherlands, Slovenia, Spain, Sweden, Switzerland, Canada, China, Taiwan, India, Pakistan and Mauritius – with roughly a third of our lab members at any given time coming from the UK, a third from the rest of the EU, and a third from non-EU countries. This fascinating mixture of backgrounds has been an absolute pleasure, both professionally and personally, and has contributed significantly to creating a productive and enjoyable working environment.

The UK benefits enormously from its rich tradition in education and science and, for centuries, has successfully attracted some of the most talented individuals of their time to work here. The prestige of its universities, the excellent facilities and resources available, and the overall strength of the UK's science base combined with the undeniable advantage of being an English-speaking country are significant advantages over other destinations.

Another factor is that the UK system offers more flexibility than many other countries, where career pathways are more restrictive. Additionally, the UK has historically been perceived as being more open to foreigners. I believe this is changing, however, and there is in fact an increasingly negative perception of the UK as a result of the charged political debate with respect to immigration and the UK's relationships with the world (for example, the EU). When viewed from overseas, the opinions voiced in these debates are undoubtedly putting off excellent candidates from applying for a UK studentship, postdoc fellowship or faculty position.

'There is an increasingly negative perception of the UK as a result of the charged political debate with respect to immigration and the UK's relationships with the world, for example, the EU. When viewed from overseas, the opinions voiced in these debates are undoubtedly putting off excellent candidates from applying.'

Attracting postdocs from overseas (and extending their contracts within the same institution) is a major bureaucratic challenge with regard to HR requirements and financial approval. The effort and cost non-EU nationals have to invest to obtain appropriate visas and get them renewed is largely underappreciated, and more than once I have seen skilled people threatened to leave the UK despite being of valuable help to their research teams, simply because the tight visa regulations did not allow them to stay longer. As an EU national, my personal experience of coming to the UK from Germany couldn't have been easier. Having said that, even I noticed that the difference between moving to the UK from within the EU and from outside the EU. Coming to the UK, for a second time, this time from Switzerland, my experience was not so straightforward and I had to fill in far more paperwork, such as lengthy customs declarations.

Case Study

Hung-Chang Chen came to the UK from Taiwan to study for a PhD at Cardiff University. Hung-Chang's thesis, which focussed on immunotherapy for breast cancer, was completed in September 2015. From May 2016, Hung-Chang has taken up a position at the Cancer Research UK Institute at the University of Cambridge as a postdoctoral research associate. As a non-EU national, Hung-Chan has experience of navigating the visa system, first as a Tier 4 (student visa) entrant before transition to the Tier 2 (general) system as a skilled worker.

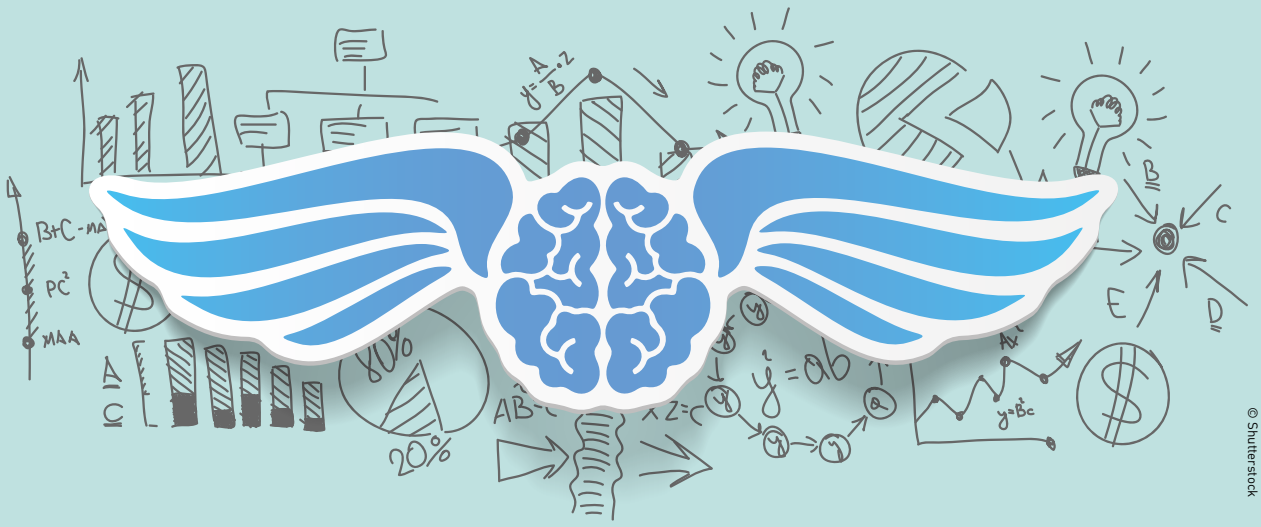
The most important factor in my choosing to do a PhD in the UK is because of its long track record in biomedical science and prestigious reputation in immunology research. I wanted to follow in the steps of Watson and Crick in uncovering the secret of life and to build on that inherited legacy to work in new areas such as immunogenetics and emerging science in translational immunology. When I first came here in 2011 the general atmosphere was very welcoming. However, since then restrictions and regulations around immigration policy have started to become tighter and there has also been a change in the public attitude. I can see these hampering the recruitment of talented international students and scientists and eventually compromising the world-leading research in the UK.

Working here has been a great pleasure and I very much enjoyed doing my PhD in a research institute comprising scientists from all over the world, each with different cultural backgrounds and having experienced different scientific training. Such a diverse environment helped expose me to unique perspectives on my work. This multiculturalism has inspired me to keep myself open minded and appreciate different approaches and aspects in designing and conducting scientific research.

I've had experience of applying for the Tier 4 student visa, an extension of the Tier 4 visa for my doctorate, and I am right now in the process of applying for the Tier 2 working visa. In general the whole visa application process is very long and can be quite exhausting. It takes around 6–8 weeks for the entire application to be finished but on top of this it takes at least a week or two to prepare all the supporting documents. The process is unpredictable and I have suffered delays which meant that I had to postpone the starting date for my job in Cambridge, causing disruption to both myself and my new employer. These delays have also meant I have missed important work conferences and also a scheduled visit home to see my family.

'The whole visa application process is very long and can be quite exhausting. It takes around 6–8 weeks for the entire application to be finished but on top of this it takes at least a week or two to prepare all the supporting documents.'

The UK should promote the migration of talented scientists, from whom it benefits greatly, and remove some of the artificial barriers that exist. International PhD students should be trusted and encouraged to stay longer and make contributions in this country. Moreover, reducing the visa processing period would be a great plus for attracting international scientists. By supporting the continued diversity of the workforce, the UK not only benefits from innovative research but also vital contributions to business and the national economy.



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Funding:

International funding supports world-class UK research

In the UK, a mixed economy of funders including private business, research councils, charities and government departments has supported the development of world-class immunological research.

From 2007–2013, the UK's gross expenditure on R&D was around €226.3 billion.[9] Nearly half of this (45%) came from the private sector. As a scientific superpower with a highly skilled workforce, the UK is an attractive location for multinational companies looking to invest in R&D, either through collaborations with academia, research councils, or by directly supporting PhD or undergraduate students. This investment is internationally mobile, and long-term government support for science funding is a key factor in attracting foreign investment, with evidence that for every 1% increase in public expenditure, an additional 0.48–0.68% is leveraged from the private sector (equating to an extra £1.13–£1.60 on every £1 from the public purse).[10] The UK's life sciences industry, which is worth an estimated £56 billion to the national economy and employs more than 180,000 people, therefore makes a valuable contribution to the overall funding mix available to immunologists.[11]

Outside of private investment, the primary source of international funding is from the EU. The EU supports research through a number of interlinked programmes, estimated to be worth €120 billion from 2014–2020.[12] Approaching two thirds of this is distributed through the European Commission's Horizon 2020 Framework Programme, which allocates funding competitively through proposal calls administered under a number of schemes, such as the European Research Council or Marie Skłodowska-Curie actions. Universities, research organisations, and small or large businesses within EU Member States are eligible to receive these funds, and they were directly responsible for over 43,000 publications (almost half of them in high impact peer reviewed journals) and more than 1,500 patent applications between 2007 and 2013.[13]

EU grants are competitive and available to all EU member states and a select number of 'associated countries' (such as Norway and Switzerland). The UK has been very successful in securing these grants, and received €6.94 billion in Framework Programme funding from 2007 to 2013 (a value second only to Germany).[8] During this time Oxford, Cambridge, Imperial College London, and University College London were awarded more Framework Programme funding than any other European universities.[8] At €0.69 billion in 2013/14 alone, EU funding now forms a major proportion of the total research income secured by UK universities. Our success in securing EU funding means that, for science and research at least, we get more out of the EU than we put in. The Office of National Statistics estimates that our contribution to the EU's research budget between 2007 and 2013 totalled €5.4 billion.[14] This compares to the €8.8 billion the UK received from the EU for research across the same period. The UK's Presidency of the European Council, planned for 2017, represents an opportunity to maximise these funding opportunities by developing an action plan to channel funding along priority health challenges, such as in cancer and autoimmune diseases.

The example of Switzerland

Participation in EU Framework Programmes is not dependent on member status. However even associate countries must agree to a number of pre-conditions set out by Brussels, including a guarantee on the free movement of persons and a commitment to contribute to the science programme's budget. Switzerland serves as a useful example of what can happen if these agreements are not met. In 2014, the country passed a vote to limit mass migration and as a consequence had its access to Horizon 2020 suspended. This compelled the Swiss government to put in place arrangements at a national level to replicate those funding decisions that already existed as part of European agreements, essentially creating a situation where the country had lost control of its science budget. Switzerland has subsequently been able to re-negotiate limited access to the programme, although this ends this year and the Swiss Government must either re-implement free movement or lose access to Horizon 2020 completely.

9. The Royal Society 2015 *UK research and the European Union: the role of the EU in funding UK research.*
10. Economic Insight 2015 *What is the relationship between public and private investment in science, research and innovation?*
11. Office for Life Sciences 2014 *Strength and opportunity 2014: the landscape of the medical technology, medical biotechnology, pharmaceutical and industrial biotechnology sectors in the UK.*
12. European Parliamentary Research Service Briefing 2015 *Overview of EU funds for research and innovation.*
13. European Commission 2013 *Seventh FP7 Monitoring Report.*
14. UK Office for National Statistics 2015 *UK Government Expenditure on Science, Engineering and Technology: 2013*

Case Study

Be The Cure is an EU funded collaboration between 24 academic and 14 industrial partners to identify new therapeutic approaches for the treatment of rheumatoid arthritis. The programme is part of the EU's Innovative Medicines Initiative (IMI), a funding framework that aims to connect those involved in academic health research with partners in the pharmaceutical industry to accelerate the development of new medicines. UK participants in Be The Cure include research groups in Glasgow, Leeds, Manchester and Oxford as well as the pharmaceutical companies AstraZeneca and GlaxoSmithKline.

IMI is the world's largest public-private partnership in the life sciences, with a budget of €3.3 billion funding more than 50 projects over 10 years. Half of this money (€1.638 billion) comes from the Horizon 2020 framework, while roughly the other half (€1.425 billion) is committed by private life sciences companies that are part of the European Federation of Pharmaceutical Industries. The rest (€213 million) is made up of smaller contributions from other participant organisations. This funding matrix ensures that for every €1 of taxpayers' money invested into the programme, an additional €1 is leveraged from private companies.

The aim of IMI is to fund collaborative research partnerships between academic life science researchers and other stakeholders, including those in the pharmaceutical industry, but also relevant regulatory bodies and interested patient groups. In doing so, the programme hopes to build collaborative networks of expertise that are the foundation of exciting innovations in healthcare, driving through new medicines, treatments and vaccines for the benefit of patients across Europe. The project has a number of specific deliverables, each geared towards improving the drug development process, including an objective to deliver a 30% better success rate in clinical trials for priority medicines identified by the World Health Organization, as well as achieving clinical proof of concept for new drug candidates against immunological, respiratory, neurological and neurodegenerative diseases.

Be The Cure brings together diverse expertise to improve research against rheumatoid arthritis (RA). The initiative involves 38 partners across 13 European countries, each co-operating in nine different work packages that are co-ordinated by a central committee to maximise research output. A main focus is to develop new and improved diagnostics to diagnose RA at an earlier stage, helping patients get effective interventions to control the condition

before it progresses. The consortium is also improving our understanding of the immune reactions underlying RA, opening up possibilities for advanced treatments in a disease for which there is currently no cure.

The enterprise has received approximately €35 million in IMI funding. Like all IMI projects, industry partners do not receive money. Their role is to contribute by providing access to other resources, such as expertise, materials and equipment. For Be The Cure, pharmaceutical participants have funded early trials and have also provided critical resources, such as serum samples and animal models. Researchers have additionally been able to utilise key technologies and equipment not usually available to university based academics. These relationships benefit participants by supporting the wider science base and helping to propel efficient drug discovery.

In 2014, the Be The Cure collaborative published 90 papers, each representing a forward step in our understanding of RA, and participants are hopeful that this success can now be exploited to accelerate the development of important new tools and diagnostics. These accomplishments have much to do with the IMI framework, including its purpose as a funding instrument, but also its function as a platform that brings together wide representation from universities, private industry, ethics bodies, regulators and patients. Facilitated by the unique conditions of the EU, nowhere else in the world does such a platform exist, and at a time when domestic research funding continues to be restricted, international funding mechanisms, such as those available through our participation in EU programmes, remain indispensable for UK immunology.

Collaboration:

UK immunologists partner with excellence across the world

In 2003, the Human Genome Project was completed after 13 years. The project harnessed the talents of thousands of researchers at 20 institutions across six countries and remains the largest and most ambitious research collaboration in the life sciences. Collaboration is an inherent component of scientific endeavour. Whether a scientific partnership involves thousands of participants or just a few, the benefits are always the same: co-operation helps bring great discoveries faster.

In the last 30 years, our total research output has more than doubled in line with other major economies. During this time, solely domestically authored papers have stayed largely static; international collaboration has fuelled the growth in the quality and quantity of scientific research.[15] Today almost half of research articles from UK researchers have at least one international co-author[16] (compared with just 33% for the US).[17] Often, these partnerships emerge from a desire by scientists to work with other outstanding figures in their field. The UK's attractiveness as a centre of global excellence is therefore underpinned by the vitality of our research base. Our status as a scientific superpower, with particular strengths in immunological research, places us at the centre of cutting edge networks of international research.

International co-authored papers have a significantly greater impact than those authored by domestic researchers only.[15, 18, 19] Collaboration increases the quality and efficiency of our research base, with cost sharing an important motivation in establishing multi-centre research partnerships. In other cases, collaboration is vital, with studies on rare diseases dependent on the ability to recruit patient cohorts that are large enough to validate research. Multi-centre, multi-country partnerships have been instrumental in the development of new treatments for type 1 diabetes[20] and multiple sclerosis[21] (for example the CAMPATH users group, which required trials at centres in Europe, Israel, Australia and South Africa to bring together patient groups large enough to evaluate the drug CAMPATH, which is now a first line treatment for multiple sclerosis).

The UK's most frequent collaborative partner has traditionally been the US. However, collaboration with European countries, and in particular France and Germany, is accelerating at a faster rate.[13] In 2011, co-authorship with EU partners made up more than 60% of the UK's international research partnerships.[13] Undoubtedly, factors such as geographical proximity, common strategic priorities and shared cultural values have facilitated this collaboration. The unique conditions of the EU – and in particular the incentives of EU Framework Programmes such as Horizon 2020 – represent fertile ground for collaboration with a politico-economic union that, with 35.5% of the world's share of citations, represents the greatest collective of science on the planet.[22]

Preserving links that allow us to tap into the European scientific powerhouse are important, but so too are efforts to forge new collaborative relationships outside Europe and the United States. The rise of Asia's competitive economies is fuelling a shift in the global scientific landscape. China, in particular, is emerging as a scientific superpower and, with annual growth in R&D expenditure averaging 21.6% per annum, the country is expected to become the world's biggest spender on science by 2022.[14] In recognition of this China, along with the US and India, hosts overseas offices for the UK Research Councils. Science was also a key focus for the recent UK state visit by the Chinese premier, Xi Jinping, with major deals for life sciences investment and collaboration on issues such as antimicrobial resistance. It is important to build upon these initiatives, and the Government should seek to showcase and export international partnerships in science at future trade missions if we are to truly capitalise on the opportunities presented by international partners, including those in the rapidly growing knowledge economies emerging in Asia.

15. Adams J & Gurney KA 2016 *The implications of international research collaboration for UK universities.* Digital Science
16. Research Councils UK 2015 *Shaping the future: UK-China collaborative research.*
17. Smith S & Adams J 2014 *'The Fourth Age of Research': implications and actions for global universities.* British Council in Tokyo
18. Nomaler Ö *et al.* 2013 Do more distant collaborations have more citation impact? *Journal of Infometrics* **7** 966–971
19. Persson O 2009 Are highly cited papers more international? *Scientometrics* **83** 397–401
20. Skyler JS *et al* 2008 Type 1 Diabetes TrialNet – an international collaborative clinical trials network. *Annals of the New York Academy of Sciences* **1150** 14–24
21. Waldmann H & Hale G 2005 CAMPATH: from concept to clinic. *Philosophical Transactions of the Royal Society of London B* **360** 1707–1711
22. Thomson Reuters 2014 *The research and innovation performance of the G20 and its impact on decisions made by the world's most influential economic leaders*

Case Study

The UNITE (Universities and National Institutes Transatlantic Eye Consortium for Human Ocular Immunology) programme is a collaborative research consortium focusing on immune-related eye disease. The programme sees British centres in Bristol and London collaborate with partners in the United States and China to lead pioneering research against common inflammatory eye diseases, such as uveitis, or conditions where inflammatory processes may play a role in disease progression.

The UNITE consortium combines the strengths of some of the world's most prestigious eye health research institutions. The project was launched in 2012, with Moorfields Eye Hospital, University Hospitals Bristol NHS Foundation Trust and the University of Bristol entering into an agreement with the National Eye Institute of the American National Institutes of Health. Later, UNITE would expand to include two of China's leading eye institutions – Zhongshan Ophthalmic Centre in Guangzhou and the Chinese University of Hong Kong.

UNITE operates as a single unified platform to co-ordinate research against inflammatory eye diseases, with the primary aim of treatment to control the inflammatory process. Early intervention is usually successful in resolving the disease, although more advanced cases are associated with serious complications, sometimes even blindness. The UNITE consortium aims to better understand the pathological processes behind these conditions in order to yield new and improved opportunities for therapeutic intervention.

Through collaboration, the centres are able to combine academic and clinical excellence in a way that synergistically drives cutting-edge research. This is brought about not least through the combined expertise of world-class scholars, with the opportunity to work with other leading people in the field a key advantage of the programme. However, UNITE is also a platform for the co-ordination and standardisation of data, resources and technologies. For example, by sharing biomaterials and other data, researchers are able to harness information from an extended cohort of patients – spanning the US and the UK – which aids the way in which researchers can test and validate their data. Participation from China adds lab resources, which play a hugely important role in powering research output.

Aside from the positive impacts on scientific output, the collaboration also produces a number of benefits that are less easy to quantify. For example, because key functions of the consortium, such as administration, are shared across all partners, the operation has been able to scale its work more appropriately as new partners have joined and the project has grown. Sharing the burden of research activity in this way also helps ensure more efficient utilisation of grant funding. Nevertheless at its heart UNITE, as with all research, remains a people driven process. Regular communication with participants is facilitated by modern innovations, such as Skype, and this frequent face to face interaction ensures the programme remains a strong platform for the sharing of ideas and knowledge that continues to expand research horizons in ocular immunology.

'Through collaboration, the centres combine academic and clinical excellence in a way that synergistically drives cutting-edge research. This is brought about through the combined expertise of world-class scholars, with the opportunity to work with other leading people in the field a key advantage of the programme.'

Data sharing:

the UK is leading the big data revolution

Research generates data to confirm or deny a hypothesis, validate a way of thinking, or generate new hypotheses and more targeted lines of inquiry. Sharing and accessing these data is a primary driver in the advancement of scientific discovery.

Sharing data is critical, especially in combatting trans-border health challenges. Outbreaks of infectious disease provide a perfect example. In February 2016, the Wellcome Trust, the Bill & Melinda Gates Foundation and the US National Institutes of Health signed a joint declaration with academic journals and other organisations to make all research data concerning the Zika virus outbreak unrestricted and free to access. They did so because the consequences of not sharing this information would severely hamper our capacity to respond appropriately to this public health emergency.[23]

Data sharing is invaluable for life science research in all domains. A firm grasp of the molecular mechanisms driving healthy immune function is fundamental to understanding how to address immune impairment. Many international collaborations are directly facilitating this understanding. For example, the 3i project, a collaborative consortium led by King's College London, is building an openly available database to describe the immunological function of almost 20,000 protein encoding genes in the mouse genome. The entire enterprise is open-source and all data are freely available on the project's website, providing immunologists with unfettered access to a catalogue of genes with relevance to immune function in health and disease. The 3i project is part of the International Mouse Phenotyping Consortium, a global collaboration building a comprehensive, open database to describe the function of genes in the mouse genome. Detailing the precise function of genes in this way is revolutionising how we approach some of the biggest challenges in immunology.

Providing more precise, targeted, effective diagnoses and treatments is a major undertaking, but one that is not beyond reach. The UK enjoys a leading position in this area and is taking bold steps to realise the future of genomic medicine, as demonstrated by the 100,000 Genomes Project, which is sequencing the genomes of 100,000 patients from the NHS. To capitalise on opportunities in this area requires large-scale, international efforts that ensure we are always at the leading edge of securing genomic data and in sharing these invaluable datasets responsibly. Managing, storing and sharing these vast volumes of data is more than any individual country can achieve alone, so it is imperative that we continue to work in the context of international, standards-driven, federated infrastructure such as the European ELIXIR network, which integrates data from across Europe.

Nonetheless, data sharing in the modern age presents new challenges. Technological advances, including those in genetics, are driving the generation of mass datasets at a scale and complexity never seen before. The 'omics' technologies (genomics, proteomics, metabolomics, transcriptomics etc) are complemented by advances in next-generation cell sequencing, DNA sequencing and high-resolution microscopy that enable immunologists to study immune processes in unprecedented fidelity. These new investigatory techniques produce staggering amounts of data, which must be stored, curated and disseminated effectively. This requires continued investment in supportive infrastructure and also a workforce that can interpret and interrogate this information intelligently. As much as the big data revolution is driving the life sciences, especially in immunology, it is also taking immunologists outside of their knowledge comfort zones. The development of skills not traditionally inherent in an immunologist's education – computational sciences and bioinformatics, for example – will be crucial in ensuring the UK can continue to remain a leading light in an increasingly data driven world.

23. Wellcome Trust 2016 *Global scientific community commits to sharing data on Zika.*

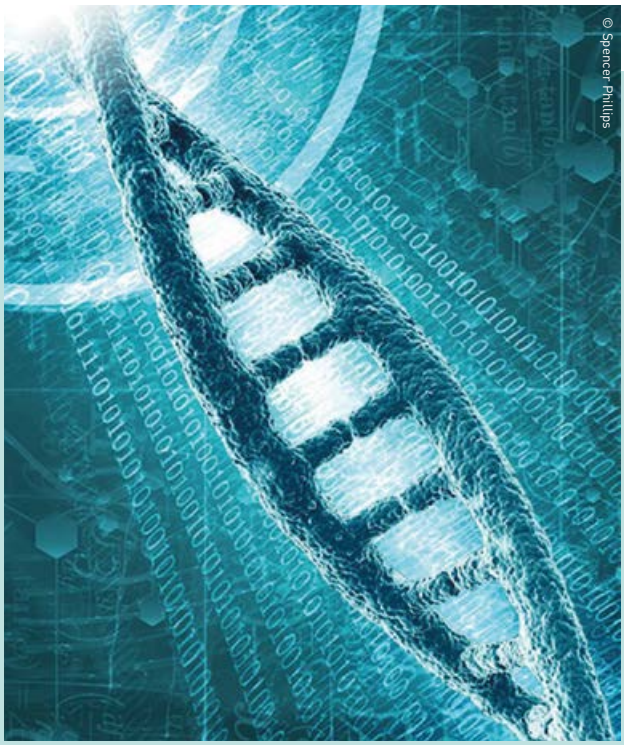
Case Study

The European Molecular Biology Laboratory (EMBL) is an intergovernmental organisation funded by 21 treaty members, representing countries primarily from Europe. EMBL acts as an international research institution with five sites across Europe each serving a specific field. The European Bioinformatics Institute (EMBL-EBI) in Hinxton, near Cambridge, is one of these sites and functions as a global hub for the hosting, development and curation of bioinformatics data.

EMBL-EBI is the embodiment of international co-operation at the cutting edge of life sciences research. A UK institution, part of a (principally) European consortium, and operating on a truly global scale, EMBL-EBI is the world leader in the collection, curation and provision of data-rich resources to researchers and industry partners across the globe. The tools and resources provided by EMBL-EBI, all of which are available free of charge, are an invaluable service in both basic and translational immunological research activities. The institution also carries out its own leading research in the field of computational biology, much of which has a direct impact on immunology.

EMBL-EBI is largely financed through its 21 European (plus Israel) member states. Additional funding is derived through bodies such as the UK Research Councils, the US National Institutes of Health) and the Wellcome Trust. The institute also competes for funding from the EU, which makes up the greatest proportion of its external funding and around 10% of its entire income. Although the UK's membership of the EU has no effect on the eligibility of EMBL-EBI to compete for this funding, leaving would be significantly disruptive, prompting uncertainty over current and future funding streams as well as existing collaborative projects with international partners.

As an internationally recognised centre of excellence, EMBL-EBI is able to attract the best scientists and researchers from around the world. The site's 550 staff represent 57 nationalities, less than half of whom are British, and many from outside the EU. As an international treaty organisation, EMBL-EBI is allowed to recruit non-EU staff through the Tier 5 (International Agreement) visa route. This streamlined visa process is of great benefit to EMBL-EBI's ability to recruit internationally. However, any disruption to the UK's obligations on free movement of people within the EU would require the institute to rely more heavily on the visa system, imposing a not-inconsiderable financial and administrative burden on the facility that would take resources away from the centre's scientific goals.



Large molecular datasets, perhaps most notably genomics datasets, are fast assuming a fundamental role in many immunological research activities. New developments in single cell transcriptomics, genomics and cell-sequencing are driving the big data revolution in immunology, allowing researchers to understand immune responses in unprecedented detail, right down to the state of individual cells. This generates huge amounts of data, which EMBL-EBI is able to efficiently store and curate as a central resource that is accessible to immunologists across the world.

Generating these biological data is often simpler than interpreting it to form and test intelligent hypotheses. Interrogating the data appropriately requires immunologists to either develop in themselves, or utilise in others, computational and numerical skills. EMBL-EBI recognises the need to help scientists get the best out of their datasets through training events and courses. Incorporating more formal computational biology and bioinformatics earlier in the education of young immunologists may be key to enabling UK scientists to maximise the benefits of data-driven research.

'Generating these biological data is often simpler than interpreting it to form and test intelligent hypotheses. Interrogating the data appropriately requires immunologists to either develop in themselves, or utilise in others, computational and numerical skills.'

Immunology serves the global public good:

science here can have profound effects around the world

In 1796, Edward Jenner purposefully inoculated the 8-year-old son of his gardener with smallpox. Jenner was testing a theory that the boy, James Phipps, would be prevented from contracting the disease because of an earlier inoculation with the milder, though related, cowpox virus. Thankfully this bold experiment, a pioneering use of vaccination, was successful, and Phipps did not develop any disease. Jenner's work in this area is credited as hugely significant in confirming vaccination as a means of preventing disease. At the time he could never have known that his research had set in motion a sequence of events that would culminate in the global eradication of a virus that had killed and maimed hundreds of millions throughout history, from the Pharaohs of ancient Egypt, to Presidents of the United States and reigning monarchs of Europe's royal families.

Jenner's research on vaccination demonstrates the universality of immunological knowledge. Working from his Gloucestershire home, Jenner had constructed the foundations of scientific thought that would later affect every living person on the planet at the end of the 20th century. When smallpox was declared eradicated in the wild in 1980, it was the first time in human history that people could live without fear of contracting one of the most devastating diseases known to science.

Like Jenner's work on smallpox, British immunologists continue to conduct research that improves the lives of those beyond the confines of our own borders. In today's globalised society, the grand challenges where immunology can make a difference (autoimmune diseases such as type 1 diabetes and rheumatoid arthritis, allergies, immunodeficiencies, infectious and insect-borne diseases, and conditions such as cancer) are increasingly cross-border in their effects. Just as rheumatic disease is not a phenomenon unique to the UK, neither are the benefits of immunological research into such conditions, which brings about new interventions to alleviate suffering, protect us from disease, and maintain good health in populations on a global scale.

The UK ranked top amongst the G7 nations for the quality of its research in infection and immunology between 2010 and 2014.[1] This means we are well placed to lead global action on health issues salient to immunology. Indeed, we have a proud history of global leadership on such issues. Most recently, UK-based immunologists were at the forefront of the scientific response to the Ebola outbreak, conducting research that spanned fundamental laboratory-based science right through to the development of candidate vaccines. Yet despite these successes the post-Ebola wash-up has prompted considerable criticism of an international response which has been characterised as slow and ineffective.[24, 25, 26] Both domestically and internationally, there remains an urgent need to improve our capacity to respond to such crises through the development of co-ordinated platforms for the research, development and manufacturing of new vaccines and treatments against novel or emerging disease threats. The UK should harness its key strengths in this area now, in the inter-epidemic period, to build global leadership, encourage international collaboration, and set in place the mechanisms that will help improve future responses.[27]

Aside from international health emergencies, we have led the way globally in other areas where immunological science can make significant contributions. For example, we have a long and proud history of research against tropical diseases, stretching back to the turn of the century and Sir Ronald Ross' Nobel Prize for his discovery that mosquitos are the vector for malaria, to the present day, where we remain the third largest funder of research on neglected tropical diseases behind the United States and the European Commission.[28] The UK Government has demonstrated commitment in this area through the £1 billion Ross Fund (named for Sir Ronald), which will sustain research into new treatments, diagnostics and vaccines against diseases in developing countries. The Department for International Development and agencies such as Public Health England have also shown commendable leadership in this area and both have significant global footprints. We urge the Government to utilise these strengths and ensure global health issues where immunology can make a significant impact are priority items for engagement at international political fora and summits.

24. World Health Organization 2015 *Report of the Ebola Interim Assessment Panel.*
25. Moon S *et al.* 2015 Will Ebola change the game? Ten essential reforms before the next pandemic. The report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola. *The Lancet* **386** 2204–2221
26. House of Commons Science and Technology Committee 2016 *Science in emergencies: UK lessons from Ebola.*
27. For example, see: British Society for Immunology 2015 *A proposal to create a 'UK Vaccine Network'.*
28. UK Coalition against Neglected Tropical Diseases 2015 *Annual Report 2014–15*

Case Study

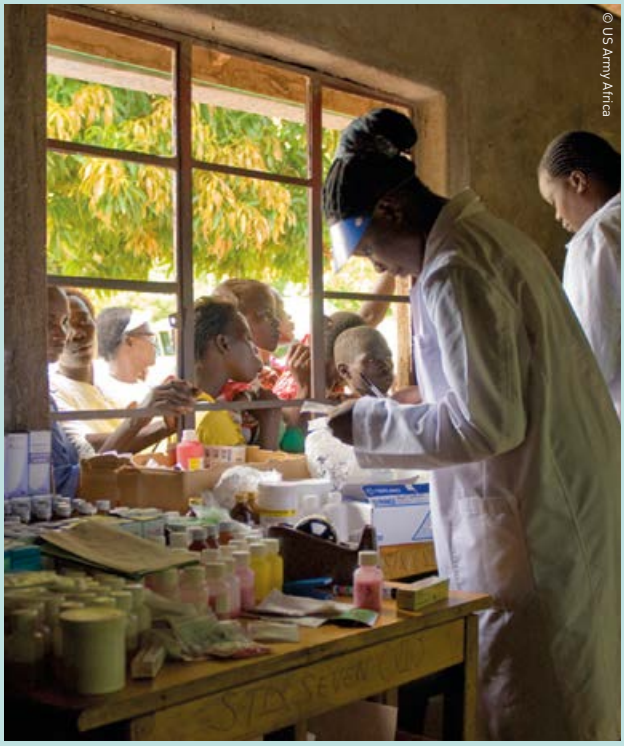
Shona Wilson is a researcher at the University of Cambridge who works on helminth infections, such as schistosomiasis. These diseases, which are especially common in low income settings, are considered neglected tropical diseases and are a key driver of poverty and ill health for more than 1 billion people worldwide. Shona's research uses immuno-epidemiological techniques (combining immunology with epidemiology) to better understand how parasitic worm infections affect vulnerable communities in Africa.

My research uses epidemiological techniques to control for confounding factors in research to better understand the progression of parasitic worm diseases. The techniques we use help control for variables such as age, gender or co-infection that could have an influence on an individual's immune response to infection. Helminths, such as Schistosoma species, are amongst the most common infections in developing countries and have a combined global burden of disease that exceeds more well-known diseases like malaria. Yet there remains so much we don't know about these infections. Improving our understanding of the fundamental processes involved is key in supporting efforts to develop new strategies for either treating the disease when someone has contracted it, or preventing them from getting it in the first place.

I am based in Cambridge and spend around 2–3 weeks in the field each year. We work closely with colleagues in Uganda, Kenya, Mali and Tanzania. These collaborations are essential for our work. Through university incentives, we are also able to bring African students to Cambridge, giving them access to academic expertise and lab facilities they would not otherwise get in their own countries. This is great not only because we can help them gain new skills which they then take back to build the research programmes in their own nations, but also because these exchanges are often the beginning of new relationships with scientists who will be crucial collaborators with us in future studies.

Our research has been supported through funding from a variety of sources, including the research councils and other UK funders, but also EU's funding frameworks. This includes successful attainment of programme funding from the EU that enabled us to recruit staff and carry out work across four sites in Africa. Internationally we are a world leader in this area and the UK has a very strong heritage in tropical medicine research. This expertise means we are well placed to support global collaborative initiatives that look to resolve these types of diseases. The UK Government has in the past supported this kind of action, such as through its endorsement of the London Declaration on Neglected Tropical Diseases, and it is right that we utilise our strengths in this area to support high quality scientific research that makes such a difference to the lives of vulnerable communities in other parts of the world.

'Internationally we are a world leader in this area and the UK has a very strong heritage in tropical medicine research. This expertise means we are well placed to support global collaborative initiatives that look to resolve these types of diseases.'



The British Society for Immunology's mission is to promote excellence in immunological research, scholarship and clinical practice in order to improve human and animal health.

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