BSI diamond anniversary:
Marking the achievements of the last 60 years

CAR T-cell immunotherapy:
achievements and challenges

Journey to clinical immunology:
career path outlined

Brexit: Implications for immunology

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Intrinsic Pathway (Mitochondria)

Snapshot of the first steps of the intrinsic apoptosis pathway.
Well, no one can accuse 2016 of being boring! It’s been an exceptionally eventful few months in the political sphere here in the UK, with Britain voting to leave the European Union and a new Prime Minister in post. These developments undoubtedly have implications for all of us in the field of immunology and our Policy Manager Chris Lowry takes a closer look on page 6.

Meanwhile, Antonella Adami and John Maher examine the achievements and challenges within the quickly developing field of CAR T-cell immunotherapy on page 12, a treatment currently on the threshold of revolutionising our approach to treating several types of cancer.

Finally, as I’m sure you’re aware, 2016 marks the BSI’s 60th anniversary. We report on a host of activities that we have underway to celebrate this on page 14. We hope that as many of you as possible are able to join us to commemorating this special milestone for the Society.

Thoughts, feedback and comments as always welcome to the email below.

Best wishes,
Jennie Evans
j.evans@immunology.org
As we watch a new Prime Minister take the helm this summer and settle in to the flat above the 'shop', it is unsettling to think that in a year's time this will be history and a new landscape for British immunology will be in sight.

In Theresa May's first speech as Prime Minister, she emphasised social justice, the system that the UN describes as 'the fair and compassionate distribution of the fruits of economic growth'. She stated, ‘When it comes to opportunity we won’t entrench the advantages of the fortunate few, we will do everything we can to help anybody, whatever your background, to go as far as your talents will take you.’

Like many learned societies, the focus of recent discussions with British and European colleagues alike has been on where science will feature in the new Government’s EU negotiations – for funding streams, for freedom of movement, for regulation and for our international relations and collaborations.

However when it comes to opening up opportunities of equality, there are some aspects of life which remain stubbornly immune to change, and one of those is a child's chances of receiving a good science education. If science is the cornerstone of the UK's future, why aren't students prioritised? Around the UK, considerable variations in the quality and quantity of science teaching persist. The amount spent on teaching science varies enormously, with one 2012 study showing the amount per secondary school pupil varied from 75p to £31. Having laboratory space, the right equipment, and time in the curriculum are all essential but often lacking factors; the difficulties in recruiting teachers are well documented and recognised by the government. With the new Education Secretary Justine Greening working with the Science Minister Jo Johnson, it would be good to see a strategy for more support in the formative years so that our fantastic achievements in science are built upon for the next generation, and are not just available to the few.

The BSI has its 60th anniversary celebrations coming up, and we hope that many of you can attend our lecture at the Royal Society on 11 October, and stay for a drink afterwards to catch up with colleagues [see page 14 for more details]. Many thanks to those of you who have sent in such good ideas for our 'Immunology in 60 Objects', which has sparked lots of thought and is being put together as we speak.

I wish you a good September.

Jo Revill
Chief Executive,
British Society for Immunology
Email: j.revill@immunology.org

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COMMITTEE NEWS

Following the recent call for nominations and subsequent election we are delighted to announce the following appointments:

**Matthias Eberl** joins the Board of Trustees, as from January 2017. The Board is the governing body of the BSI and is responsible for ensuring that the organisation operates properly and effectively.

**John Curnow** will take over as Groups & Meetings Secretary from January 2017, (he will shadow the present Secretary, Rob Barker, from July 2016), and will work closely with the BSI team to coordinate our numerous Regional and Affinity Groups and their activities.

We have five new members on the Forum: Louise Cosby (Northern Ireland rep), Rebecca Newman (Early Career), Maria Montoya (Veterinary), and Antonios Psarras & Fane Mensah (PhD). The Forum is the BSI’s ‘think tank’ and the place where the issues and ideas that are of importance to the Society and its members are raised, discussed and developed.

**Gary Entrican** was elected as Congress Secretary (with 51% of the vote), and will start shadowing the present Secretary, Leonie Taams, from October 2016, before taking over from December 2017. Gary will chair our Congress Committee, and work closely with the BSI team to organise the BSI Congress. Welcome to Gary, and a huge thank you to Simon Milling who also stood in this election, coming a close second with 49% of the vote. Gary will be joined by our new Congress Committee members, Paul Bowness, Luke Foster, Ian Humphreys and Irina Udalova who take up their posts from October.

We’d like to thank all of our committee members past and present for their hard work and commitment to the BSI, and would like to encourage all of our members to apply for committee opportunities as they arise.

**Emilie Thomas**  Committee & Governance Manager, British Society for Immunology
**SOCIETY NEWS**

**New Impact Factors**

The 2015 Impact Factors for journals have been announced, and we are delighted to say that the impact factors for both of the BSI journals have increased.

*Clinical & Experimental Immunology*

2015 Impact Factor: **3.148**

*Immunology*

2015 Impact Factor: **4.078**

We are particularly encouraged by the performance of *Immunology*, as this marks its sixth consecutive rise in a fluctuating climate, and sees it break into the 4s. These figures are a testament to the continued hard work of the Editors-In-Chief, Mark Peakman and Danny Altmann, their associate editors, and the journals teams at both the BSI and Wiley. We must also credit our authors and readers – many of whom are BSI members – whose devotion to the field of immunology and interest in our journals is vital to their rude health.

May the upward trajectory continue!

**BSI Medical Elective scheme**

We are pleased to announce the renewal of our Medical Elective and Summer Placement Award Scheme (MESPAS) for 2016–17. This funds medical students to undertake a medical elective or research project with immunological relevance. Awards of up to £1,500 are available. Click [http://bit.ly/2aoG5tX](http://bit.ly/2aoG5tX) for more information.

**New BSI website coming soon**

Here at the BSI, we’ve been hard at work developing our new website which will give our members an improved user experience as well as allowing us to reach out and communicate with new groups. The website will be fully mobile compatible and will launch later this year.

**EFIS Ambassadors**

The European Federation of Immunological Societies (EFIS) is looking to recruit early-career ambassadors from each national immunology society to work with them to highlight to early-career scientists what EFIS can offer to them. If you are interested in filling this post for the BSI, please email Emilie Thomas at e.thomas@immunology.org.

**Listen again! Cheltenham Science Festival 2016**

Visit our SoundCloud page to listen to the recordings from our recent Cheltenham Science Festival events. With talks featuring ‘disgustologist’ Val Curtis, oncologist Siddhartha Murghejee and immunologists such as Jim Kaufman, Dan Davis and Salim Khakoo, there’s plenty to discover. If it’s music you’re after, you can find a range of T cell and pathogen inspired tracks on the page as well! Visit [https://soundcloud.com/brit-soc-for-immunology](https://soundcloud.com/brit-soc-for-immunology).

**Upcoming BSI meetings**

Visit [www.immunology.org/events](http://www.immunology.org/events) for more information.

**CAMBRIDGE IMMUNOLOGY FORUM**

22 September 2016, Cambridge

**JOINT BSI & NVVI CONGRESS 2016**

6 – 9 December 2016, Liverpool

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**New Bite-Sized Editorial Board**

We’re delighted to welcome Lewis Cawkwell, Timothy Donnison, Hannah Jeffery, Louisa Jeffery, Kylie Morgan, Mezida Saeed and Sonali Singh to the newly formed Editorial Board for Bite-Sized Immunology. The new board will be working with Helen Collins, the BSI Education Secretary, to develop and update the content on our highly used education resource.
“I would be absolutely flabbergasted if the UK electorate vote to leave the UK,” Barry Orr, spokesperson for online betting company Betfair, told the Daily Telegraph on 23 June. Indeed, Betfair’s odds on the day of the referendum offered an implied probability of 74% for ‘Remain’. Bookmakers William Hill and Ladbrokes were offering a 76% and 78% chance, respectively. Even investors seemed to be banking on a remain vote, with markets across Europe surging in the days before the referendum. And yet, as would later become only too clear, the predictions of experts were a rapidly diminishing currency.

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A unified voice

It is perhaps an understatement to say that the referendum outcome took a few people, Barry presumably included, a little off-guard. Many in the scientific community in particular will be shocked by the result. Whereas the country was deeply divided on the issue of immigration and a perceived erosion of national sovereignty, scientists spoke with one voice on the value of EU funding, collaboration, and the benefits of open borders and free movement of people.

Therefore, as the country begins to contemplate the implications of a post-EU landscape, many immunologists will have more than a few questions on their mind: What now for European grant funding? Or participation in research consortia? How does this affect shared international facilities like the European Bioinformatics Institute? And what does the result mean for friends, colleagues and students who have come here from overseas to study or contribute so valuably to vitally important research?

Unchartered waters

Without access to a functioning crystal ball definitive answers to these questions are impossible to find. The very nature of the circumstances the country now finds itself in, a geopolitical shift unprecedented in scale and complexity in the modern era – perhaps matched only by the gradual collapse of the British Empire, means that we face a period of great uncertainty. But whereas the plans for partitioning India and Pakistan – thus creating the two sovereign states – were said to have been drawn up over lunch, the UK’s separation from the EU will be a much more protected affair, with a multitude of different exit scenarios possible. Indeed, even in David Cameron’s government, Brexit appeared to mean different things to different people. Take this, and couple it with a divisive referendum campaign marked throughout by bombast and bluster (of which both

sides, to a greater or lesser extent, were guilty) and you have the present mood of ‘Remainers’: uncertain, even pessimistic.

For these reasons it is worth reflecting on the facts as they exist now. Nothing has changed in legal terms. The UK will remain a full EU member (with all the rights and obligations that affords) up to and during the two-year renegotiation process triggered by Article 50. The government has already moved to reassure EU students at British universities (as well as those beginning courses in September) that their funding will be protected for the duration of their study. The Science Minister, Jo Johnson (who retained his post in Theresa May’s reshuffle), has also stated that it is “business as usual” for participation in Horizon 2020 schemes.

Concerns already surfacing

These reassurances, however, probably mean little to those people on the ground from whom disconcerting stories are beginning to bubble to the surface. Anecdotal accounts of researchers being asked to leave EU-consortia or for lead investigators pressured to step down because of uncertainty over future funding arrangements are beginning to appear in the media. There are also reports of researchers who are reluctant to bid for EU grants and institutions that are unwilling to participate in collaborations for fear of being seen as a potential ‘weak link’.

Such reports are concerning. One of the most important roles a learned society or membership body can perform in these times is to act as a direct link between the membership and decision makers in government. We would be very grateful to receive information, which will be treated in confidence, on how the referendum has impacted (or is likely to impact in the future) your area. We will combine this information with the recommendations of our recent report Immunology: An international, life-saving science and, working with partners, seek to ensure science, and

immunology in particular, features prominently as the new government negotiates the UK’s divorce from Brussels.

Celebrating our international community

One final thing is worth considering in the immediate aftermath of the referendum. The rising tide of xenophobia and racism experienced across the country (and in some universities) has been an ugly consequence of the vote. In some ways science is an antidote to this.

The UK is a world leader in immunology precisely because we are able to attract the best talent from across the world to work and study here. We recognise the contribution of international researchers to immunological research in the UK as something worth celebrating. That is why the first recommendation of our internationalism report implores government to take every opportunity to make it clear that the UK welcomes overseas talent. For all the prophesying and prognostication over what the vote might or might not mean for science, one thing is absolutely clear: this recommendation, which seeks to send a strong message to the international community that the UK remains a welcoming and open country, is important now more than ever.

Chris Lowry
Public Affairs Manager,
British Society for Immunology
Email: c.lowry@immunology.org

BSI teaching survey findings

We recently carried out a teaching survey of our members to find out who and how they teach and what the BSI can do to support their work. Here, we present a summary of the initial findings from the 184 responses that we received. Our staff and trustees are now analysing the implications of this and we will bring you more news shortly on future BSI activities in this area.

Respondants’ career level

![Respondants’ career level chart]

Percentage of time spent teaching

![Percentage of time spent teaching chart]

What activities should the BSI offer to support immunology teaching?

Training and a Mentoring Programme were the most popular choices for Early-Career Researchers; whereas Lecturers and Professors were most supportive of a virtual network of educators/teachers.

Activities carried out

<table>
<thead>
<tr>
<th>Activities</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Face-to-face lecturing</td>
<td>90%</td>
</tr>
<tr>
<td>Distance/e-learning</td>
<td>13%</td>
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<tr>
<td>Small group tutoring</td>
<td>73%</td>
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<tr>
<td>Practical labs</td>
<td>53%</td>
</tr>
<tr>
<td>Lab project supervision</td>
<td>82%</td>
</tr>
<tr>
<td>Career skills</td>
<td>31%</td>
</tr>
<tr>
<td>Course organisation</td>
<td>45%</td>
</tr>
</tbody>
</table>

Had received training prior to commencing teaching

45%

Hold a teaching qualification

42%

Said they received adequate ongoing training from their institute

60%

Said there was a clear promotion track within their institute for educators

36%
What’s in your sample?

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The editors of Clinical & Experimental Immunology, one of the BSI’s official journals, are looking for submissions of exciting and innovative clinical and translational research, particularly in the areas of immunotherapy, disease mechanisms, new diagnostics, and clinical guidelines, pathways and consensus statements.

In addition to research papers, we also publish reviews and perspectives. If you have an article in mind that you would like to write for us, please contact the editorial office at imm@immunology.org, with an outline of your proposed article. Don’t forget, when you publish in Clinical & Experimental Immunology, you can expect:

- a rapid time to first decision, with an average of 12 days
- highly visible, search engine optimised publication on Wiley Online Library and PubMed Central
- up-to-date altmetrics and citation information for real-time monitoring
- promotion of your articles by specialist journals marketers at both Wiley and the BSI
- no publication charge for full BSI members, or a fixed charge of £95 per paper for non-members.

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Early bird registration deadline: 20 OCTOBER 2016

For further information and continuous updates, please visit: WWW.BSICONGRESS.COM
Clinical Excellence Awards for NHS consultants (England & Wales)

Clinical Excellence Awards (CEA) recognise individuals who make exceptional contributions to the NHS. Applications can be either at a local (employer based awards) or national level. The latter category of higher level awards is aimed at NHS consultants who perform ‘over and above’ the standard expected of their role. This includes those who do so through their contribution to academic medicine. To be considered for an award, you must demonstrate achievements in developing and delivering high quality patient care, and contribute to the continuous improvement in NHS service organisation and delivery.

Annually, approximately 300 awards are given in England, and 18 in Wales. As there are a limited number of new awards agreed by Ministers, this makes the process very competitive. The success rate for achieving CEA awards in 2014 was approximately 20%.

BSI support

Applications are assessed at an employer level initially with higher value awards assessed by the Advisory Committee on Clinical Excellence Awards (ACCEA) for England and Wales. These awards (levels 9–12) are known as bronze, silver, gold or platinum CEAs.

Professor Graham Lord, MRC Centre for Transplantation, King’s College London

“Thanks to support from the BSI, I achieved a silver level CEA award in 2015, which means a great deal professionally. It’s great to have your work acknowledged in this way, and to be endorsed by a national body such as the BSI makes a big difference. The process can be complicated, so having the support of your membership society is really useful.”

Professor Paul Klenerman, Nuffield Department of Medicine, University of Oxford

“I received a bronze CEA award last year – the BSI supported my application and I am really grateful they did. I had been unsuccessful numerous times in the past and had pretty much given up hope. The system is a bit complicated and some of the sections don’t apply as obviously to people in the lab or a research environment – so having support from a national body like the BSI is really important in giving a bit of overall context. I would certainly encourage anybody applying to talk to the BSI – often ACCEA set quite tight deadlines, so it all can feel a bit stressful – but the BSI were helpful and encouraging. I’d certainly like to thank all those involved and wish good luck to anybody applying this time around.”

Emilie Thomas
Committee & Governance Manager, British Society for Immunology
Email: e.thomas@immunology.org

The BSI also represents immunology on the scoring panel of the Royal College of Physicians (one of the national nominating bodies). We’d like to say a huge thank you to all those who have supported the BSI in this process over the years, both by scoring and writing citations, and wish the current applicants success for the 2016 round. The round closed in May, with results expected in January 2017.

Look out for a call in Spring 2017 for the next round of awards; more information at http://bit.ly/29UHnJQ
CAR T-cell immunotherapy
– a perspective on achievements and challenges

After decades of failure, immunotherapy has recently begun to revolutionise the treatment approach taken for several cancer types. Harnessing the power of the immune system to seek and destroy transformed cells has the potential to achieve long-term remission and prevention of cancer recurrence.

CAR T-cell immunotherapy success in ALL

One of the roles of the immune system is to identify cancer cells through the recognition of tumour antigens and to eliminate these cells through a process of immunosurveillance. Unfortunately, due to the immunosuppressive nature of the tumour micro-environment, cancer cells can often escape this process, expand and become a poor target of immune responses. Immune checkpoint blockade is a logical approach that helps to re-invigorate tumour-specific immune responses, impacting meaningfully in the treatment of several solid tumours such as melanoma and non-small cell lung cancer. Perhaps even more remarkable has been the recent success of cellular therapies in which patient derived T-cells are genetically retargeted using chimeric antigen receptors (CARs). When applied to the treatment of patients with refractory acute lymphoblastic leukaemia (ALL), CAR T-cell immunotherapy achieves complete remission of disease in over 80% of cases. In that setting, T-cells are re-targeted against the ubiquitous B-cell antigen, CD19. The efficacy of CAR T-cell immunotherapy of ALL is unprecedented for a new cancer medicine but a key question is whether comparable success can be achieved in other cancer types.

Construction of chimeric antigen receptors

Chimeric antigen receptors are membrane spanning fusion molecules that couple the direct binding of a specific cell surface-associated target to the delivery of an immune cell activating signal. Targeting is most commonly achieved using a single chain antibody fragment, although peptides and ligand derivatives may be used alternatively. This element is separated from the signalling domain by a hinge/spacer and transmembrane domain.

Chimeric antigen receptors are delivered by gene transfer, most commonly using retroviral or lentiviral vectors. The most commonly used host cells are patient-derived peripheral blood T-cells, although these fusions can also be expressed in other immune cell subsets [e.g. NK cells], or even in stem cells. Owing to their antibody-like binding properties, CAR T-cells bypass the need for HLA restriction and circumvent immune evasion mediated by tumours that downregulate HLA class I expression at the cell surface. T-cells that are re-targeted using CAR molecules mediate anti-tumour responses through direct cytotoxicity and the release of a panoply of immunomodulatory molecules.

Construction of CARs remains a largely empiric process since all elements of the fusion may require refinement and optimisation. Based upon the endodomain of these molecules, several CAR generations have been described in which a CD3 zeta [or functional equivalent] module is found alone [first generation] – a perspective on achievements and challenges

‘Several other examples of on-target off-tumour toxicity have been reported which have resulted in death or significant organ damage, highlighting the need for careful target validation.’

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or is coupled to one (second generation) or more co-stimulatory elements.

First generation CARs were developed by Eshhar, establishing proof of concept for this emerging technology. However, clinical efficacy required the additional provision of co-stimulation by CD28 or 4-1BB, leading to enhanced proliferation and reduced anergy or activation induced cell death. Second generation CARs were originally described by Finney and colleagues and were first shown to be functional in human T-cells by Maher and Sadelain. The alternative 4-1BB-based second generation CAR platform was originally developed by Campana and Imai. Both second generation variants have demonstrated compelling efficacy in patients with ALL, treated at multiple independent clinical centres. Third generation fusions have also been described in which two co-stimulatory modules are present, although improved functionality compared with second generation iterations remains uncertain.

**Limitations of CAR T-cell immunotherapy**

Despite the success of this technology in patients with ALL, response rates have been somewhat less impressive in patients with more indolent B-cell malignancies. Most disappointingly however, results in patients with solid tumours remain unimpressive. Lack of efficacy in this context has been ascribed to several challenges, including the paucity of safe tumour-specific targets, inadequate homing of CAR T-cells to tumour deposits and susceptibility of these cells to suppression within the tumour micro-environment.

CAR T-cell immunotherapy is also limited by potentially severe toxicity. In patients treated with CD19-targeted CAR T-cells, B-cell depletion commonly leads to impaired antibody-forming capacity and hypogammaglobulinemia. This predictable ‘on-target off tumour’ toxicity can be mitigated by immunoglobulin replacement therapy. However, many patients also develop cytokine release syndrome, which is a profound systemic inflammatory response driven by the interaction between CAR T-cells and cells of the mononuclear phagocyte lineage. Treatment of cytokine release syndrome may require intensive medical support, including the administration of pressor agents and mechanical ventilation. In addition, biological agents such as the anti-interleukin 6 receptor antagonist, tocilizumab, can prove dramatically effective in some cases. Neurotoxicity is also emerging as a common and sometimes fatal toxicity and may relate to the ability of CAR T-cells to enter the central nervous system. This can manifest with deficits such as impaired speech, vision, confusion or seizure activity. Several other examples of on-target off-tumour toxicity have been reported which have resulted in death or significant organ damage, highlighting the need for careful target validation.

**Expensive production**

Immunotherapy using CAR T-cells imposes high manufacturing costs since cell products are generally autologous (e.g. patient-derived) and good manufacturing processes and manufacturing facilities are required. In general, patients undergo a leukapheresis to provide sufficient cells from which to generate a product; although some investigators have developed systems to allow the use of whole blood as an alternative. T-cells are generally activated ex vivo and, following gene transfer, cell products are expanded over a period of 10–14 days. Prior to administration, quality control assays must be performed on the CAR T-cell product, followed by a concentration and sometimes a cryopreservation step. This allows the shipping of cell products from centralised manufacturing facilities to the site of the patient.

**Commercial interest**

Until recently, CAR T-cell immunotherapy has largely been an academic activity. However, there is increasing commercial interest in this sector, leading to the launching of several spin out companies and partnerships between academic centres and pharmaceutical companies. To facilitate more widespread rollout of this technology, there is increasing interest in the development of universal cell therapy products. Examples include the use of allogeneic CAR T-cells that have been genetically engineered to minimise risk of graft versus host disease and immune-mediated rejection.

We have reached a truly exciting stage in the development of this new modality of cancer therapy. To make major impact, it will be necessary to adapt this technology for the treatment of solid tumours. Success in that arena will certainly prove transformative to cancer medicine.

Antonella Adami
Research technician and GMP production scientist

John Maher
Consultant and Senior Lecturer in Immunology
CAR Mechanics Group, Division of Cancer Studies, King’s College London
60 years of the British Society for Immunology

2016 marks the 60th anniversary of the British Society for Immunology. We have a number of activities planned, centred around the key date of 11 October. We hope that as many as of you as possible are able to join in celebrating this important milestone for our Society.

BSI 60th Anniversary Lecture: The changing face of research
18:00 – 19:30, Tuesday 11 October 2016
Royal Society, London, UK

Join us in the celebration of the 60th anniversary of the British Society for Immunology as we explore how biomedical research has changed over the past 60 years and where it may lead us in the future.

When a small group of immunologists founded the British Society for Immunology 60 years ago, they could hardly have foreseen the explosion of knowledge that would follow. So much has changed: the technology, the nature of research, the levels of insight and the financial investment in making each new discovery.

Throughout this period, the BSI has remained a constant force in the life of its members, encouraging and supporting the study of immunology and helping us to share and discuss ideas. Despite all these changes and progress, so much about the immune system remains a mystery. We have an exciting future.

As a member, you are the lifeblood of the BSI. I hope you will join us in marking our 60th anniversary by attending a very special event, and now formally invite you to the BSI’s 60th anniversary lecture and drinks reception.

I will be joined on stage by Professor Sir Robert Lechler, President of the Academy of Medical Sciences and Professor Fiona Powrie, Director of the Kennedy Institute at Oxford University to discuss: ‘The changing face of medical research’.

We will examine how biomedical research has evolved over the past 60 years, from self-experimentation that would be unimaginable today, to big data and global collaboration. We anticipate a lively debate and stimulating discussion between our speakers and the audience, all chaired by Professor Adam Hart (author and broadcaster), so please bring your reminiscences and predictions of the future to what will undoubtedly be a memorable event.

The event is free and will take place at the Royal Society, London at 18.00 on Tuesday 11 October. I hope you are able to join us. We anticipate that this will be a popular event, so please reserve your place now.

With best wishes,

Professor Peter Openshaw
President, British Society for Immunology

All BSI members are warmly invited to join us at our anniversary lecture and at the drinks reception afterwards. To book your free place for the BSI anniversary lecture, please visit http://bit.ly/BSIat60.

Speakers
Professor Peter Openshaw, BSI President and Professor of Experimental Medicine at Imperial College London

Professor Fiona Powrie, Director of the Kennedy Institute of Rheumatology and the Translational Gastroenterology Unit at University of Oxford

Professor Sir Robert Lechler, President of the Academy of Medical Sciences and Vice-Principal (Health) at King’s College London

Chair
Professor Adam Hart, author and broadcaster and Professor of Science Communication at University of Gloucestershire
The UK currently ranks first amongst the G7 for the quality of our research in infection and immunology. At the BSI, we want to use our 60th anniversary to celebrate the breadth and depth of immunological research in this country and beyond. More than that, we want to engage with Government, decision makers and funders to tell the story of just how important immunological research is to the life sciences, patient care and the economy. Ensuring that immunology, in all its rich diversity, is appreciated and understood provides us with a much stronger platform to advocate on the key issues that affect both our members and the discipline as a whole as well as the health and wellbeing of the public.

To do this, we have commissioned a report to discuss key areas where immunology has and will have a significant impact in our understanding of human and animal biology, our ability to treat and even cure common diseases, and our capacity to deal with emerging threats on a global scale. We will launch this publication on Tuesday 11 October at our anniversary lecture. We hope this will prove an enjoyable read for you and will have a big impact on our ability to show how important immunology research is all sectors of society as a public good.

Immunology has the ability to make a difference and we want everyone to know this!

Immunology: the past, present and future

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**Immunology in 60 objects**

The discipline of immunology has a long and proud history, but if you had to pick 60 items to tell the story of immunological research through the ages, what would you choose?

The BSI has tried to answer this with our ‘Immunology in 60 objects’ project. Each object has been suggested by a BSI member to tell the tale of a specific discovery, new technique or step change in thinking in our wonderful discipline.

From October onwards, we will release one object per day to chart the tale of immunology from Edward Jenner’s discovery of the smallpox vaccine right up to the present day. We really hope that you, as our members, will again get involved with this project when launched, helping us to publicise to a wide audience and giving us your feedback on the items chosen.

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Keep an eye on our website for more details and follow #60objects.
UKPIN has the overall aim of advancing care in PID. We are progressing and supporting a range of PID-related activities including the UKPID registry, QPIDS accreditation, guideline development, the UKPIN biennial conference and enhancing communication and collaboration with academic and research initiatives.

The UKPID registry
In October 2015 the registry switched to the new European Society for Immunodeficiencies (ESID) structure, which is simpler to use, includes checks to improve data integrity and enables more reliable data to be generated. Currently the registry only collects the Level 1 dataset, which includes basic demographic data, consent details, diagnosis, genetic results and treatment details (immunoglobulin replacement therapy, transplant and gene therapy). In the new design, any entry without a genetic mutation must have the diagnosis validated against the ESID Registry diagnostic criteria and all entries must have the level 1 dataset completed before accepted into the ESID registry. In the new design, data are also collected on date and cause of death for deceased patients.

The level 2 datasets have not yet been finalised by ESID and there is currently no date set for their completion and adoption by the UK registry. Level 2 is disease specific and includes fields such as laboratory results, other diseases, infections and quality of life data. Development and completion of level 2 data will incrementally increase the quality of data and knowledge on outcomes and response to treatment in these very rare conditions.

The UK registry continues to include patients with hereditary angioedema (HAE) and secondary antibody deficiency, although they are no longer included in the ESID Registry. The staff supporting the registry, and funded by UKPIN, have been instrumental in ensuring the success of the registry to date.

QPIDS
The UKPIN clinical PID service accreditation scheme has successfully transferred to the Royal College of Physicians (RCP), where it is now known as the Quality in Primary Immunodeficiency Services (QPIDS) scheme. The accreditation standards have had light touch revision and the accreditation pathway has been aligned to the RCP’s methodology. Updates on the status of accreditation and registration can be found on the UKPIN and QPIDS websites. The QPIDS scheme is recognised by the NHS England service specification for specialised immunology, which requires specialist units to be working towards accreditation in order for their services to be commissioned.

A total of 22 services have registered for the scheme so far, with seven of these previously accredited under the UKPIN scheme. Registered services are working towards accreditation and we hope to see the first QPIDS accredited service soon.

The first training day for services registered for accreditation was held in January 2016, with excellent feedback received from delegates. The day will be held regularly, with a further day planned for later in 2016.

Biennial conference 2015
The UKPIN biennial conference was held in Belfast in November 2015 and was a great success. The meeting focus was ‘New Entities in Primary Immunodeficiency’, an exploration of how genomic medicine has impacted on discovery in PID and its treatment. There were parallel sessions with an update on new diagnostic tests and helping patients manage long-term conditions. For the first time, patient representatives were hosted...
within the main meeting space and this was extremely important in networking between all professional groups.

The great debate – now a regular feature – considered whether genomic medicine would replace functional immunology testing. As always, the purpose of this session was to provide lively discussion, and the audience were enthusiastically engaged.

The conference finished with a session that covered the genomic projects currently underway and a final thought-provoking talk on how pathogen as well as host genomics is an essential part of ongoing research in understanding the immune-pathogen interface.

Who attended the 2015 conference?

357 delegates
197 separate organisations represented
131 clinicians
100 consultants
62 nurses
44 healthcare scientists
11 researchers

‘The staff supporting the registry, and funded by UKPIN, have been instrumental in ensuring the success of the registry to date.’

Videos of sessions, photos and poster abstracts are available for members to view online, including a report by Suzanne Elcombe providing a trainee’s perspective on the meeting.

Biennial conference 2017

The 2017 meeting will take place in Brighton on 7–8 December. This follows immediately after the British Society for Immunology Annual Congress (4–7 December), with a single overlapping day and a joint plenary session. Please save the date. The organising committee is being led by Kimberly Gilmore for UKPIN in collaboration with the BSI.

Guideline development

UKPIN is working with the BSI on the development of clinical guidelines for primary immunodeficiency diseases. Stephen Jolles is leading this initiative for UKPIN in collaboration with the BSI.

Research collaboration

The refresh of the UKPIN website has also allowed the creation of an area dedicated to research. The 100,000 genomes project is an exciting research development that aims to sequence 100,000 genomes from 70,000 people by the end of 2017. Sophie Hambleton, the Genomics England Clinical Interpretation Partnership (GeCIP) Immune Disorders Lead for UKPIN, has provided UKPIN with a brief summary of the project, which can be accessed via the website.

Tomaz Garcez
Chair, UKPIN

Useful links

Registry page http://ukpin.org.uk/registry/registry-intro
UKPIN accreditation page http://ukpin.org.uk/accreditation
UKPIN clinical guideline updates: http://ukpin.org.uk/guidelines/ukpin-guidelines
UKPIN steering committee http://ukpin.org.uk/about/present-steering-committee
UKPIN research page: http://ukpin.org.uk/research/research-current-initiatives
QPIDS website: www.qpids.org.uk
GECIP UKPIN Forum: http://ukpin.org.uk/interest-groups/gecip

Become a UKPIN member

Please consider joining the UKPIN membership by following the appropriate links on the UKPIN website. Together we can improve the care of patients with PID.

UKPIN membership: http://ukpin.org.uk/members/membership
This joint event between the British Society for Immunology and the Dutch Society for Immunology brings together two of Europe’s most established immunology organisations for a jam-packed programme full of the latest immunology research, top speakers and diverse networking opportunities. Join over 1,000 delegates from around the globe for four days of immunological delights!

**BSI Congress bursary**
All BSI members can apply for a Congress bursary to assist with the costs of attending the meeting. Application deadline is **20 September** and you can find more information at http://bsicongress.com/bursaries-and-grants.

**Bright Sparks in Immunology**
13:00 – 17:00, Tuesday 6 December 2016

Our flagship session to showcase the work of early-career researchers in immunology is back, more popular than ever! If you’re a PhD student or postdoc, make sure you register your abstract for these sessions on your submission form. It’s a fantastic opportunity to discuss your work with a large network of peers and debate immunology in a friendly atmosphere.

**Keynote lecture**
Akiko Iwasaki
Professor of Immunobiology and Molecular, Cellular and Developmental Biology, Yale University
18:30, Tuesday 6 December
The BSI congress offers a good chance to see the latest progress in areas of immunology that I am familiar with and to explore new areas that I am curious to know more about. I’ll be heading to the parallel session on ‘Immunology at the extremes of age’ organised by Fiona Culley, Sian Henson and Jessica Teeling as this is an expanding area with new and exciting work of relevance to the demographic challenges of 21st century. The parallel session on ‘Innate host defence peptides and proteins’ interests me as this is an area that we are starting to study in my lab. Inevitably, some interesting sessions will clash in the timetable: for me the session on ‘Thymus development’ organised by Frank Staal and Dan Pennington covers an area that I have been interested in for 20 years. But I will miss it as I will be chairing, together with Peter Katsikis, the session on ‘The molecular regulation of T cell mediated immunity’; our session will cover post-transcriptional regulation of mRNA in the control of gene expression. As some others from my lab will attend Congress, I hope we can cover the different sessions and compare notes later!

Martin Turner
Babraham Institute

I always love coming to Congress and meeting up with old lab mates for a reunion in one of the bars around the conference centre. It’s really the only conference that everyone I know attends, which means I meet up every night with old friends and their labs. The discussions we have at these dinners have led to many new ideas and collaborations for my work.

At this year’s Congress, I am particularly looking forward to all the career-based sessions, which I help to organise. I find the sessions and the discussion afterwards to be really incredibly useful as they are so focused on people with immunology PhDs. This year we are dividing into two streams, so we can discuss pushing our careers forward either as academics – with advice on writing grants and fellowships – or outside academia, for people who want to pursue different paths. As someone currently writing fellowship proposals, I know I’m going to find masses of useful advice.

Emily Gwyer Findlay
University of Edinburgh

This joint Congress has been almost three years in the making, culminating in a truly excellent and inspiring programme that covers virtually all aspects of immunology. Our call for parallel sessions had a fantastic response from members from both the UK and Dutch societies, and this is reflected in a varied and exciting program. On the first day, before the official opening, we will have our – by now traditional - Bright Sparks session showcasing the groundbreaking research performed by our bright population of PhD students and early postdocs. Congress will kickstart with our opening address followed by the keynote seminar by Professor Akiko Iwasaki from Yale University, who will describe her recent findings on the initiation and maintenance of anti-viral immunity at mucosal surfaces. This will be followed by an opening reception where you can meet and greet your friends and colleagues from the UK and Netherlands and many other countries, whilst enjoying a bite to eat and some refreshments.

The next three days will be filled with outstanding sessions on vaccination, molecular and cellular regulation of conventional and unconventional T cells, B cells and antibodies, macrophages, granulocytes, innate lymphoid cells, innate sensing, mucosal immunology, in vivo tracking and imaging, tumour immunology, and much much more. There will be plenty of opportunities for academic and social interaction during our highly popular poster sessions. And of course we will have the Congress party! Even though it’s summer now, I can’t wait for December!

Leonie Taams
BSI Congress Secretary
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Congratulations

This is the section of the magazine where we celebrate the achievements of our members. Our congratulations to all who are mentioned here.

Communicating Immunology Grants

The BSI is delighted to fund two projects through our Communicating Immunology Grants. Oxford Hands-On Science, a student run organisation, received £1000 to support their summer roadshow visiting science festivals and schools in Oxfordshire and South Wales. Katherine Walwyn-Brown (The University of Manchester) received a grant to support her participation in the Manchester Soapbox Science event, with a talk on natural killer cells. The next grant deadline is 1 October. For more details, visit: http://bit.ly/1rpXUXj.

Wellcome Trust awards

The following BSI members have been awarded a Wellcome Trust Investigator Award in the recent grant round:
• Ken Smith (University of Cambridge)
• Martin Turner (Babraham Institute).

Congratulations

Congratulations to Sheena Cruickshank who won postgraduate supervisor of the year at the University of Manchester student union teaching awards.

Top honours to immunologists

We’re delighted to see immunology well represented in recent award rounds, with BSI members playing a prominent role. Past BSI President Professor Adrian Hayday from King’s College London has been elected as a Fellow of the Royal Society in recognition of his work employing molecular biology approaches to understand how lymphocytes function within tissues and how this contributes to human health and disease.

Similarly, the Academy of Medical Sciences announced their new list of Fellows recently and the following BSI members are recognised: Professor Arne Akbar, University College London; Professor Judith Allen, University of Manchester; Professor Gordon Brown, University of Aberdeen; Professor Graham Lord, King’s College London; Professor Mala Maini, University College London; Professor Peter Parham, Stanford University. Our congratulations to all of you.

New appointment

Many congratulations to Professor David Wraith who has recently taken up the appointment of Director of the Institute of Immunology and Immunotherapy at the University of Birmingham.

Travel grant success

The following members were recently awarded BSI travel grants:

The following members have been awarded ICI 2016 travel grants:


We would love to hear from you about your achievements. Have you or a colleague recently received grant funding, passed your PhD viva or accepted a new appointment? If so, let us know by emailing media@immunology.org.
On 28 June I completed my specialist training in immunology and was signed off as competent by a panel of senior colleagues. What a strange feeling: a shake of hands, smiles in the room, congratulations, and off I went. It was over! It was still difficult to believe I am a clinical immunologist now, after a long and challenging journey, which felt like a 3000m steeplechase – you have to jump over hurdles, you inevitably end up in the water, you sweat, you may fall, you get tired but, you eventually get there, after seven and a half laps.

‘Manyimmunology trainees develop a passion for research during training and they take time out of their training to obtain a PhD or MD degree.’

“I became an immunologist because this speciality married my interests of clinical care and biological sciences. The rewards and challenges go hand-in-hand in clinical immunology and, being a diverse speciality, it requires an in-depth specialist knowledge of allergy, autoimmunity, immunodeficiency and laboratory medicine; good clinical, laboratory and time management; and all the clinical skills of medicine. There are all the research and academic opportunities and the need to ‘keep up to date’ in such a developing field. These factors keep it interesting but are also very demanding.”

Dr Tanya Coulter (Dublin)

“I wanted to pursue a medical career with a strong scientific basis, and with the potential for research. Immunology and allergy seemed to be the most dynamic and interesting of the areas. I enjoy the fact that I can engage with one patient for a longer period of time; I appreciate a holistic approach towards patients as the immunological disorders tend to present as multisystem disease; I also value the fact that a career in clinical immunology facilitates a good work–life balance.”

Dr Nada-Lee Al-Muhandis (Hull)
‘A sound knowledge of internal medicine was a massive help to me once I decided to pursue my passion for immunology and started my second specialist training – clinical immunology’

“I was fortunate during my foundation years to have a placement in immunology and rheumatology at Manchester Royal Infirmary. I was inspired by my mentor, consultant immunologist Dr Matthew Helbert, to look into a career in immunology. I value the chance of combining clinical, academic and laboratory fields and working in a rapidly advancing specialty with cutting-edge science. I enjoy working as part of a multidisciplinary team, providing integrated care for patients. I feel that working within a small speciality enables me to get to know my colleagues both on a national and international level.”

Dr Shuayb Elkhalifa (Manchester)

“I specialised in clinical immunology in Slovakia, and am currently working as an SpR at the Royal Free Hospital in London. Having had the opportunity to practice immunology and allergy, I’ve always felt more attracted by immunology, as being an incredibly fast-advancing interdisciplinary field. In my opinion, the complexity, broad spectrum and constant development makes clinical immunology a great multidisciplinary tool, continuously enriching medical knowledge, giving possibilities and hope to treat or even cure what has not been possible so far. I am fascinated by what our understanding of the immune system has already taught us, and what new diagnostic treatment options it can offer in the near future.”

Dr Jaroslava Orosova (London)

“Immunology impacts on every part of the human body, making clinical immunology the only truly ‘multi-organ speciality’. I like the challenge of being in a young evolving speciality where much is still to be found out; with small patient groups we have to be more flexible as there will never be the numbers to conduct robust clinical studies, unlike in other diseases.”

Dr Arthur Price (Leicester)

through the UK and into Europe. Trainees at the Royal Free benefited from having an opportunity to learn directly from Professor Bodo Grimbacher, a renowned scientist and clinician from the Centre for Chronic Immunodeficiency, Freiburg.

Some of our patients with an umbrella diagnosis of antibody deficiency are now characterised with genetic mutations accounting for their disease. So, learning from our patients we can recognise what phenotype is associated with a gene defect, unlike in the past when we had to rely on animal models to predict what would happen in humans. Many immunology trainees develop passion for research during training and they take time out of their training to obtain a PhD or MD degree.

The immunology speciality is very small and there are about 20 training centres in the UK with approximately 30–40 trainees. Therefore, to exchange ideas and to get to know fellow trainees, we attend ‘hitchhiker’ training days. These topic-based training events give us an opportunity not only to learn but also to network, and to share advice on how to defeat the much dreaded FRCPath examinations.

**Why clinical immunology?**

So, you may ask, who wants to embark on the difficult and demanding training in clinical immunology, knowing that other medical specialties are more straightforward with much easier exit exams and more jobs waiting?

I became fascinated by immunology in the early nineties while training in internal medicine at the University of Ancona, Italy. At that time the differences between Th1 and Th2 cells were the hot topic and I found it intriguing how immune polarisation determines clinical conditions. Like many of us, I was ‘infected’ by the contagious passion for immunology in the department. Professor Giovanni Danieli inspired me and encouraged to undertake a PhD in immunological sciences, in addition to my specialist training in internal medicine. A sound knowledge of internal medicine was a massive help to me once I decided to pursue my passion for immunology and started my second specialist training – clinical immunology.

I have shared insights from my fellow trainees in this article. I think we all agree that clinical immunology is a holistic speciality and a close link between clinical practice and research and basic science is essential. The opportunity to provide a more individualised and less rushed clinical contact with our patients is a bonus.

I hope that this article will inspire medical students and junior doctors to embark on this fascinating, tortuous, trek through clinical immunology training. I have met many extraordinary people who have chosen this speciality and I was privileged to train with them. I am certainly very grateful to Dr Ronnie Chee, my Educational Supervisor, for his guidance and support throughout my training. I am looking forward to my next challenge as Consultant Immunologist and Allergist at UCLH, where I will complement a multidisciplinary team of specialists.

Dr Magdalena Dziadzio
Consultant in Immunology and Allergy at UCLH, previously Specialist Registrar in Immunology at the Royal Free Hospital,

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FUTURE FOCUS

Biomedical Picture of the Day (BPoD)

With even the briefest flick through the vast array of today's biomedical journals you're likely to come across a host of eye-catching images. From fluorescing cells and glowing model organisms in a variety of poses, to highly magnified life in super-resolved detail, you don't have to be a scientist to be captivated by their astonishing visual beauty. But before Biomedical Picture of the Day (BPoD) it was only those associated with research deemed newsworthy by the media that were routinely seen by the non-scientists.

Inspired by NASA's Astronomy Picture of the Day (APOD), the director of the MRC Clinical Sciences Centre (CSC) – Professor Amanda Fisher – realised that biomedical research imagery had the same potential to amaze and stimulate interest, and so created BPoD (www.bpod.mrc.ac.uk). Showcasing the weird and wonderful however isn’t just to demonstrate a diversity in eye candy. Each image is accompanied by a concise 150-word summary of the science behind the image. At least once a week an image will derive from work carried out by researchers linked to the MRC-CSC, and written by somebody at the Institute. The majority come from professional science writers, all with the non-scientist in mind. The aim is not only to tickle the taste buds of those looking for a career in one of the many facets of biomedicine, but also simply to engage those who love science.

The first BPoD was published on 1 January 2012; four and a half years later we now have an archive of over 1600 images from all walks of biomedicine – from immunology and virology – to biophysics and psychiatry. Occasionally we have ‘Theme Weeks’ for example featuring entries from image competitions, or of a research theme such as ‘Medicinal Plants’, or to tie in with one of the MRC-CSC’s public engagement activities. Each month we feature a BPoD focused on a biomedical personality, past or present. As most images come from research that is timely, the archive represents an extensive record of what could be called the ‘state of the art’ of science.

Besides the daily visitors to the website, BPoD also reaches thousands worldwide through Facebook, Twitter and, with over 40,000 followers, Tumblr.

As a non-profit making resource, if it’s not already published with a free-to-use creative commons licence, we find that most journals and scientists are more than willing to allow us to feature their work. Each BPoD is accompanied by credits and copyright ownership details, and links to the scientists’ and institution homepages.

If you have a picture, either as a stand-alone image or as part of a published article that you would like to contribute to BPoD, we’d be delighted to consider it. Please contact us at bpodteam@csc.mrc.ac.uk.

Lindsey Goff
Editor-in-Chief, BPoD
BSI Undergraduate Prizes

Each year, the BSI’s Immunology Undergraduate Prize scheme aims to promote excellence in the study of immunology at undergraduate level, and encourage gifted students to pursue further postgraduate study, or a career in the discipline. Here’s a selection of the 2016 winners.

University of Glasgow

Claire Martin was awarded the 2016 BSI Delphine Parrott Prize in recognition of her outstanding performance on the University of Glasgow’s BSc (Hons) Immunology programme. This prize was established in memory of Delphine Parrott who was the first female professor at the University of Glasgow where she started the first BSc devoted to immunology in the UK.

Dr Pasquale Maffia, coordinator of the final year of the Immunology programme said: “Claire was the top student of this year’s class and a very deserving winner. She graduated with a first class honours degree, achieving an exceptional overall programme grade point average of 19.83. We are also extremely grateful to the BSI for the 2016 Undergraduate Prize awarded to Rebecca Cairns for the best laboratory project.”

University of Aberdeen

The BSI Undergraduate Prize 2016 was awarded to David Sünderhauf who gained a first class BSc Honours degree in Immunology from the University of Aberdeen. David gained the highest average mark across the whole Immunology course and the highest marks in the class for his excellent research project. He will be continuing his interest in immunology in a different vein with an MRes at Exeter University.

University of the West of Scotland

Well done to Diana Onodelia Rios Szwed who was awarded the Immunology Undergraduate Prize by the University of Strathclyde. Diana plans to start a PhD at the University of Dundee in September.

University of Strathclyde

Congratulations to Melissa Craig from the University of the West of Scotland who was awarded the BSI Undergraduate Immunology Prize.

You can find out more about the BSI Immunology Undergraduate Prize scheme and how your department can apply for funding at http://bit.ly/29S5kUM.
Immunological research does not stop at borders. Fighting HIV, Ebola and multidrug resistance is a truly global endeavour, as are novel approaches to diagnose, treat and prevent autoimmunity, chronic inflammation and cancer. The BSI South Wales Immunology Group believes that it is of vital interest for the scientific community to have access to international funding and facilities, to be embedded in collaborative networks with the best experts in their fields, and to be able to influence national and international policies. In this respect, the European Union has played a crucial role in fostering cutting-edge science in the UK.

**Threat to European funding**

Cardiff researchers working in infection and immunity have been highly successful in obtaining funding from the EU, ranging from incoming Marie Curie fellowships and ERC grants to active participation in EU-wide networks such as EPAD (European Prevention of Alzheimer’s Dementia Consortium), EE-ASI (Enhanced Epidermal Antigen-Specific Immunotherapy Against Type 1 Diabetes), and EuTRiPD (European Training & Research in Peritoneal Dialysis), to name a few. These international consortia tackle some of the biggest challenges to public health, by using state-of-the-art technologies and providing access to well-defined patient cohorts and outstanding training environments.

There is an imminent threat of jeopardising access to EU funding, with UK scientists already experiencing problems with EU consortia and Horizon 2020 applications. These increasing difficulties combined with the likely restrictions of free movement of students and staff to and from EU countries and the tightened visa regulations for workers from overseas will have profound consequences for the scientific landscape in the UK and beyond.

The BSI South Wales Immunology Group is therefore campaigning to emphasise the international nature of science and to celebrate the diversity of researchers working in the UK, in support of the BSI’s own ‘Internationalism of Immunology’ report and inspired by activities by the Academy of Medical Sciences, the Royal Society, the actions of >100 university VCs across the UK, and groupings such as Scientists for EU.

**Power of social media**

Some of the photos posted on our social media channels have already been re-tweeted up to 120 times – including by the Royal Society, the President of the Royal College of Pathologists and the local MP for Cardiff Central (with our top tweet earning 12,000 impressions within a week), and have had more than 200 shares and 700 likes on Facebook after being shared by Scientists for EU.

While the great majority of local researchers and the public have expressed their support of our campaign, Brexit of course is one of the most controversial topics of our generation and the divide of the country can easily be felt by feedback like “You talk some nonsense” or simply “Lie!” and harsh discussions between leavers and remainers in the comments sections.

**Have your say**

This is a time of risks and worries with regard to funding, collaborations and recruitment but there may also be new opportunities. As a scientific community we currently have a unique chance to influence the agenda during the Brexit negotiations and highlight areas of particular importance and relevance to us. So please be proactive and voice your concerns, wishes and ideas by contacting the BSI, by submitting evidence to the Science and Technology Committee of the House of Commons, contacting your local MP and by helping to monitor the impact of the Brexit vote on UK science.

**Matthias Ebert**
South Wales Immunology Group

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South Wales Immunology Group

Research needs free movement and ideas. #FreedomofMovement #bIEUMonday #ProfRefRacism #ScientistsGlobal

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Immunology News | September 2016

Vitamin D immunoregulation through dendritic cells

Vitamin D (VD3) has been linked to immunological processes, and its supplementation may have a role in treatment or prevention of diseases with underlying autoimmune or pro-inflammatory states. As initiators of the immune responses, dendritic cells (DC) are a potential target of VD3 to dampen autoimmunity and inflammation, but the role of DC in VD3-mediated immunomodulation in vivo is not understood. In addition to being targets of VD3, DC can provide a local source of bioactive VD3 for regulation of T-cell responses. Bscheider and Butcher review existing studies that describe the tolerogenic potential of VD3 on DC, and discuss them in the context of current understanding of DC development and function.


The T helper type 17/regulatory T cell paradigm in pregnancy

There are circumstances where the fine balance of the healthy immune system is disrupted. In pregnancy, the foreign foetal antigens challenge the maternal immune system and Treg cells will dominate Th17 cells to guarantee foetal survival. In other situations – such as autoimmunity, where the Th17 responses are often overwhelming, the immune system shifts towards an inflammatory profile and attacks the healthy tissue from the self. Interestingly, autoimmune patients have meliorating symptoms during pregnancy. This connects with the antagonist role of Th17 and Treg cells, and their specific profiles during these two immune-challenging situations. In their review, Figueiredo and Schumacher put into perspective the Th17/Treg ratio during pregnancy and autoimmunity, as well as in pregnant women with autoimmune conditions. They further review existing systems biology approaches that study specific mechanisms of these immune cells using mathematical modelling and point out possible future directions of investigation. Understanding what maintains or disrupts the balance between these two opponent yet reciprocal cells in healthy physiological settings shed light into the development of innovative pharmacological approaches to fight pregnancy loss and autoimmunity.


Clinical & Experimental Immunology

Cut to the chase: a review of CD26/dipeptidyl peptidase-4’s (DPP4) entanglement in the immune system

CD26/DPP4 is a surface T cell activation antigen and has been shown to have DPP4 enzymatic activity, cleaving-off amino-terminal dipeptides with either L-proline or L-alanine at the penultimate position. It plays a major role in glucose metabolism by N-terminal truncation and inactivation of the incretins glucagon-like peptide-1 (GLP-1) and gastric inhibitory protein (GIP). In 2006, DPP4 inhibitors were introduced to clinics and have been demonstrated to efficiently enhance the endogenous insulin secretion via prolongation of the half-life of GLP-1 and GIP in patients. However, a large number of studies demonstrate clearly that CD26/DPP4 also plays an integral role in the immune system, particularly in T cell activation. Therefore, inhibition of DPP4 might represent a double-edged sword. Apart from the metabolic benefit, the associated immunological effects of long-term DPP4 inhibition on regulatory processes – such as T cell homeostasis, maturation and activation – are not understood fully at this stage.


From the bench to clinical practice: understanding the challenges and uncertainties in immunogenicity testing for biopharmaceuticals

Unlike conventional chemical drugs where immunogenicity typically does not occur, the development of anti-drug antibodies following treatment with biologics has led to concerns about their impact on clinical safety and efficacy. Hence, the elucidation of the immunogenicity of biologics is required for drug approval by health regulatory authorities worldwide. Published ADA ‘incidence’ rates can vary greatly between same-class products and different patient populations. Such differences are due to disparate bioanalytical methods and interpretation approaches. In this context, Gunn et al’s review article discusses the complex nature of ADA and key nuances of the methodologies used for immunogenicity assessments, and attempts to dispel some fallacies and myths.

PSGL-1 is an immune checkpoint regulator that promotes T cell exhaustion

Current checkpoint inhibition therapy in cancer is efficacious in a minority of patients highlighting the need for additional targets. Tinoco and colleagues show that the adhesion molecule PSGL-1, important in migration of haematopoietic cells, also acts as a negative regulator of T cell function. Using the Cl13 chronic LCMV infection model, they show that PSGL-1 deficient (Selplg−/−) mice have increased T cell accumulation in lymphoid and non-lymphoid tissues, enhanced T cell survival and effector function, but also high mortality due to immunopathology. Ligation of PSGL-1 on exhausted CD8+ T cells silenced TCR signals, increased PD-1 expression and reduced T cell survival. Importantly, PSGL-1 deficiency enhanced anti-tumour T cell responses by preventing the development of T cell exhaustion indicating PSGL-1 as a potential target for immunotherapy.

Tinoco et al. 2016 Immunity44 1190–1203.

RBPJ controls development of pathogenic Th17 cells by regulating IL-23 receptor expression

IL-23R signalling skews Th17 cells towards a pathogenic phenotype. RBPJ is found downstream of Notch, which regulates Th17 development. Using CD4CreRBPJfl/fl mice, Meyer zu Horste and colleagues show RBPJ deficiency in T cells decreases IL-17 significantly in vitro under pathogenic Th17 conditions (IL-1β, IL-6, IL-23) but not under non-pathogenic Th17 conditions (TGF-β1, IL-6). RBPJ also regulates pathogenic Th17 cells in vivo, as RBPJ deficiency reduces severity and exhibits faster recovery in EAE-induced CD4CreRBPJfl/fl mice. RBPJ’s dominant role involves directly affecting transcriptional Th17 regulation by binding the Il23r promoter, shown by ChIP PCR. RBPJ and RORγt in combination additively activate Il23r. RBPJ also represses IL-10 production in Th17 cells through the transcription factor c-MAF and can bind the IL-10 locus in Th17 cells, promoting their pathogenicity.

Meyer zu Horste et al. 2016 Cell Reports16 392–404

Activin A programs the differentiation of human Tfh cells

T follicular helper (Tfh) cells are a specialist subset of CD4+ T cell critical for regulating the quality of antibody responses. Recently Locci and colleagues developed a high-throughput screen to identify factors important for the differentiation of Tfh cells in humans. A ‘secretomics’ library was used to test 2000+ human extracellular proteins for their ability to modulate the differentiation of naïve T cells to Tfh cells in vitro. Using flow cytometry to measure surface expression of the Tfh markers CXCR5 and PD-1, the authors discovered that Activin A is a potent inducer of Tfh cells. Activin A had no effect on CD4+ T cells from mice, highlighting the value of this novel approach in understanding Tfh cell biology in humans.

Locci et al. 2016 Nature Immunology17 976–984

The human thymus is enriched for autoreactive B cells

The thymus represents the primary lymphoid organ responsible for the development of T cells. However, we have known for some time that B cells reside in the thymus, although their role and origin remains to be fully elucidated. To gain further insight, Rother and colleagues examined human thymic B cells, from paediatric thymi and observed that thymic B cells exhibit a naïve mature phenotype and have a diverse Ig gene repertoire similar to paediatric BM-derived B cells; which unlike mature foetal B cells they noted had a skewed repertoire. However, a greater proportion of thymic B cells contained reactivity towards protein autoantigens. In contrast, foetal B cells showed high reactivity towards dsDNA. From these results, the authors suggest that thymic B cells are resident cells and may participate in negative selection by presenting autoantigens.

Rother et al. 2016 Journal of Immunology197 441–448
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