BRITISH PHARMACOLOGICAL SOCIETY

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PHARMACOLOGY MATTERS

- **Strimvelis – Drug Discovery of the Year 2018:** A View for the Future of Personalised Medicine
- Introducing the Nagoya Protocol to the Pharmacologist
- Calling on Pharma to Publish in PR&P!

Neuropharmacology | Bioprospecting and drug development | Supporting young pharmacologists

EDITORIAL

In the aftermath of the chill brought by the Beast from the East, I would like to wish a warm welcome to the first *Pharmacology Matters* of 2018. In this edition we celebrate the successes in drug discovery and showcase the multiplicity of our members' activities.

Since our last edition we have welcomed two new recruits to our editorial team, Aisah Aubdool and Ted Wickstead, who replace Chris Tsantoulas and Karolina Gherbi. I'd like to thank Chris and Karolina for all of their hard work and for dedicating their time to support *Pharmacology Matters* through the years.

With the Society's new five-year strategy in mind, Jono provides insight into the key objectives and the how these will benefit the Society and its members going forward. The engagement of our Young Pharmacologists Advisory Group (YPAG) has truly been remarkable as Vedia updates us on their activities and the other Society committees that its young members are now involved in. The strength of leadership on display from our early career members is further demonstrated by Jessica, Joseph, Colleen and Amelia as they share their experiences as organisers of the 'Frontiers in Musculoskeletal Health, Ageing and Disease' Young Life Scientists (YLS) symposium.

In the wake of the stem cell therapy Strimvelis (GSK) being named the Society's Drug Discovery of the Year 2017, we hear views from Janet Nicholson and Tom Blackburn on the outlook for personalised medicine. This is swiftly followed by the perspectives from our new editorial team member Ted, on the challenges which face neuroscience drug development. Continuing with this theme, Clare Stanford and Mark Tricklebank provide an update from the neuropharmacology Affinity Group (AG), whilst James Dear and Daniel Antoine share toxicology AG news.

We pass the mic to our international members in Australia where we hear from Andy Lawrence as he shares his life in two parts – one as a surf lifesaver (p16) and the other as the new Editor-in-Chief of PR&P (p22) in a call for Pharma to publish their reports in the journal. Nicola Smith from the Victor Chang Cardiac Institute in New South Wales then takes us on a journey of her career as a GPCR molecular pharmacologist.

Thomas Murphy breaks down the Nagoya Protocol into R&D terms for the pharmacologist, which is followed by Katherine Duncan as she explores the ocean of potential for marine-based biosources for the development of new drugs.

Finally, congratulations go to David Webb who received the Tomah Masaki Award at the Fifteenth International Conference on Endothelin. Anthony Davenport shares his highlights from this meeting. In other prize winner news, we interview Simon Hirota and Pieter Okkerse as winners of the 2017 BJP and BJCP early career researcher prizes respectively.

Judging by the meetings lined up for 2018, it looks like there is an exciting year ahead on the pharmacology front! **Enjoy!**

Margaret

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YOUR SOCIETY

JONO BRÜÜN
Chief Executive

I want to take this opportunity in the first *Pharmacology Matters* of 2018 to share a few thoughts about the Society's new five-year strategy.

New strategy, new focus

If you haven't had a chance to read our new strategy yet I would urge you to do so – as with all our work, our members were at the forefront of our minds as we developed it. I would particularly like to draw out a couple of new aspects of what we want to achieve over the next few years, and how we want to go about it.

Firstly, it is no accident that the very first objective we set out in the strategy is "To remove barriers to participation and success, while welcoming equality and celebrating diversity, and being inclusive in all we do". I would like to think that this has always been one of our underpinning values as a Society, but in thinking about the new strategy we recognised that it is far too important not to be explicit about. One of the wonderful things about our membership is that as it grows, it continues to become more and more diverse. We want not only to welcome that but to champion it.

Another pre-existing but now, I hope, more powerfully articulated objective for the Society is "To deliver clear, relevant and accessible advice to policy makers". Over the past year or two we have invested more effort and resources in our policy work than ever before. This has already enabled us to get seats at the table and our voices heard in debates where we may have struggled to have an impact before.

> "To deliver clear, relevant and accessible advice to policy makers"

To give just one recent example, Anna Zecharia, our Director of Policy and Public Affairs, was recently invited to represent the Society at the Commons Science and Technology Committee's Brexit Science and Innovation summit. Being able to participate in high-level forums like this allows us to follow through on the promise we made to members after the June 2016 referendum, which was that we would ensure the voice of pharmacology and clinical pharmacology is heard on the most important and complex of issues.

I'd also like to expand on our stated intention to "develop sustainable, ethical new sources of revenue and ensure more of the Society's activities are self-sustaining". First and foremost this means continuing to develop develop the British Pharmacological Society Assessment Ltd (BPSA), the subsidiary company we spun out of the Society in 2017 to explore revenue-generating opportunities for our prescribing skills platform (delivered in the UK since 2014 as the Prescribing Safety Assessment, in partnership with the Medical Schools Council).

2018 is going to be a big year for BPSA, we will be pursuing opportunities to introduce our prescribing assessment and skills offer around the world.

Staff news

This step-change at BPSA leads me neatly into welcoming Angus Metcalfe to the Society. Angus joined us in February, taking on the brand new role of Sales Director for BPSA. He brings with him a wealth of top-level commercial experience in scientific, technical and medical publishing, elearning and securing global commercial deals.

February also saw the departure of our Head of Meetings & Events, Susanne Schweda, after three years as a much valued member of the team at the Schild Plot; and the arrival of her successor, Lindsay McClenaghan, who joins us after several years at the British Society for Rheumatology.

By the time you read this we will also have said goodbye and good luck to Alison Bate, who has been with us since August 2017, first as an intern and latterly as interim Education, Training and Policy Officer. I'd also like to welcome her successor in that role, Abigail Harris, who joins us fresh from completing an internship at the Royal Society and a PhD in genetics at the University of Oxford.

I should finish by acknowledging how much I have been enjoying working with Steve Hill and Munir Pirmohamed in their new roles as President and President-Elect, respectively.

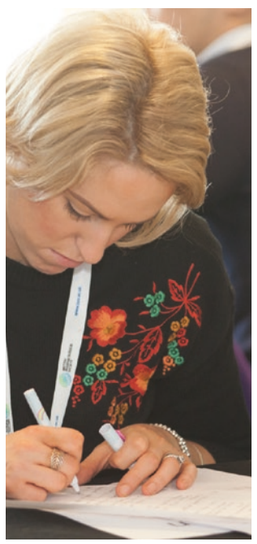
Steve and Munir have both made significant contributions to the Society over a number of years; notably Steve as President-Elect for the past two years, and Munir as Vice-President Clinical for the past six. They have been important contributors to developing our new strategy, and I'm greatly looking forward to working with them to put it into action this year and beyond.

YOUNG PHARMACOLOGISTS ADVISORY GROUP

GOING FROM STRENGTH TO STRENGTH

VEDIA CAN
University of Westminster

Vedia is a Doctoral Researcher at the University of Westminster, UK, specialising in immunopharmacology. She is also a member of the British Pharmacological Society's Young Pharmacologists Advisory Group and the Editorial Board of Pharmacology Matters. Her primary research focus is exploring how inflammatory pathways in an osteoarthritic model can be inhibited using novel compounds. Previously, she completed a Bachelor's degree in Biomedical Sciences and a Master's degree in medical molecular biology.



The Young Pharmacologists Advisory Group (YPAG) aim to improve representation, involvement and engagement with young and early career members as much as possible. The continued support from the British Pharmacological Society allows us to achieve this.

The majority of the YPAG members now sit on other committees of the Society (see Table 1), allowing young pharmacologists to voice their opinions and share their ideas across a multitude of platforms. We feel that the Society has made a concerted effort to ensure that younger members feel supported and valued, and we hope to carry this effort into 2018. We echo the message delivered by the Society's President President Steve Hill:

> "It's crucial that we are totally engaged with our early-career pharmacologists and there has been real progress in this area. Young members are now represented on nearly all of the Society's committees, and its Council. It's all part of moving the Society from being a club to a vibrant society that invests in and champions the activities of all of its members – whatever level they are at in their career"

We are determined to ensure that younger members are involved with and supported by our Society.

Table 1. Members of the YPAG and the other Committees of the Society that they are also members of.

Members	Committee/Group
Aidan Seeley	Council
Clare Stanford (Chair)	Council, Membership & Awards Committee, Finance Committee, Neuropharmacology Affinity Group Co-chair
Laura Ajram	Women in Pharmacology Advisory Group, Meetings Committee
Adebayo Aibinu	Membership & Awards Committee
Caroline Copeland	Policy & Public Engagement Committee
Ross King	Policy & Public Engagement Committee
Vedia Can	Pharmacology Matters Editorial Board

The YPAG takes pride in listening to and taking on the feedback we receive from our younger peers and as a result, we were able to expand our Committee from 8 to 15 members in July 2017 to represent a wider demographic of young pharmacologists[1]. The new YPAG group consists of current AJ Clark students and two members who are based at international institutes. Our new members were instantly involved with important tasks and activities during the annual *Pharmacology* conference in 2017, as the new recruits were paired with senior members of the Society to help judge the YPAG BSc undergraduate posters for prize awards, to chair the flash poster presentations, and to deliver the student choice award presentation during the annual dinner. In addition, for the first time in the history of the British Pharmacological Society, YPAG members were given the opportunity to co-chair and judge the oral communication sessions held during the conference, giving younger members the opportunity to learn more about conference proceedings from their paired senior academic peers. Chloe Peach, one of the new members of YPAG, had the opportunity to co-chair a session on molecular and cellular pharmacology with Professor Barbara McDermott. Chloe found the session very enlightening as this opportunity gave her an insight into how to successfully chair a session, which she will be able to apply in her future academic endeavours.

> "It was a good way to get to know the co-chair and speakers, to gain exposure and confidence speaking in front of an audience, and to learn how to chair a session. I will be able to use these skills when delivering future presentations. I also enjoyed being more involved in the conference by helping to keep people to schedule and judging prizes"
>
> Chloe Peach.

Other members of the YPAG such as myself, Laura Humphrys and Adebayo Aibinu also echo this response. It is important to highlight that this experience helped us improve our confidence in public speaking in front of a sizeable audience and we would like to thank the Society for giving us this prestigious opportunity. Personally, I felt that co-chairing an oral communication session was brilliant preparatory experience for chairing future conference events. I was extremely honoured to share the neuropharmacology stage with the exemplary Dr Alistair Corbett. This experience prepared me for the symposium I was due to co-chair the following day with my colleague Aidan Seeley.

For 8 consecutive years, the YPAG has delivered symposia at the Society's annual *Pharmacology* conferences. In 2017, Aidan Seeley and I were honoured to chair our symposium entitled 'Membrane Trafficking – The Highway to Novel Pharmaceutical Targets'. The symposium was designed to represent research from a diverse range of speakers from PhD to Professor level, and to highlight novel research generated by our peers in the UK. The speakers for the symposium included Professor Gwyn Gould (University of Glasgow), Dr Graeme Cottrell (Reading School of Pharmacy), Jean Iyinikkel (a final year PhD student at the University of Aberdeen), Dr Kirsty McMillan (University of Bristol) and Dr Emmanuel Boucrot (University College London). Dr Boucrot concluded the symposium with his presentation on the endophilin controls of GPCR endocytic pathways, with a in depth discussion on his recent research in the identification of new pathways of endocytosis such as the Fast Endophilin-Mediated Endocytosis (FEME) pathway, which has been published in Nature. The symposium highlighted the plethora of exciting research occurring across the country in membrane trafficking.

> "Having chaired the event, it was great to see so many of our young and early career members attend and for them to feel comfortable enough to engage and ask questions"
>
> Aidan Seeley.

What awaits us in 2018?

Coming up this year, the Federation of European Biochemical Societies will host the 2018 Golgi meeting 'Membrane trafficking in cell organisation and homeostasis' in Italy, and the Gordon Research Conference will host the Protein Processing, Trafficking and Secretion meeting in the United States. Both meetings will feature cutting-edge research on the cell biology of the secretory and endocytic pathways. So, if you missed our symposium at *Pharmacology 2017* and would like to present your novel research you could submit an abstract for one of these upcoming meetings and help us to continue raising the profile of pharmacology globally.

In other plans for this year, we will be re-launching our YouTube video series on 'How do Drugs Work?' to make them even more engaging and creative, submitting our proposals for symposia at *Pharmacology 2018*, collaborating with other societies and continuing to support young pharmacologists in all capacities.

The YPAG works hard and works together to pave the way for novelty.

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EXPERIENCES OF ORGANISING A YOUNG LIFE SCIENTISTS SYMPOSIUM

FRONTIERS IN MUSCULOSKELETAL HEALTH, AGEING AND DISEASE

JESSICA CEGIELSKI
University of Nottingham, UK

Jessica Cegielski is an Abbeyfield Foundation funded PhD student, undertaking her studies within the MRC-ARUK Centre for Musculoskeletal Ageing Research, University of Nottingham. Jessica's research primarily focuses on the development of minimally-invasive stable isotope tracer techniques in the measurement of muscle protein synthesis, breakdown and total muscle mass, with an additional aim of identifying potential biomarkers of sarcopenia.

JOSEPH BASS
University of Limerick, Ireland

Dr Joseph Bass completed his PhD investigating the molecular mechanisms that Vitamin D and the Vitamin D receptor (VDR) have upon muscle protein synthesis. This encompassed utilising novel *in vivo* electroporation techniques to modulate VDR expression, and the analysis of anabolic/catabolic signalling pathways in both *in vivo* and *in vitro* models. Joe is currently a post-doctoral researcher at the University of Limerick, undertaking human nutritional studies.

The YLS 2017 organising committee presenting Hannah Lithgow (Edinburgh Napier University) the award for the best poster communication.

The Young Life Scientists' (YLS) symposium is an annual conference supported by the Biochemical Society, British Pharmacological Society and Physiological Society and organised by PhD students and Post-Doctoral researchers for other early career researchers. Each year, proposals are put forward by young scientists to host their own conference on a theme of their choice. On 25 November 2017, exactly 6 months after finding out we were successful with our proposal, we held our one-day symposium entitled "Frontiers in Musculoskeletal Health, Ageing and Disease" at the MRC-ARUK Centre for Musculoskeletal Ageing Research, University of Nottingham.

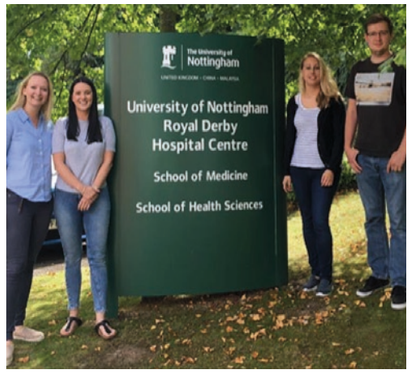
Our organising committee comprised of a PhD student (Jessica Cegielski) and three Post doctorates (Dr Amelia Pollard, Dr Colleen Deane and Dr Joseph Bass). Despite being dispersed across three different institutions, we all work within the same field and had worked at the MRC-ARUK Centre for Musculoskeletal Ageing Research. Therefore, the theme of this year's symposium focussed on the regulation of musculoskeletal health during ageing and disease, whilst discussing potential nutritional, pharmacological, and exercise interventions to delay the onset of age-related and/or disease-related muscle loss. We aimed to provide a great opportunity for young scientists to showcase their research to their peers, and encourage open discussions in a friendly and constructive environment.

The day proved to be a great success, with over 70 delegates from over 40 different institutions, including overseas. We had 3 main session themes: nutrition, exercise and metabolic diseases in ageing. Each session was chaired by a keynote speaker and renowned researcher from the field. Our invited keynotes were: Dr Carolyn Greig (University of Birmingham), with specific interests in healthy ageing and nutrition, Professor Philip Atherton (University of Nottingham), a leading expert on human muscle metabolism and exercise, and finally, Dr Iskander Idris (University of Nottingham) an honorary consultant physician, specialising in diabetes and metabolic disease in ageing.

A group photo of the YLS 2017 organising committee, keynote speaker (Carolyn Greig, bottom left) and delegates.

Additionally, there were 9 oral communications and a poster communication session that provided young scientists with a platform for their research. Furthermore, two workshops were held, one on grant writing success (led by Dr Adam Gordon, University of Nottingham) and the other discussing life beyond a PhD, by invited speakers Dr Anna Selby, Dr Helen Bradley and Dr Daniel Owens. All communications on the day were of a high calibre. Oral communications were judged by internal and external adjudicators, and the posters were assessed by the organising committee. The award for the best oral communication went to Sam Scott (Liverpool John Moores University, PhD Student) and the best poster communication prize was won by Hannah Lithgow (Edinburgh Napier University, PhD student).

Overall, the day was a great success and we received very positive feedback for the high quality of presentations, workshops and the symposium itself. It was great to see our 6 months of work come together as such an enjoyable experience.



The organisers (left to right) Jessica Cegielski, Colleen Deane, Amelia Pollard and Joseph Bass.

With thanks to our additional sponsors Abbott Nutrition, MRC-ARUK Centre for Musculoskeletal Ageing Research, University of Nottingham, Primer Design and BioTechne.

If you're interested in organising your very own YLS symposium, then submit your proposal now! The call for proposals in 2018 is now open and closes on 6 April 2018! Email getinvolved@bps.ac.uk to receive further information on how to apply.

COLLEEN DEANE
University of Exeter, UK

Dr Colleen Deane's past research has centred around understanding the age-related regulation and regeneration of skeletal muscle using *in vivo* and *in vitro* models and techniques. Since completing her PhD in collaboration with the University of Nottingham, Colleen is currently investigating the effects of improved mitochondrial function on skeletal muscle function in ageing humans at the University of Exeter.

AMELIA POLLARD
University of Nottingham, UK

Dr Amelia Pollard has utilised a variety of proteomic and lipidomic techniques to explore the role of mitochondria in brain and skeletal muscle with ageing as part of her PhD. Now, Amelia is a BBSRC funded post-doctoral researcher at the University of Nottingham and is using *C. elegans* to investigate the molecular mechanisms underpinning muscle decline in space. This project involves working closely with the European Space Agency as well as collaborating laboratories in Japan, Greece and America.

STRIMVELIS – DRUG DISCOVERY OF THE YEAR 2018: A VIEW OF THE FUTURE FOR PERSONALISED MEDICINE

JANET NICHOLSON
Boehringer Ingelheim, Germany

Janet Nicholson is Director and Group Leader of CNS Diseases Research at Boehringer Ingelheim (BI), Germany. She received her PhD in pharmacology from the University of Cambridge in collaboration with Parke-Davis Neuroscience Research Centre. Dr Nicholson conducted a post-doctoral research fellowship at the Mental Health Research Institute, Michigan, USA, before returning to Europe to take up a position at the University of Basel, Switzerland, where she worked in collaboration with Santhera Pharmaceuticals. Dr Nicholson spent several years at Pfizer, Sandwich, UK, before joining BI in 2011. In her current position, Dr Nicholson leads a multidisciplinary team working in the field of neuropsychiatry.

TOM BLACKBURN
Translational Pharmacology
BioVentures Ltd

Tom has held senior executive positions with major pharmaceutical and biotech companies in the UK and USA. His expertise in discovering innovative therapeutics led to the development of several clinical candidates and marketed drugs (Paxil/Seroxat®). He has directed pre-clinical and clinical drug development of novel antidepressants, anticonvulsants, antimigraine, Parkinson's disease and cognitive enhancers. Tom has authored over 100 scientific publications and book chapters, is an inventor on several patents and is a board member of a number of biotech companies.

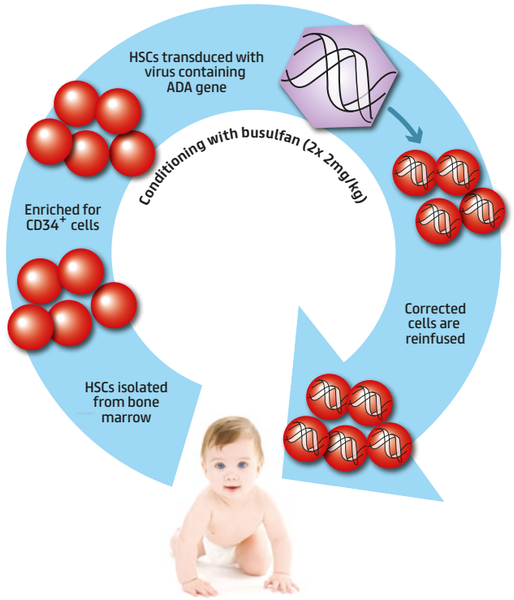


FIGURE 1
Strimvelis *ex vivo* stem cell gene therapy treatment process. HSC refers to Hematopoietic Stem Cells.

Bone marrow is collected from the patient under general anaesthesia. The bone marrow is transported to the manufacturing centre where the first step is to purify and concentrate the stem cells (CD34-mediated immunomagnetic separation). Stem cells are then cultured *in vitro* with cytokines, growth factors and a viral vector which transduces them and inserts a functional human ADA gene. These genetically corrected cells are now able to express functional ADA protein, and, after low dose chemotherapy, are reinfused into the patient.

A significant advance in medical innovation was recently achieved with the approval of Strimvelis, an autologous stem cell therapy for the treatment of adenosine deaminase severe combined immunodeficiency (ADA-SCID).

ADA-SCID is an ultra-rare inherited orphan disease. Babies with SCID lack virtually all immune protection from bacteria, viruses, and fungi and are prone to repeated and persistent infections. Those affected usually live in isolation due to their vulnerability to infection which has led to the condition being named 'bubble baby syndrome'. Without effective treatment, survival beyond two years is rare.

It is estimated that ADA-SCID affects as few as 50 patients per year in EU/US, 17 of which are in the UK[1] but nonetheless the disease still represents a significant unmet medical need for children who suffer from this life-threatening disorder.

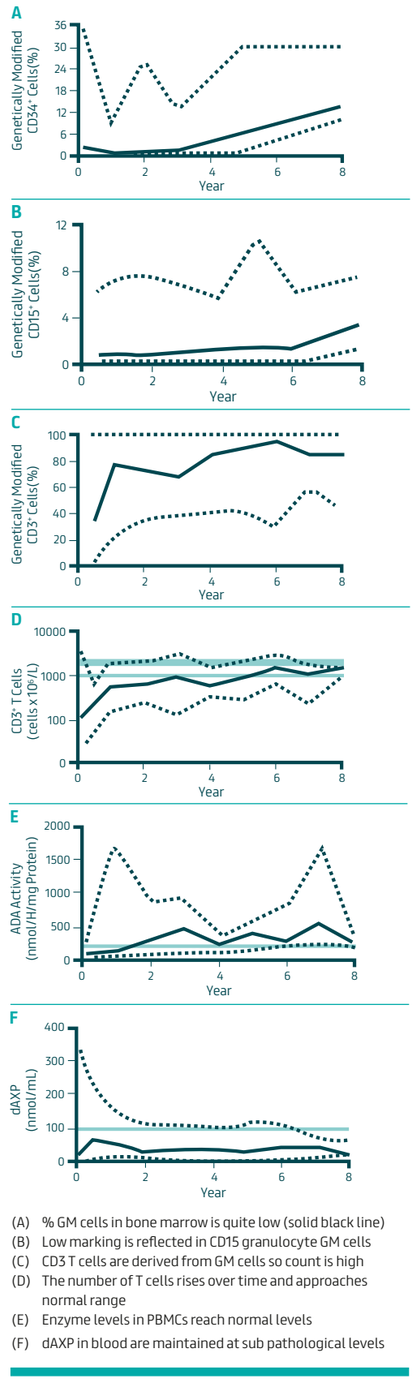
Strimvelis is the first *ex vivo* stem cell gene therapy to receive regulatory approval anywhere in the world and represents an important milestone in medical innovation[2]. The British Pharmacological Society's Drug Discovery of the Year award is chosen annually by the Society's Industry Sub-Committee, and this year was presented to the researchers at GlaxoSmithKine's (GSK) rare disease division responsible for developing Strimvelis.

Adenosine deaminase (ADA) is an enzyme which is essential for the maintenance of healthy white blood cells that fight off infections; in patients with ADA-SCID this enzyme is defective. Strimvelis acts by correcting this deficiency, resulting in functional ADA and restored immune function for the patient.

The treatment process starts with collection of bone marrow from the patient, followed by purification and concentration of stem cells (Figure 1). The stem cells are then cultured *in vitro* with cytokines, growth factors and a viral vector that inserts a functional human ADA gene into the cell's DNA. These genetically corrected cells are now able to express functional ADA protein and after low dose chemotherapy are reinfused into the patient. The cells take root in the patient's bone marrow, replicating and creating cells that express functional ADA protein and thus leading to restored immune function. Thus, Strimvelis is personalised for each patient and is a one-off treatment, intended to provide life-long benefit. The methodology used for the collection and analysis of stem cells followed the basic principles of the pharmacological primary bioassay, the cornerstone of concentration effect (potency) and potential clinical efficacy - as first described by Paul Ehrlich in the 19th century. Thus, for the first time, the full realisation of the clinical application of the human stem cell *ex vivo* bioassay has now been allied in the development of the innovative drug Strimvelis to treat ADA-SCID.

ADA itself is expressed in all cell types with highest levels in lymphocytes of the immune system. The absence of functioning ADA leads to an accumulation of both deoxyadenosine (dAdo) and deoxyadenosine triphosphate (dATP) in cells. Too much dATP leads to the inhibition of ribonucleotide reductase which is important for DNA repair, and to the inhibition of terminal deoxynucleotide transferase which is important for VDJ recombination. The accumulation of dAdo leads to the inhibition of S-adenosyl lymphocyte activation. The overall consequence of these cellular perturbations is profound lymphopenia and dysfunctional cells. Treatment with Strimvelis has been demonstrated to increase functional enzyme levels over time and to normalise the number of T cells while keeping adenosine metabolite levels in the blood at sub pathological levels. The overall result is a long term stable presence of the gene modified cells in blood, and a functioning immune system that can allow treated children to live a normal life, with dramatically reduced risk from life-threatening infection[3] (Figure 2).

FIGURE 2
Mechanism of the action of Strimvelis



(A) % GM cells in bone marrow is quite low (solid black line)
(B) Low marking is reflected in CD15 granulocyte GM cells
(C) CD3 T cells are derived from GM cells so count is high
(D) The number of T cells rises over time and approaches normal range
(E) Enzyme levels in PBMCs reach normal levels
(F) dAXP in blood are maintained at sub pathological levels

> "It is estimated that ADA-SCID affects as few as **50** patients per year in EU/US"

As is typical for any drug discovery process, the development of Strimvelis took place over a number of years. The treatment concept was developed at San Raffaele Telethon Institute for Gene Therapy between 1995 and 2010, when GSK licensed the project from Telethon and initiated the collaboration. GSK also worked with the biotechnology company MolMed S.p.A, to develop a robust manufacturing process suitable for a commercial supply. Pivotal clinical trial data for Strimvelis showed that, after a median of 7 years of follow up, treated patients have a 100% survival rate, and 75% of patients who received treatment need no major intervention for ADA-SCID (i.e. long term enzyme replacement or bone marrow transplant). In April 2016, the European Medicines Agency recommended marketing approval for the use of Strimvelis in children with ADA deficiency, for whom no suitable matched HSC donor was available. The first child to be treated with commercially approved Strimvelis was in March 2017. Prior to this, only a single other individual, also from Europe, had ever accessed gene therapy to treat an inherited ailment outside of a clinical trial or early access scheme. Following a review in the UK by the National Institute for Health and Care Excellence, Strimvelis was recently approved for commissioning. Strimvelis is only available at San Raffaele Hospital in Milan but patients can access it via EU laws covering cross-border health care provision. Currently patients from four other EU countries have been referred for treatment.

Professor Carole Longson, Director of the Centre for Health Technology Assessment at the National Institute for Health Care Excellence (NICE), said: "Strimvelis represents an important development in the treatment of ADA-SCID, offering the potential to cure the immune aspects of the condition and avoid some of the disadvantages of current treatments. We believe this means that children born with ADA-SCID will now have a better chance of being able to lead as near normal a life as possible, going to school, mixing with friends, free from the constant threat of getting a potentially life-threatening infection."

At the British Pharmacological Society's *Pharmacology 2017* meeting, Strimvelis was named as the Society's Drug Discovery of the Year. David Webb, Society President and Christison Professor of Therapeutics and Clinical Pharmacology at the University of Edinburgh, presented the award to Jonathan Appleby, Chief Scientific Officer for Gene Therapy in GSK and Rare Diseases and Project Leader for Strimvelis, at a prize-giving ceremony during the conference.

"For many of my colleagues in GSK, working on Strimvelis with our collaborators from the Telethon Institute for Gene Therapy in Milan has been the highlight of our professional careers. To see this innovative therapy successfully given to patients in a commercial setting is very rewarding. I truly hope that this achievement will lead to other similar treatments being approved for use in other diseases."

Jonathan Appleby

The discovery and development of Strimvelis is a significant achievement and has provided a road map for similar approaches. What was previously unprecedented has become possible and a source of inspiration for the evolution of drug discovery. Furthermore, new modalities such as gene therapy permit an increased level of precision to treatment and potential for improved efficacy. Tailoring of drugs to an individual patient is an approach already being taken up in the oncology field and could soon be applicable to many others such as neurological, ocular and metabolic disorders[4]. The development of gene therapy opens up the possibility of treating previously untreatable diseases and holds vast potential for the future of medicine.

The Strimvelis story also highlights an important element for successful drug discovery, and that is collaboration. As mentioned above, the discovery and development of Strimvelis was a joint venture between the San Raffaele Telethon Institute for Gene Therapy and GSK. The concept for Strimvelis had been proven by years of research funded by Telethon, however to gain regulatory approval it took the development, manufacturing and commercial input of an experienced pharma company like GSK. This example highlights the importance of scientists being open to joining forces to share creativity and knowledge, to leverage expertise and thus to enable the development of ideas and concepts that might otherwise not be brought to fruition. In the example of Strimvelis, collaboration was essential to the development of a highly innovative drug that has already transformed the lives of numerous patients and their families.

Strimvelis represents the beginning of tomorrow's medicines today - an exciting time for personalised medicine and a launch-pad for a gene therapy platform that tackles more prevalent disorders.

> "The Strimvelis story also highlights an important element for successful drug discovery, and that is collaboration"

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ACKNOWLEDGEMENTS

With thanks to Jonathan Appleby for kindly reviewing the article and providing helpful comments.

NEURODEGENERATIVE DRUG DEVELOPMENT: IS THIS THE BEGINNING OF THE END?

EDWARD WICKSTEAD
Queen Mary University of London, UK

Ted is a neuroscience PhD student studying at Queen Mary University of London and the University of Westminster. His research focuses on the role of inflammation in neurodegenerative disease. He has a BSc from King's College London, which included a year studying at the National University of Singapore. He is a STEM ambassador, local group representative for the British Neuroscience Association (BNA), alongside being a blogger, writer and advocate for mental health awareness.

Image sourced from Pfizer Inc.

In January 2018, Pfizer Inc; one of the world's largest pharmaceutical companies, announced they will be abandoning research into new therapeutics aimed at treating both Alzheimer's and Parkinson's disease. This was due to a succession of clinical trial failures. A spokesperson for the company expressed that "this was an exercise to re-allocate spend across our portfolio, to focus on those areas where our pipeline, and our scientific expertise, is strongest"[1].

However, the controversial decision will also result in the loss of 300 jobs in its drug discovery and early development programmes across the United States, including Cambridge, Andover, and Groto[2]. The layoffs will occur over several months. This is following the closure of two manufacturing sites in the UK during 2016 and 2017, which resulted in a further 370 job losses. This news now overshadows the backlash against Merck & Co. in early 2017 upon their announcement they would be halting their mid-to-late stage clinical trial treatment (verubecestat) for Alzheimer's disease[3].

Over the last two decades, Pfizer has supported at least 100 clinical trials of 24 potential Alzheimer's disease drugs[4]. Unfortunately, only donepezil (Aricept) – a drug developed by both Pfizer and Eisai – was approved for clinical use[5]. Aricept has now been available to Alzheimer's disease patients for over 20 years. However, like all currently available therapeutics for the disease, their clinical benefit becomes limited over time. A similar story is true for levodopa as a treatment for Parkinson's disease. Approved by the Food and Drug Administration (FDA) in 1970, leveodopa is a staple in Parkinson's disease treatment. However, it is plagued with unwanted side-effects triggering psychological distress in patients[6,7].

In recent memory, practically every clinical trial for Alzheimer's and Parkinson's disease drug candidates has ended in failure – a far from extensive list for Alzheimer's is shown in Table 1[8]. This was either due to toxicity or limited-to-no clinical benefit. The exception of this is an extended-release formulation of amantadine (Gocovri), which was approved by the FDA in 2017 for use for dyskinesias in Parkinson's. However, dyskinesias are a symptom of levodopa treatment, rather than a symptom of the disease itself. Further, for Alzheimer's, no new therapeutic has been approved in the last 15 years, despite expansive clinical trials aimed at the disease. Failures are frequent and newsworthy. Most recently, on 13 February 2018, Merck confirmed the discontinuation of their APECS study, following the halt of their EPOCH study in 2017. Similarly, like EPOCH, APECS utilised verubecestat. However, it was given for the treatment of prodromal Alzheimer's patients[9]. With all of this in mind, alongside the fact that each clinical trial has the potential to cost hundreds of millions of pounds, from a business perspective, Pfizer may be the first, but not the only pharmaceutical company to abandon research into these diseases.

TABLE 1
Selected anti-Alzheimer's disease drugs which have failed at clinical trial since 2002.

DRUG	TRIAL	TARGET	OUTCOME/YEAR	COMPANY	CLINICAL TRIAL NUMBER
Verubecestat	Phase II (APECS)	BACE1 inhibitor	No clinical efficacy, 2018	Merck & Co.	NCT01953601
Verubecestat	Phase II/III (EPOCH)	BACE1 inhibitor	No clinical efficacy, 2017	Merck & Co.	NCT01739348
Intepirdine	Phase III	5-HT6 receptor antagonist	No clinical efficacy, 2017	Axovant Sciences	NCT02586909
LY2599666	Phase I	Passive immunotherapy (Aβ)	Insufficient target engagement, 2017	Eli Lilly & Co.	NCT02614131
Solanezumab	Phase III	Passive immunotherapy ($Aβ_{16-24}$)	Discontinued – missed primary endpoint, 2016	Eli Lilly & Co.	NCT01127633
TRx0237	Phase III	Tau aggregation inhibitor	No clinical efficacy, 2016	TauRX Therapeutics Ltd.	NCT01689233
EVP-0962	Phase II	y-Secretase inhibitor	Discontinued, 2016	FORUM Pharmaceuticals	NCT01661673
GSK239512	Phase II	H_3 receptor antagonist	No improvements in memory test, 2014	GlaxoSmithKline	NCT01009255
Bapineuzumab	Phase III	Passive immunotherapy (Aβ)	Discontinued 2012, no clinical efficacy	Janssen, Pfizer	NCT00667810 NCT00676143
Latrepirdine (Dimebon)	Phase III	Nonselective antihistamine	Terminated, 2012	Pfizer	NCT00912288
AN-1792	Phase II	Active immunotherapy ($Aβ_{1-42}$ peptides)	Discontinued 2002, adverse effects: meningoencephalitis	Janssen, Pfizer	NCT00021723

Pfizer are one of several big pharmaceutical companies, including GlaxoSmithKline and Eli Lilly that are a part of the Dementia Discovery Fund (DDF). The DDF was launched in 2015 by industry and government to develop Alzheimer's treatments. Currently, it is not certain how significantly this development will impact the DDF. Generous donations from philanthropists may be able to somewhat plug the hole that Pfizer will inevitably leave. Bill Gates, for example, has promised to donate £38 million to the DDF. "I believe we are at a turning point in Alzheimer's research and development, which the Dementia Discovery Fund is playing an important role in by exploring new approaches to treat the disease," said Gates following the announcement[10].

Regardless of your standpoint, these are potentially dark times in neurodegenerative research. The news may well intensify the 'health care for people, not for profit' debate, and may damage the public perception of Pfizer. The onus may begin to fall ever more on academic research groups to provide much needed reassurance and hope.

Unfortunately, in the minds of Pfizer executives, injecting billions of pounds into Alzheimer's and Parkinson's disease research does not appear to be a fruitful business model, and they appear to be jumping ship. This move has its clear advantages from a business perspective, whereby the company can introduce greater funds into different areas of research. However, as a consequence, advancements in neurodegenerative research could be considerably reduced.

Around the globe, approximately 10 million people are living with Parkinson's disease[11], whilst 48 million currently live with some form of dementia[12]. Thus, the payoff for new FDA approved drugs would be priceless.

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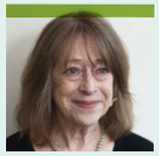
UPDATES FROM OUR AFFINITY GROUPS

NEUROPHARMACOLOGY



CLARE STANFORD
University College London, UK

Clare studied physiology at University College London (UCL), followed by postgraduate and postdoctoral research at the University of Oxford – investigating neurochemical mechanisms that regulate noradrenergic transmission in the brain and periphery. Since returning to UCL, her research has focused on the neurobiology of mood and behaviour and the mechanism of action of drug treatments for psychiatric disorders. This work has involved preclinical research *in vitro* and *in vivo*, as well as human studies. She is currently Professor (Emerita) of Translational Neuropharmacology at UCL, a member of Council of the British Pharmacological Society and the Laboratory Animal Science Association and of the A(SP)A Animal Science Committee.

MARK TRICKLEBANK
Kings College London, UK

Mark Tricklebank is a behavioural neuroscientist/psychopharmacologist who graduated with a joint honours degree from the North East London Polytechnic in Psychology and Biochemistry in 1971. He then undertook a Master's degree in Neurochemistry at the Institute of Psychiatry and completed a PhD at the University of Manchester in 1975. Mark then moved into the pharmaceutical industry, which took him to Merrell-Dow, Strasbourg; Merck Sharp and Dohme, Harlow; Sandoz, Basel; Novartis, Basel and Eli Lilly, Windelsham. Mark remained in industry until suffering a stroke in 2012. Not wishing to retire, he applied for, and won, a Wellcome Trust career re-entry fellowship working with Professor Steven Williams in the Centre for Neuroimaging Sciences, Institute of Psychiatry Psychology and Neuroscience King's College London, where Mark is currently based. Mark was awarded the degree of DSc from the University of Manchester in 2015 and a fellowship from the British Pharmacological Society in 2012.

The Neuropharmacology Affinity Group serves all members of the Society with an interest in neuropharmacology. We cover topics ranging from intracellular signaling to translational research and so there is a wide pool of expertise within the group. The Neuropharmacology Affinity Group has 225 members, with women accounting for 45% of these recruits.

Since our last update in *Pharmacology Matters*, we have been doing our best to ensure that neuropharmacology has made a prominent contribution to several national and international meetings. One of these was a symposium on Trace Amine Associated Receptors, at the EPHAR meeting in Istanbul in June 2016, which was remarkably well attended, considering the catastrophic event at the airport the night before. Another symposium, on melatonin, at *Pharmacology 2016*, covered material ranging from the genetics and pharmacology of melatonin receptors to its promising clinical applications. A collection of review articles on melatonin pharmacology and potential pharmacotherapy will soon be published in a Themed Issue of the *British Journal of Pharmacology*.

We are delighted that Society members are engaging more in the Affinity Group's activities and submitted several proposals for symposia for *Pharmacology 2017*. Three were selected for the meeting: One of these, "A new look at imidazolines, their receptors and emerging therapeutic applications" was co-chaired by David Nutt and provided an update on recent developments in this fascinating, yet neglected, field of pharmacology. The second symposium in the neuropharmacology track was: "Pharmacological strategies for disease modification in the treatment of neurodegenerative proteinopathies". This interdisciplinary symposium drew attention to the diverse pharmacology underlying efforts to develop disease modifying therapies for neurodegenerative proteinopathies. The third was "Sigma-1 receptors as therapeutic targets". This was another interdisciplinary symposium, which again emphasized new directions for research in this field. Without doubt, the neuropharmacological highlight of *Pharmacology 2017* was Graeme Henderson's lecture on opiate overdose, given in memory of Gary Price. This was a truly fascinating talk, which drew on his expertise in several fields, combining pharmacokinetics and pharmacodynamics to explain unintended perils of polypharmacology in drug abuse.

Looking to the future, we are pleased that a symposium from this Affinity Group has been accepted for inclusion in the programme for the World Congress of Pharmacology, to be held on Kyoto in 2018. The title of this session is "New perspectives on the function and pharmacology of the renin-angiotensin system" and will draw attention to the exciting evidence that the renin-angiotensin system (RAS) has a key role in systems that are distinct from cardiovascular regulation and include modulation of mood and behaviour. The symposium will be co-chaired by Clare Stanford (British Pharmacological Society) and Kouichi Tamura (Yokohama City University) and the four talks are:

- **Pleiotropic mechanisms and actions of the brain renin-angiotensin system** (*Robert Speth*: Nova Southeastern University, USA)
- **A role for the neuronal renin-angiotensin system in treatment of obesity and metabolic syndrome?** (*Kouichi Tamura*: Yokohama City University, Japan)
- **The neuronal renin-angiotensin system: a new strategy for PTSD and fear-related disorders** (*Paul Marwar*: George Washington University, USA)
- **Targeting the neuronal renin-angiotensin system in prevention of neurodegeneration and dementia** (*Ursula Quitterer:* ETH, Zurich, Switzerland)

We hope to see lots of Society members there.

In the meantime, we strongly encourage members of the Neuropharmacology Affinity Group, who are keen to arrange a symposium or a themed meeting, to make contact with us, or the Society's Meetings Secretariat. We would be pleased to help you turn your ideas into a British Pharmacological Society event.

TOXICOLOGY

JAMES DEAR
University of Edinburgh, UK

Dr Dear began his medical training at University College London and completed a PhD in Pharmacology before finishing his clinical training at Oxford University. After junior medical jobs at the John Radcliffe Hospital in Oxford and a variety of London teaching hospitals, Dr Dear spent 2 years as a research fellow at the National Institutes of Health, Bethesda, USA. Since 2005, Dr Dear has been at Edinburgh University as Reader in Clinical Pharmacology with a particular interest in translational toxicology.

DANIEL ANTOINE
University of Edinburgh, UK

Dan is a Principal Investigator at the MRC Centre for Inflammation Research and part of the Pharmacology, Toxicology and Therapeutics group at the University of Edinburgh. He obtained is PhD in pharmacology in 2009 at the University of Liverpool. His research interest centres on drug-induced liver injury and he has previously worked in industry (AstraZeneca) and conducted postdoctoral research at the Harvard Medical School, USA and the MRC Centre for Drug Safety Science, UK. Dan sits on the British Pharmacological Society's membership and awards committee, acts as Councilor for the IUPHAR Drug Metabolism and Drug Transport Section Executive Board and was elected to serve on the Hepatotoxicity SIG steering committee for the American Association for the Study of Liver Diseases. Dan also serves on the training fellowship awards panel for the NC3Rs and is an Editorial Board member for the *British Journal of Pharmacology* and *Pharmacology Research & Perspectives*.

The Toxicology Affinity Group serves members with interests in all aspects of toxicology. This includes a wide range of pre-clinical areas such as biological modelling, cardiovascular toxicology, drug discovery toxicology, *in vitro* and alternative methods for toxicity evaluation and nanotoxicology. This Affinity Group is very keen to integrate clinical and translational toxicology with pre-clinical science, and have a strong representation across regulatory science.

At *Pharmacology 2016* a number of symposia were aligned with toxicology. These included:

- Organ-on-a-chip technology – the future of physiological profiling?
- Clinical application of systems pharmacology models
- Nanomedicine in pharmacology

In addition, Professor Kevin Park (University of Liverpool) gave an outstanding Lilly Prize Lecture that was highly relevant to both pre-clinical and clinical toxicologists. The title of the lecture was 'Adverse drug reactions – from man to molecule and back again'.

At *Pharmacology 2017* the following sessions were particularly aligned with our group:

- Engaging with ethical review: strengthening relationships between ethical review bodies and researchers
- When less is more; rational drug design through fragment-based drug discovery
- Mind the gap: clinical pharmacology in the NHS and pharmaceutical industry
- Advances in drug development and regulation, MHRA

The Grahame-Smith Prize Lecture entitled 'Paracetamol as a model of precision toxicology' was delivered by Dr James Dear. This lecture described the full translational pathway of biomarker development from pre-clinical models through to human multi-centre studies in patients with this common clinical toxicology emergency.

In 2018, we are planning a specific Toxicology Affinity Group focussed meeting on the safety of stem cell therapy – please stay tuned for more information.

Our long-term goal is to bring UK pre-clinical and clinical scientists together to promote toxicology within the Society and engage with others interested in toxicology across the UK and Europe.

The Society would like to thank Mark and Daniel for their hard work over their 2 year terms as co-chairs of the neuropharmacology and toxicology Affinity Groups retrospectively. We would also like to warmly welcome the new co-chairs - Francisco Molina Holgado from the University of Roehampton, UK for neuropharmacology, and Heather Wallace from the University of Aberdeen, UK for toxicology.

SURF LIFESAVERS

ANDY LAWRENCE
The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Professor Andrew Lawrence is an NHMRC Principal Research Fellow and Associate Director at the Florey Institute of Neuroscience and Mental Health, where he is also Head of the Mental Health Research Theme and runs the Addiction Neuroscience laboratory. Andrew has published over 200 original articles and reviews, and been cited >8000 times (H index 49). Andrew was treasurer of the Australian Neuroscience Society (2002-2008) and is a Fellow of the British Pharmacological Society. He was Senior Editor of the *British Journal of Pharmacology* (2007-2014) and is currently a Reviews Editor with the *British Journal of Pharmacology*. He is Editor-in-Chief of *Pharmacology Research & Perspectives*, Associate Editor of both *Neurochemical Research* and the *Journal of Pharmacological Sciences*. He sits on the Editorial Board of *Addiction Biology*. Andrew was recently President of the Asian-Pacific Society for Neurochemistry (2014-16) and is currently a Council member of the International Society for Neurochemistry. In 2017 Andrew delivered the Lawrie Austin Plenary lecture at ANS.

Surf lifesaving has a proud history in Australia, starting around the Sydney ocean beaches in 1907. The stated mission of Surf Lifesaving Australia is "Surf Life Saving exists to save lives, create great Australians and build better communities".

Living near the beach in Melbourne, I am a member of our local lifesaving club, Hampton. Which was established in 1913. Over many years I have taken on numerous roles, including grant writing, powercraft officer, chief instructor and director of lifesaving. Currently I am both chief instructor and director of lifesaving, which is a bit of a handful at times! In addition to these roles I am a patrol captain, and organise all of our patrol teams and roster for the season.

My role as chief instructor involves organising annual skills requalification (all lifesavers must renew their awards every year) as well as organising training sessions for new awards. Most start out around 13 years old with a Surf Rescue Certificate (SRC), which graduates to a Bronze Medallion from 15 years upwards. Other awards that I train include Spinal Management, Advanced Resuscitation, Rescue Boat Crew and Driver. Each year we put on courses for each of these awards, and we get lots of adults as well as teenagers involved. I am also an assessor for Lifesaving Victoria, which involves going to clubs and acting as the external examiner for requalifications and new awards. All of this is purely in a volunteer capacity. I have been recognised by my club and I am now a life member.

Obviously, our main role is to provide a safe beach for the public, but we also train to compete in surf lifesaving carnivals around the state and country. For example, I compete for Hampton in the Inflatable Rescue Boat (IRB) racing team, which is very exhilarating, especially when there is a big swell. I also compete for the Hampton Masters team in regular lifesaving events (board rescues, sprints etc.). Each year we compete at state championships, usually in Lorne on the Great Ocean Road. This year I went one up on my previous 2 silver medals and came back with a gold medal in the men's 50-55 age group beach relay!

Lifesaving is incredibly family and community oriented, with lots of social events all year round. My wife and daughter are also members. My wife has previously served as club secretary and my 18-year-old daughter is currently manager of the IRB racing team. It was a great feeling last season competing alongside my daughter in IRB racing, even being in the same team for some events. A lifesaving club is an amazing cross-section of society, people from all walks of life come together. Many of my closest and dearest friends come from lifesaving. One thing is for sure, a mate from lifesaving will always be there for you.

SPOTLIGHT ON... ANTIPODEAN MOLECULAR PHARMACOLOGY OF G PROTEIN-COUPLED RECEPTORS

NICOLA SMITH
Victor Chang Cardiac Research Institute, Australia

Dr Nicola J Smith is a National Heart Foundation Future Leader Fellow and head of the Molecular Pharmacology Laboratory at the Victor Chang Cardiac Research Institute. She is a conjoint Senior Lecturer at the University of New South Wales. Nicola graduated from the University of Melbourne with a BA, BSc (Hons) and PhD and received a National Heart Foundation/NHMRC CJ Martin Fellowship to undertake post-doctoral training first with Professor Graeme Milligan at the University of Glasgow and then Professor Bob Graham at the Victor Chang. Her passion is the study of orphan G protein-coupled receptors in health and disease.

It's OK. I get it. My enthusiasm is a little over-the-top. But 'c'mon!' (to borrow a phrase from fellow enthusiastic-type, Australian tennis player Lleyton Hewitt), G protein-coupled receptors (GPCRs) are awesome!

With more than 800 members, GPCRs are the largest membrane protein family in the human genome. They follow a universal template of an extracellular N-terminus, seven transmembrane-spanning helices and an intracellular C-terminus, but beyond this they all have their own little personalities. Some have crazy hairdos, some need a friend to get to their destination, some are more like swingers, coupling with different partners depending on their mood. Through their various binding sites, GPCRs can be turned on, turned off or very precisely tuned to achieve a biological outcome. The ones I am most interested in are a little lost – these orphan GPCRs are yet to be paired with their endogenous ligand. This means that they are tough nuts to crack... let me tell you that a pharmacologist without a ligand is a sad sight indeed.

Australia has an established international presence in GPCR pharmacology and I was lucky enough to be an undergraduate at the University of Melbourne when Arthur Christopoulos and Patrick Sexton were first starting to build their formidable partnership. In a strong pharmacology department run by Jim Angus, former colleague of Sir James Black, I was put through my analytical pharmacology paces by Michael Lew[1], who taught me to love GPCRs and the things they could do. I undertook an Honours year in the fledgling Christopoulos laboratory alongside Lauren May, well known to the British Pharmacological Society's members from her time in Nottingham with Steve Hill, and there was no turning back – I was hooked on GPCRs.

Coming from a family riddled with cardiovascular disease, I combined both of my passions by joining the laboratory of Wally Thomas at the Baker Heart Research Institute for my PhD. Wally is a wonderful man and he taught me many things in the laboratory, but his greatest gift was encouragement to believe in myself, flee the nest and aim for the biggest GPCR labs in the world. And with that, I found myself on a four year overseas research fellowship in wonderful Glasgow (I mean this genuinely – I love the city and miss all the 'Weegies' I left behind) in the laboratory of Graeme Milligan, GPCR guru. I blame Graeme for my journey into the difficult world of orphan GPCRs (although he did warn me!) as he introduced me to the free fatty acid receptor family of GPCRs. They were deorphanised in 2003 and beasts to work with, at that time lacking any ligands with decent potency (or even solubility). I liked the idea that we had to push these metabolite receptors and our assay systems to their very limits in order to squeeze out any clues that might help us understand them more[2]. This is even more so the case with orphan GPCRs and I am often overheard to use stronger words than 'beasts' to describe them.

In early 2011, I returned to Australia with the desire to learn *in vivo* pharmacology so that I could take orphan GPCR targets from *in silico* models all the way to animals[3]. And thus I find myself still at the Victor Chang Cardiac Research Institute today, running a lab with two post-docs, a research assistant, two PhD students and three interns.

Science in Australia is wonderful but different to what I experienced in the UK. You have to be more organised, for starters, as reagents aren't kept in stock nearby and are often shipped from Europe or the USA. We also operate on a yearly grant cycle so our summers are lost to grant and fellowship submissions while the rest of our countrymen sun themselves on beaches or attend Test matches and tennis tournaments. Funding here is as bad as the rest of the world so it is very competitive to get a break, although there is a strong emphasis on supporting early career researchers and there are plenty of opportunities for talented young pharmacologists from overseas. So, on a parting note, I encourage fellow GPCR fans to visit us all in Australia – we have our annual ASCEPT pharmacology meeting this year in Adelaide (27 to 30 November 2018) followed by the high-calibre 10th Molecular Pharmacology of GPCRs meeting in Melbourne (2 - 4 December 2018). I hope to see you there!

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INTRODUCING THE NAGOYA PROTOCOL TO THE PHARMACOLOGIST

THOMAS MURPHY
Policy Advisor: Convention on Biological Diversity and Nagoya Protocol

Thomas is part of the Department for Environment and Rural Affairs' International Ecosystem and Climate Change team and is the UK's policy lead for the Convention on Biological Diversity, the Nagoya Protocol, and also acts as the Nagoya Protocol Focal Point for the UK.

Thomas has advised and assisted ministers in debates on the Protocol and contributed to negotiations at an international level. As part of the UK delegation at several EU ABS Expert groups Thomas has helped steer implementation of the Protocol within the EU.

Before moving into public policy, Thomas graduated with an Environmental Management (land use) degree from the University of Greenwich and worked in the not-for-profit sector to help businesses and the public sector take action on energy efficiency and air quality.

Throughout history, genetic material from plants and animals to microbial organisms has provided an extremely rich source for pharmacological study.

Despite the rapid advancements in technology over recent years and the application of synthetic chemicals, genetic material still represents an important pool for the identification of novel drug leads. In particular, medicinal plants, evolutionarily optimised for serving different biological functions, have proven their value as a source of molecules with therapeutic potential.

It is widely recognised that biological diversity holds a bounty of beneficial bioactive compounds, many of which have not been fully investigated as new and effective medicines. Furthermore, in the context of drug discovery, genetic material often comes with the additional advantage of well documented ethno-pharmacological information about the traditional use. This has and can be used to guide the identification and development of therapeutic compounds, thereby speeding up the process.

However, despite this valuable resource of genetic material and associated knowledge, it is also widely reported that biological diversity is under threat and we risk losing these resources for future generations. In a bid to protect global biodiversity, the international community has sought to halt such loss, notably through the Convention on Biological Diversity which focusses its attention on the conservation and sustainable use of biological diversity and through a supplementary article, the Nagoya Protocol, on the fair sharing of benefits arising from the use of genetic resources.

What is the Nagoya Protocol?

The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Their Benefits from Their Utilization came into force in 2014.

A supplementary agreement to the 1992 Convention on Biological Diversity (CBD), the Protocol aims to fulfil the third objective of the CBD:

> "the fair and equitable sharing of the benefits arising out of the utilisation of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources"

A genetic resource, as defined by the Protocol, is any plant, animal, microbe or material of other origin which contains functional units of heredity and is of actual or potential value. Importantly, human genetic resources are not covered by the Nagoya Protocol.

Recognising the sovereign rights of countries that have signed and implemented the Protocol over their genetic resources and providing a frame work for the sharing of benefits when a genetic resource is utilised, the Protocol creates an incentive to these countries to conserve biological diversity.

To date, 105 countries (including the UK) have signed and ratified the Protocol. The Protocol requires these countries to implement both national access legislation (legislation that governs how genetic resources in their jurisdiction can be accessed) and compliance measures to ensure that those within their country undertaking utilisation of a genetic resource have acquired the resource in line with the access legislation of the country where they sourced it.

For example, the UK does not have legislation in place to regulate access to its genetic resources but it has put in place compliance measures to ensure that UK users exercise due diligence when utilising genetic resources from other countries.

Why does the Nagoya Protocol matter to Pharmacologists?

In the UK there are a number of regulations in force that implement the Nagoya Protocol;

- *Regulation (EU) No. 511/2014 on compliance measures for users from the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilisation in the Union*
- *Implementing Regulation (EU) 2015/1866* - laying down the detailed rules for the implementation of Regulation (EU) 511/2014

Under these regulations, those who seek to conduct Research and Development (R&D) are required to exercise due diligence to demonstrate that genetic resources and/or any associated traditional knowledge are accessed and utilised in accordance with the applicable legislation of the providing country.

The first step is to visit The Access and Benefit sharing Clearing House (ABSCH). This useful tool allows a potential user to identify which countries are party to the Protocol, the national legislation in that country and the relevant contacts to find out more.

Depending on the national measures that apply in the provider country the user may need to demonstrate Prior Informed Consent (PIC) has been obtained and Mutually Agreed Terms (MAT) have been established.

In the UK, this is done through submitting a due diligence declaration to the UKs Competent National Authority, the Department for Business, Energy & Industrial Strategy. This can be done using the online system DECLARE.

A declaration is required at two designated checkpoints in the R&D process:

- When in receipt of research funding in the form of a grant, for work involving utilisation of genetic resources and/or associated traditional knowledge (aTK);
- At the stage of final development of a product developed via the utilisation of genetic resources and/or aTK with such resources. The definition of when final development has occurred is available in *Implementing Regulation (EU) 2015/1866*.

For Pharmacologists, operating in a notably R&D intensive sector means that awareness of these regulations is essential.

> "To date **105** countries (including the UK) have signed and ratified the Protocol"

Want to know more?

The Protocol can be initially daunting but help is at hand, visit the BEIS site here for more information and contact details for further support.

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MARINE BIOMEDICINE: 21ST CENTURY BIOPROSPECTING TO COMBAT ANTIMICROBIAL RESISTANCE

KATHERINE DUNCAN
University of Strathclyde, UK

In 2016, Katherine started her research group as a Chancellor's Fellow and Lecturer in Drug Discovery at the Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde. With over 12 years of international interdisciplinary research experience in marine natural products, Katherine completed a MChem (Scotland), an International MChem research placement (Florida), a PhD in Biomedical Sciences (Canada), and two post-doctoral fellowships (Marine Biomedicine, University of California and Marine Biotechnology, Scottish Marine Institute). Katherine's interdisciplinary research encompasses molecular biology, genomics, microbiology, phylogenomics, chemistry, oceanography and comparative metabolomics to discover new antibiotics from our oceans.

Bacteria are rapidly becoming resistant to our most widely used antibiotics[1], resulting in a severe worldwide threat to human health. Multidrug resistant infections result in 25,000 annual deaths in the EU[2] and 700,000 worldwide, a figure that is predicted to rise to 10 million by 2050 if new chemistry is not discovered[3]. The severity of these "superbugs" was recently illustrated through the isolation of Enterobacteriaceae, found to be resistant to 26 antibiotics including carbapenem (a drug of last resort)[4].

Scottish Island sediment bank

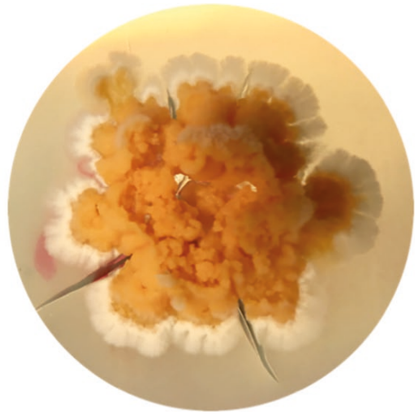

Figure 1. Bacteria isolated from Antarctica.

Following the treatment of tuberculosis in 1944 with streptomycin[5], bacteria have been the primary source of bioactive natural products. In fact, 73% of all approved antibacterial agents discovered between 1981 and 2016 were unaltered natural products, or natural product derivatives[6], many of which are produced by bacteria. Natural products can be divided into primary metabolites (essential for organism survival, i.e. amino acids) and specialised metabolites (which confer an adaptive advantage to the producing organism). In evolutionary terms, antibiotics are specialised metabolites, as they provide a competitive advantage to the producer. In particular, one order of bacteria, the actinomycetales, have been unsurpassed in their ability to produce clinically relevant chemistry, with over 10,000 bioactive microbial metabolites ascribed to these strains[7].

Since the first bacterial genome was sequenced in 1995, whole genome sequencing has uncovered the truly remarkable chemical potential of these bacterial strains. This has revealed that up to 90% of the blueprint (biosynthetic gene clusters) that encode the production of these specialised metabolites remain cryptic, with no known product[8]. Eliciting this chemistry represents an incredible opportunity to uncover new antibiotics.

To enable antibiotic production, we need to first understand the evolutionary, biogeographic and ecological switches that enable these biosynthetic gene clusters to be expressed. We know that bacteria sample their biosynthetic gene clusters from their environment through horizontal gene transfer. This has great implications on bioprospecting (the search for new natural product resources), as their taxonomy (which species they are), evolution (how they are related) and biogeography (where they are isolated from) influence their chemical ability.

> "Multidrug resistant infections result in 700,000 annual deaths worldwide"

The oceans cover over 70% of the Earth's surface, representing an incredibly biodiverse and chemically understudied ecosystem. My research group isolates actinomycetes from marine ecosystems such as Scottish islands and and Antarctic sediment cores. We use this marine bacteria culture collection to study chemical potential (through genome sequencing), chemical ability (using comparative metabolomics) and bioactivity (against clinically relevant pathogens). These specialised metabolites and bioactivities are then related to evolution, environmental parameters and biogeography across tens to hundreds of strains. By combining these 'omics' technologies, it enables us to both inform future bioprospecting and accelerate antibiotic discovery.

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CALLING ON PHARMA TO PUBLISH IN PR&P!

ANDY LAWRENCE
The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Professor Andrew Lawrence is an NHMRC Principal Research Fellow and Associate Director at the Florey Institute of Neuroscience and Mental Health, where he is also Head of the Mental Health Research Theme and runs the Addiction Neuroscience laboratory. Andrew has published over 200 original articles and reviews, and been cited >8000 times (H index 49). Andrew was treasurer of the Australian Neuroscience Society (2002-2008) and is a Fellow of the British Pharmacological Society. He was Senior Editor of the *British Journal of Pharmacology* (2007-2014) and is currently a Reviews Editor with the *British Journal of Pharmacology*. He is Editor-in-Chief of *Pharmacology Research & Perspectives*, Associate Editor of both *Neurochemical Research* and the *Journal of Pharmacological Sciences*. He sits on the Editorial Board of *Addiction Biology*. Andrew was recently President of the Asian-Pacific Society for Neurochemistry (2014-16) and is currently a Council member of the International Society for Neurochemistry. In 2017 Andrew delivered the Lawrie Austin Plenary lecture at ANS.

Pharmacology Research & Perspectives (PR&P) is jointly owned by the British Pharmacological Society, American Society for Pharmacology and Experimental Therapeutics (ASPET) and Wiley. We are an Open Access journal that aims to promote the publication of all types of pharmacological studies: original articles, reviews, hypotheses, opinions – including what has historically been perceived as "negative data", for example failed replication, target (in)validation and similar. A historical example would be the development of tricyclic antidepressants that were derived indirectly from an antihistamine program, and monoamine oxidase inhibitors which came from antitubercular compounds, both of which contributed to the development of rational drug design.

On the other hand, multiple teams in Pharma and Biotech have been working on projects that have been stopped for various reasons, in many cases unrelated to scientific issues, generally referred to as "strategic considerations". Sometimes, such projects have led to development of candidates that may have been explored in the clinic. In other cases, projects have at least led to the production of tool compounds that may be of great value for the scientific community to validate or invalidate targets or pathways. Indeed, such projects may have been stopped because the data that have been published earlier in high profile journals, could not be reproduced; yet the teams did not publish the data, as the team members were allocated to other projects and publication was not a priority. At times, teams may also have been disbanded, and some of the scientists may have joined academia or have retired. In these cases, the data could be written up (traditionally, when projects are stopped, a "post mortem" has been written to allow management to proceed) and submitted to PR&P, as there is now renewed interest in such reports.

We believe publication of such studies is important for a number of reasons:

1. It promotes transparency
2. It should aid in reproducibility
3. It could very well prevent unnecessary time, expense and animals being used in experiments that are not warranted if all the facts are available
4. Even if a target fails, the program may still result in the provision of new molecules that could be highly useful tools for fundamental discovery-based research

Accordingly, in 2018 we will publish reviews that highlight historical cases where what was initially perceived as a "negative" result in fact turned out to change the field and/or lead to new medications, even if not for the originally intended condition! We have some already "locked in" but if you have ideas please feel free to contact me (Andrew.Lawrence@florey.edu.au).

From the perspective of original articles, we would like to call on those engaged in Pharma research and development to actively consider publishing data from shelved projects (for the reasons enunciated above). We acknowledge that when a program is ceased and the researchers are aligned with new projects that priorities may change. Therefore, in order to facilitate the process and minimise the time factor for manuscript writing, we would be happy to accept submissions in the form of internal reports, simply reformatted for PR&P style. In addition, we would be happy to consider monograph-style submissions. To start the ball rolling, I am delighted to announce that Professor Daniel Hoyer will contribute such articles from his time in Pharma. Please consider doing the same.

DAVID WEBB RECEIVES THE TOMAH MASAKI AWARD FOR HIS PIONEERING ENDOTHELIN RESEARCH

ANTHONY DAVENPORT
University of Cambridge, UK

Anthony Davenport is Reader in Cardiovascular Pharmacology and directs the Human Receptor Research Group in Experimental Medicine and Immunotherapeutics, University of Cambridge. He is an executive committee member of NC-IUPHAR that oversees the databases GuidetoPharmacology.org, GuidetoImmunopharmacology.org and is a contributor to the Concise Guide to PHARMACOLOGY. He is a member of the Editorial Board of the *British Journal of Pharmacology*. His research concentrates on understanding the role of G protein-coupled receptors, together with their transmitters in the human cardiovascular system and how these are altered with disease. A major focus for over two decades has been endothelin peptides and more recently, the apelin signalling pathway.

David Webb receiving the Tomoh Masaki Award from Mashi Yanagisawa. (Photo courtesy of We Make Media, Ltd).

The Fifteenth International Conference on Endothelin took place in Prague from 4 - 7 October 2017, and was co-chaired by Ivana Vaněčková (University of Prague) and John Pernow (Karolinska Institute, Sweden). A highlight of the meeting was the presentation to Professor David Webb (University of Edinburgh and past President of the British Pharmacological Society) of the Tomah Masaki Award, for his pioneering research into the clinical pharmacology of endothelin, agonists and antagonists, published in over two hundred papers and reviews.

His most highly cited paper on endothelin appeared in the Lancet[1] in 1994 propelling endothelins from the laboratory into the clinic. With Bill Haynes, he showed that the highly selective ET_A receptor antagonist, BQ123, when co-infused with endothelin-1 into the brachial artery of volunteers, abolished the vasoconstrictor action of the peptide. Crucially, BQ123 infused alone caused progressive vasodilatation, demonstrating unequivocally that endothelin-1 contributed to the maintenance of peripheral vascular tone, opposing the actions of nitric oxide[1]. In the current era now dominated by mice, this milestone study was an elegant demonstration of the power of selective pharmacological tools, in this case an antagonist, to investigate physiological function on humans. The study utimately fostered the development of small molecule endothelin receptor antagonists for clinical use.

The inaugural biennial Tomoh Masaki Award[2] was established in 2011 and first presented at the very sucessful Twelfth International Conference on Endothelin in Cambridge, UK[3], that was hosted by the British Pharmacological Society. The award honors the scientific achievements of Tomoh Masaki, who obtained his M.D. from the Faculty of Medicine (University of Tokyo) in the late 1950s and was appointed Professor of Pharmacology at the

> "Masaki's scientific legacy is remarkable. jkiThe field remains vibrant with new discoveries and over **30,000** papers have been published to date"

Institute of Basic Medical Sciences (University of Tsukuba, Japan) where he led the team that identified endothelin as the Endothelium Derived Constricting Factor (EDCF) in 1988[4], and first cloned the endothelin ET_B receptor[5].

The existence of an EDCF had long been suspected since Robert Highsmith's group (University of Cincinnati College of Medicine, USA) characterised the vasoconstrictor action of a compound obtained from media conditioned by bovine endothelial cells and showed that it was likely to be a peptide, since activity was abolished by trypsin[6]. One of Tomoh Masaki's graduate students, Masashi Yanagisawa (molecular biology) together with Hiroki Kurihara (cardiology) suggested the identification of the peptide as a subject for his PhD thesis. The project expanded to include the late Katsutoshi Goto (pharmacologist) and Sadao Kimura (biochemist) and resulted in the *Nature*[4] paper published on 31 March 1988. The paper described the structure of endothelin-1, a 21 amio acid peptide with not one but two disulphide bridges, a feature unsual for a biologically active peptide, together with its function as the most powerful and long lasting vasoconstrictor discovered to date. The impact of the *Nature* paper was phenomenal, igniting new research around the world. Although the structure was not disclosed until March, nearly 50 papers were published in 1988 and over 450 during the following year. Progress was so rapid in the summer of 1988 that within seven months, Sir John Vane (William Harvey Research Institute, London) had convened the First International Meeting on Endothelin[7].

Masaki's scientific legacy is remarkable. The field remains vibrant with new discoveries and over 30,000 papers have been published to date. 75 papers on endothelin have been clasified by ISI Web of Science as 'highly cited' - meeting the criterion of having received enough citations to place them in the top 1% of their academic fields based on a highly cited threshold for the field and publication year. The most recent of these is an an IUPHAR review[8]. In 1991, he moved to the Faculty of Medicine (Kyoto University) and was appointed Director of the Research Institute of the National Cardiovascular Center (Osaka) in 1997, President of Osaka Seikei University in 2003 and finally Professor at Tokyo Women's Medical University from where he retired in 2009[2].

Previous receipients of the award include Professor Masashi Yanagisawa in 2011 (University of Texas in Dallas and University of Tsukuba), Dr Katsutoshi Goto (2013) also part of Dr Masaki's team and Dr Martine Clozel (2015), who led the discovery and development of bosentan[9], the first in class endothelin receptor antagonist to enter the clinic.

At the meeting in Prague, a highlight of the invited speakers was Dr Rajat Gupta (Harvard Medical School,USA), who delivered the British Pharmacological Society's Distinguished Lecture describing his recent research published in *Cell*[10] where a Single Nucleotide Polymorphism (SNP) regulating endothelin levels has been shown to be associated with five vascular diseases including coronary artery disease and hypertension. This discovery has the potential to be used to stratify patient groups for personalised treatment with endothelin receptor antagonists.

This conference currently rotates between Japan, North America and Europe every two years. The Sixteenth International Conference on Endothelin (ET-16) will be held 22-25 September 2019 in Kobe, Japan, and will be chaired by Dr Noriaki Emoto (Kobe University) and Dr Bambang Widyantoro (University of Djakarta, Indonesia).

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Q&A WITH THE 2017 WINNERS OF THE BJP AND BJCP EARLY CAREER RESEARCHER PRIZES

At the annual joint dinner for the editors of the *British Journal of Pharmacology (BJP)* and the *British Journal of Clinical Pharmacology (BJCP)*, the prizes for the best paper published by an early career researcher in BJP and BJCP over the previous year are awarded. Awardees receive £1000 in prize money, a certificate, and one year of complimentary membership of the Society.

The early career researcher prize was introduced to recognise and encourage the submission of outstanding work done by young investigators working in pharmacology. The award is a part of the Society's ongoing commitment to inclusivity, engagement and support for young pharmacologists. The 2017 winners were Simon Hirota for BJP, and Pieter Okkerse for BJCP, we got in contact to learn more about our prize winners.

SIMON HIROTA (SH)
University of Calgary, Canada

Simon's laboratory focuses on the pathogenesis of the inflammatory bowel diseases (IBD; Crohn's disease and ulcerative colitis), with a specific focus on the pathogenic tissue remodelling resulting in bowel wall thickening and luminal narrowing. Especially prevalent in patients with Crohn's disease, fibrosis and smooth muscle hypertrophy lead to bowel obstruction, requiring surgical resection. Currently there are no approved treatments for this component of IBD. Simon's lab are currently characterizing the anti-fibrotic/anti-proliferative effects of various nuclear receptors in the intestinal mesenchymal cell populations that contribute to remodelling in IBD, in the hopes of finding new therapeutic targets.

PIETER OKKERSE (PO)
Leiden University Medical Centre, The Netherlands

For Pieter's PhD thesis he performed clinical pharmacology research in the field of neurology and pain at the Centre for Human Drug Research (Leiden, The Netherlands). He developed a battery of human pain models to detect analgesic properties of existing and new drugs. Currently he is working as a medical doctor as specialist registrar in anaesthesiology at Leiden University Medical Centre in the Netherlands.

DESCRIBE THE KEY DISCOVERIES FROM YOUR ARTICLE AND THEIR IMPLICATIONS FOR THE PHARMACOLOGICAL COMMUNITY

SH: In our article, we reported a novel role for the constitutive androstane receptor in the repair response within the intestinal epithelium (*in vitro*) and intestinal mucosa (*in vivo*). While most of the focus on xenobiotic receptors has been on their regulation of drug detoxification responses, our data, along with other recent publications, suggest that these receptors may play additional roles to regulate mucosal homeostasis.

PO: The aim of the study was to investigate the ability of a battery of human pain models to detect analgesic properties of commonly used analgesics in healthy volunteers. We showed that the battery of pain models was able to detect changes in pain detection and pain tolerance thresholds after administration of different classes of analgesic compounds in healthy subjects. Compounds with different mechanisms of action demonstrated a distinct response pattern on the different pain models. The battery of pain models can be used to benchmark analgesic properties of new drugs against established analgesics in early phase clinical studies.

WHAT INSPIRED YOU TO TAKE UP RESEARCH?

SH: As an undergraduate student, I was fortunate to be accepted into a small group-driven pharmacology training program at McMaster University (Hamilton, ON, Canada) under the mentorship of Drs. Denis Crankshaw and Patangi (Chari) Rangachari. As part of the course requirements, we performed hands-on studies using common experimental approaches (e.g. organ bath assays; radioligand binding assays; colorimetric CYP activity assays; patch-clamp electrophysiology). After finishing our 3rd year research project, where we sought to correlate the polyphenol content in various wines with endothelial-dependent relaxation responses, I was hooked on scientific research!

PO: During my medical studies, I became involved in a pain research project at the anaesthesiology department of the university hospital. It was here that my interest in research was aroused. After graduating from medical school, I had the option to begin clinical work or pursue research. I decided to work as a clinical scientist at the Centre for Human Drug Research (CHDR) in Leiden, The Netherlands, to enable me to both use my practical medical skills and help advance field of medicine. It was at CHDR where I performed the work described in the article.

Simon receiving his prize at the joint BJP and BJCP Editorial Board dinner, from BJP Editor-in-Chief Amrita Ahluwalia.

WHAT POSITION ARE YOU CURRENTLY WORKING IN? WHAT DOES THIS INVOLVE AND WHAT YOU ARE WORKING ON?

SH: I am currently an Assistant Professor in the Department of Physiology & Pharmacology at the University of Calgary. My work profile requires 25% commitment to administrative duties and teaching, within which I act as the Director of our Intestinal Inflammation Tissue Bank and Deputy Chair of our Animal Ethics Committee. The balance of my time is protected for my research, which is focused on the pathogenesis of IBD. In addition, we have a variety of internal collaborations focusing on studying the role of the intestinal microbiota on vascular function.

PO: Currently I am working as a medical doctor as a specialist registrar in anaesthesiology. It is a 5 year program and I am currently in my fourth year. As an anaesthetist, you monitor the patient's conditions before, during and after anaesthesia. Furthermore, you are responsible for analgesia during and after the surgery, airway management in trauma patients and so on. Last month, I defended my thesis and was awarded my PhD. At the moment I am not involved in any research projects, though I am expecting to get involved in new projects in the upcoming months.

CAN YOU TELL US ABOUT YOUR CAREER PATH TO DATE?

SH: After finishing my doctoral training in smooth muscle physiology and electrophysiology, under the supervision of Dr. Luke Janssen (McMaster University), I sought to apply my expertise to the gastrointestinal tract to characterize the changes in smooth muscle function in the context of infection and inflammation (Drs. Paul Beck & Justin MacDonald; University of Calgary). However, as my fellowship progressed, I began to focus on the biology of the intestinal epithelium and innate immune signalling pathways (the NLRP3 inflammasome). This 'switch' has led me to where I am now, with a research program focused on understanding the pathogenesis of IBD. Most recently, I've returned to my 'roots', starting a line of study to better understand how aberrant intestinal fibroblast and smooth muscle function contributes to bowel obstruction in Crohn's disease.

PO: In 2010, I received my qualification as medical doctor at Leiden University. After graduation, I started working as research physician at the CHDR in the field of neurology and pain, where I carried out the research described in the article. In 2015, I started my residency in anaesthesiology at the Leiden University Medical Centre. In 2016, I completed my registration as a clinical pharmacologist and last January I finished my thesis 'The use of a battery of evoked pain models in early phase drug development' and obtained my PhD degree.

WHAT DO YOU FIND MOST REWARDING ABOUT YOUR WORK?

SH: The trainees. Watching their progression over the course of a summer or the completion of a degree is the best part of my job.

PO: The rewarding part of the research I performed is that the methodology that we investigated and validated is still being used in clinical research. The battery of pain models is used to screen the effects of analgesic compounds with new mechanisms of action. It is rewarding to see that the work that we initiated, is being picked up by others.

The rewarding part of my current job is the patient satisfaction, getting patients through major surgery and have them wake up without too much pain.

HOW DID YOU FEEL WINNING THE PRIZE?

SH: I was very surprised and extremely honoured. I grew up as a young scientist reading BJP. In fact, my first publication as an undergraduate was in BJP. So this award is very meaningful to me.

PO: I was mainly surprised when I received the message that I had won the BJCP young investigator prize. I received the award during the BJP and BJCP Editorial Boards dinner during the *Pharmacology 2017* conference.

WHAT ARE YOUR PLANS FOR THE FUTURE?

SH: Keep focused on training and mentorship, while working hard to provide the resources for my lab to do curiosity-driven research.

PO: In two years' time, I will complete my training to be an anaesthetist. Anaesthesiology is divided in several subspecialties - intensive care medicine, pain medicine, cardiothoracic anaesthesiology and so on, and in the coming year I will have to make a decision about where to specialise. I certainly want to combine my clinical work with research as I believe that combining the two makes your job far more challenging.

IN YOUR OPINION, WHAT ARE THE BIGGEST CHALLENGES FACING EARLY CAREER RESEARCHERS AND HOW WOULD YOU SUGGEST THESE ARE TACKLED?

SH: Getting into the funding system is toughest challenge for a new investigator. Without increasing the budgets for federal granting agencies, new investigators will continue to struggle to gain traction. When I first started my lab, I focused on generating preliminary data and publishing papers for over a year and a half before writing my first grant. During this process, I worked with a variety of senior colleagues who reviewed my proposal at various stages. With a track record of early independence, a bunch of preliminary data, and some great mentorship, I was successful in my first grant application.

PO: For medical doctors like me, it can be challenging to combine patient care with research. A big part of the research work needs to be done in your own spare time, so you can end up working long hours.

For my colleagues who work solely in research, there is a lot of competition, whether that's when getting your work published in a journal or applying for research grants. It is important that there are sufficient grants available dedicated to early career researchers. The Dutch Organisation for Scientific Research offers special grants to young scientists, however last year only 14% of the proposals were approved. I think there is some room for improvement there.

DO YOU HAVE ANY ADVICE FOR EARLY CAREER RESEARCHERS?

SH: Find a group of mentors and seek guidance/feedback from them as much as possible in the first years of your appointment. Plan grant submissions early, and always seek multiple rounds of feedback from your mentors. Lastly, keep things in balance. There's a pretty good chance that people won't remember the paper you just published in 20 years' time. On the other hand, your friends and family will remember the time you've spent with them for a lifetime.

PO: Follow your heart. Pick a subject that really interests you. For medical doctors who want to do a PhD program – do it because you're interested in science and not because you have to. A four-year long PhD program is a long time if that's not where your heart is.

WHAT DO YOU ENJOY DOING OUTSIDE OF WORK?

SH: I am a competitive cyclist, racing enduro mountainbike in the summer and cyclocross in the fall. I co-manage a racing team (Steedz Enduro) and am the vice-president of a local cycling club (Bicisport Calgary) with a focus on developing junior racers for national and international competition (we've developed four Olympians to date!). In the rest of my spare time, I play in an 80's metal band (Hellrazer).

PO: I really enjoy riding my racing bike. Leiden is near the beach, dunes and forests, so that's a great starting point to make some nice trips. Furthermore, I like to travel, enjoy good food and go out with friends.

BJCP Editor-in-Chief Adam Cohen presenting Pieter with his prize.

Q&A

AN UPDATE FROM OUR MEETINGS TEAM

CHARLOTTE CORDREY
Events Manager

Charlotte's role involves logistical support to the Meetings and Education function – including Focused Meeting organisation, Meetings Committee & Affinity Groups administration, as well as supporting the organisation for the annual meeting. Charlotte joined the Society from the Royal Society of Medicine where she looked after a number of medical specialities and organised clinical and non-clinical meetings and events. Prior to that, Charlotte worked in the corporate sales team for Hilton Hotels, and studied Events Management at Leeds Metropolitan University.

NIALL HYLAND
Vice President – Meetings

Niall is a Lecturer in pharmacology in the School of Medicine at University College Cork, Republic of Ireland. He also holds a Faculty position at the APC Microbiome Institute, a Science Foundation Ireland research centre where his research focuses on the microbiota-gut-brain axis. Niall has a PhD in Pharmacology from King's College London and trained in both the USA and Canada. He is co-chair of the Society's Systems and Integrative Pharmacology Affinity Group and on the Editorial Board of the *British Journal of Pharmacology*. He also contributes to the activities of the European Society of Neurogastroenterology and Motility and The American Gastroenterological Association Institute Council.

PHARMACOLOGY 2017
11–13 December 2017 | London, UK

At our recent annual meeting, *Pharmacology 2017*, we welcomed 1,112 guests from 51 countries to the Queen Elizabeth II Conference Centre in Central London.

The Society hosted the biggest programme to date with 15 symposia, 7 workshops and 6 plenary lectures alongside oral communications and poster presentations.

Pharmacology again offered a number of 'firsts' for the Society. It was the first year that we accepted late-breaking abstracts with a view to showcasing the very latest research and encouraging undergraduate project submissions. This resulted in a total of 376 abstracts submissions, of which 70 were late breaking abstracts.

Another first, was the business-focused plenary; the culmination of a year-long dialogue with industry. This session featured three leading experts, each with a different perspective on 'hot trends in pharmacology: new science and the business landscape'. We also continued from the success of the previous year and began each day with a career bootcamp, and welcomed more flash poster presentations - with a dedicated session showcasing work from 'Clinical Pharmacology Month'.

To encourage networking, and in order to offer more delegates the opportunity to attend, we held the Welcome Reception at the QEII Conference Centre. The evening was a great success, with attendees enjoying musical entertainment, a taste of traditional British food, a doughnut machine and a photo booth - all whilst catching up with friends and colleagues overlooking some of the best views of London at night!

Keeping abreast of technology, the *Pharmacology 2017* app was downloaded by a record number of attendees. We will now be looking into improving the app and user experience, to ensure all visitors who want to can benefit and engage with the app for future *Pharmacology* conferences.

For further information on *Pharmacology 2017*, please visit **www.bps.ac.uk/pharmacology2017** and to keep an eye on key dates, deadlines and programme information for *Pharmacology 2018* visit **www.bps.ac.uk/pharmacology2018**.

FUTURE MEETINGS

PHARMACOLOGY FUTURES 2018 - EXPLORING FUTURE DRUG DEVELOPMENT
17 May 2018 | Edinburgh, UK

Pharmacology Futures 2018 is a one-day focused meeting, which will explore the technologies and skills that will drive drug development over the next 10 to 15 years, with speakers sharing their visions of the future to celebrate 250 years of pharmacology in Edinburgh. The University of Edinburgh's Cameron Prize for Therapeutics will be awarded during the meeting.

Deadlines to note:

Abstract submission deadline: **Friday 16 March 2018 (11:59pm GMT)**.
Bursary submission deadline: **Friday 16 March 2018 (11:59pm GMT)**.
Early-bird registration deadline: **Monday 16 April 2018 (11:59pm GMT)**.
For further information please visit **www.bps.ac.uk/pharmacologyfutures2018**.

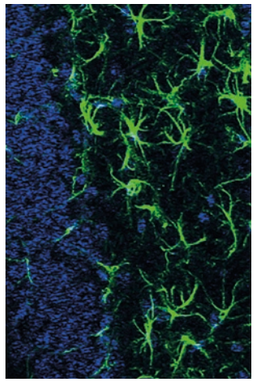
CURRENT TRENDS IN DRUG DISCOVERY – YOUNG SCIENTISTS AND TOMORROW'S MEDICINES
7 June 2018 | London, UK

The British Pharmacological Society and the Society for Medicines Research are pleased to announce their first joint meeting, which aims to increase understanding of current trends in drug discovery in order to accelerate the development of new drug therapies. It will also aid evaluation and interpretation of drug properties and data to allow accurate reporting. The meeting aims to enhance the understanding of drug action and identification of ways to improve experimental design and the drug discovery process.

The one-day programme will bring together presentations from both internationally accurate reporting. The meeting aims to enhance recognised speakers and young scientists, giving them an opportunity to discuss their research through either oral or poster presentations.

Deadlines to note:

Oral presentation submission deadline: **Friday 16 March 2018 (11:59pm GMT).**
Poster presentation submission deadline: **Friday 30 March 2018 (11:59pm GMT).**
Bursary submission deadline: **Friday 30 March 2018 (11:59pm GMT).**
Early-bird registration deadline: **Thursday 10 May 2018 (11:59pm GMT)**.
For further information please visit: **www.bps.ac.uk/drug-discovery-meeting**



7TH FOCUSED MEETING ON CELL SIGNALLING
16 – 17 April 2018 | Nottingham, UK

This two-day Focused Meeting on Cell Signalling will give 200 participants the opportunity to hear leading experts in cell signalling from across the world present their research. This Focused Meeting is the seventh in a highly successful series of Cell Signalling meetings supported by the Society and for the first time, the meeting will include the JR Vane Medal plenary lecture. The meeting provides a unique opportunity for participants working in the field to network with pharmacologists from the UK and overseas and present their work as oral and poster presentations.

Deadlines to note:

Abstract submission deadline: **Friday 23 February 2018 (11:59pm GMT)**.
Bursary submission deadline: **Friday 23 February 2018 (11:59pm GMT)**.
Early-bird registration deadline: **Monday 19 March 2018 (11:59pm GMT)**.
For further information please visit **www.bps.ac.uk/cellsignalling2018**.

BRITISH PHARMACOLOGICAL SOCIETY

UPCOMING **BRITISH PHARMACOLOGICAL SOCIETY** MEETINGS IN 2018

7th Focused Meeting on Cell Signalling

16–17 April 2018
Nottingham, UK

Focused Meeting: Pharmacology Futures 2018 – Celebrating 250 years of Pharmacology in Edinburgh

17 May 2018
Edinburgh, UK

Focused Meeting: Current trends in Drug Discovery – Young Scientists and Tomorrow's Medicines

A joint meeting with the Society for Medicines Research (SMR)

7 June 2018
London, UK

President's Lecture

26 June 2018
London, UK

Focused Meeting on Immunopharmacology: challenges, opportunities and research tools

1–2 October 2018
Edinburgh, UK

Pharmacology 2018

18–20 December 2018
London, UK

For more information on attending or presenting at these meetings, please contact **meetings@bps.ac.uk** or visit **www.bps.ac.uk/future-meetings**

BRITISH PHARMACOLOGICAL SOCIETY

RSE The Royal Society of Edinburgh
KNOWLEDGE MADE USEFUL

Submit your abstract and register now:

PHARMACOLOGY FUTURES 2018

Exploring future drug development

17 May 2018, National Museum of Scotland, Edinburgh, UK

Pharmacology Futures 2018 will explore the technologies and skills that will drive drug development over the next 10 to 15 years, with speakers sharing their visions of the future to celebrate 250 years of pharmacology in Edinburgh.

The University of Edinburgh's Cameron Prize for Therapeutics will be awarded during the meeting.

PhD students and early career researchers* are invited to submit a scientific abstract showing how their work contributes to the 'Future of Pharmacology'. The best three from each category will be invited to give an oral presentation. Two winners will be selected, one from each category (PhD students and early careers researchers) to receive certificates and prizes of £250. The authors of all other accepted abstracts will be invited to present a poster.

For more information about attending or presenting please contact **meetings@bps.ac.uk** or visit **www.bps.ac.uk/pharmacologyfutures2018**

Speakers

How do we make the UK a world leader in drug discovery?
Professor Chas Bountra, University of Oxford, UK

Human pluripotent stem cell models for future drug discovery and disease modelling
Professor Christine Mummery, Leiden University Medical Centre, The Netherlands

Minding the gap: Linking preclinical studies to the development of novel therapeutics at the National Institutes of Health
Professor Susan Amara, National Institute of Mental Health, USA

Drugging transcription: Progress and potential for treating human diseases
Dr Rab Prinjha, GlaxoSmithKline, UK

The pharmacology of turning thoughts into local blood flow in the brain
Professor Mark Nelson, University of Vermont, USA

The role of biomarkers in translational pharmacology
Dr James Dear, University of Edinburgh, UK

GPCR allostery: From theory to medicine
Professor Arthur Christopoulos, Monash University, Australia

2017 Cameron Prize for Therapeutics lecture: Building and maintaining a global response to antimicrobial resistance (AMR)
Professor Dame Sally Davies, Department of Health, UK

Early bird registration rate expires: 16 April 2018 **Registration deadline**: 10 May 2018
Abstract submission deadline: 16 March 2018 **Member bursary deadline**: 16 March 2018

Early bird registration fees from £50.
Please visit www.bps.ac.uk/pharmacologyfutures2018 to book your place.

*Early careers researchers: oral communications – for those with up to 7 years' full-time equivalent post-doctoral experience as of May 2018