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PHARMACOLOGY MATTERS

Gender inequity | Leadership and mentoring | Encouraging inclusion in pharmacology

EDITORIAL

In the 10th anniversary of *Pharmacology Matters*, I am proud to deliver our 30th edition of the magazine on behalf of the Editorial Board as we celebrate 250 years of pharmacology.

To kick-off our edition, Jono places the focus well and truly on the long-term visions of the Society on leadership in pharmacology with emphasis on the many ways the Society continue to invest and support future leaders through initiatives aimed at enhancing leadership opportunities, education and skills development. One successful initiative, introduced by the Society in 2015, has been the Ambassadors scheme. We catch up with one Ambassador, Dr Yvonne Dempsie, who used funding from this scheme to start up the Glasgow Pharmacological Society (GPS), which continues to grow in strength with a highly motivated early career membership (pages 4 and 5). Further information on the future plans for the Ambassadors Scheme is provided by the Society's Engagement Manager, Teesha Bhuruth (pages 28 and 29).

In other initiatives, the Society's curriculum development team highlight the launch of a new curriculum (with partner organisations) to support skills development in the use of animals in biomedical research (pages 9 and 10). This will be welcome news for our early career pharmacologists who will benefit from gaining all-important *in vivo* research skills and awareness of appropriate experimental design. The current challenges in this area in the context of drug discovery are covered by our long-standing *Pharmacology Matters* editor, Dr Mike Curtis (pages 23 and 24).

Leadership within the Society is further demonstrated through our Affinity Groups. This time, we hear from members of our 'Drug Discovery, Development and Evaluation' group as David and Sarah cover issues with opioid dependency and emerging targets, whilst our Molecular and Cellular Pharmacology group provide updates on the contributions they have made over the past year to pharmacology meetings world-wide (pages 11-14). Other initiatives supported by the Society include the AllTrials Campaign (pages 25-27) and movements towards improving Equality, Diversity and Inclusion (EDI, page 30).

Gender inequality in STEM subjects continues to be a major concern, and as Dr Karen Gregory (pages 31-34) illustrates, the field of pharmacology has room to improve in this area. Earlier this year I was fortunate to be selected to become part of the Ingenious & Enterprising Women Programme (supported by the Scottish Funding Council) and as a result I have gained tremendously from the experience and the supportive network that has since formed. Here, we showcase other opportunities that exist in the form of world-wide leadership (pages 35-37) and UK mentoring schemes (pages 38 and 39) for early career female scientists, in the hope that we can inspire our young members to seek out similar opportunities to support their career development.

I hope you enjoy the latest edition of *Pharmacology Matters*.

Margaret

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YOUR SOCIETY

JONO BRÜÜN
Chief Executive

> "our new curriculum challenges educators to place greater focus on experimental design, data interpretation, ethics and animal welfare"

In my last article for PM I shared a few thoughts about our new five-year strategy. As you would expect from me as Chief Executive, our long-term goals are never far from my mind, so I want to return to the subject here to consider how we have begun to take that plan forward.

All about leadership

In the new strategy, Council wanted to commit the Society to demonstrating leadership. The language of the strategy is peppered with talk of being proactive, "setting the agenda", "being the leader". So it has been great to see that being taken forward in some of the recent work that the Society has delivered.

For example, last month we launched – with support from some 30 organisations across the life sciences – a new curriculum for the use of research animals. The UK is already a world leader in the appropriate and ethical use of animals in research. But as well as being designed to build on that strength, our new curriculum challenges educators to place greater focus on experimental design, data interpretation, ethics and animal welfare. We wanted to build a cross-sector coalition to create a highly skilled and well informed next generation of researchers, and I'm delighted to see that we have been able to take the first steps towards that. Please do take a look at the curriculum itself, and the article explaining the thinking behind it on pages 9 and 10 of this edition.

Another example of how our stated aim to "set the agenda in education and skills" is coming to life is the ongoing development of the education and assessment offer from BPS Assessment Ltd (BPSA). BPSA has recently gone live with a new website – www.bpsassessment.com – which showcases the new and developing prescribing eLearning and assessment capabilities available through its Prescribing Skills Assessment. The purpose of BPSA is to drive improvements in medication safety worldwide through safer prescribing and a knowledge of clinical pharmacology and therapeutics. We hope that the example we have set by delivering the Prescribing Safety Assessment in partnership in the UK will be helpful to medical educators and healthcare systems in other countries. The project is a great example of the Society contributing to a hugely important issue on a global stage.

Young members setting the agenda

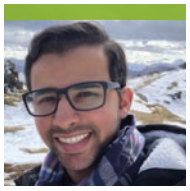
Where the strategy talks about "support[ing] the next generation of learners" and "support[ing] pharmacology educators in their personal and professional development", it's important to be clear that this is about far more than the Society doing things for our members. It is also about members taking an opportunity or a platform that we give them and making it their own.

That is why I was so impressed by the timely and articulate blog we posted in June by two of our younger members about their fears for a looming mental health crisis among PhD students and early career researchers. Aidan Seeley, our Young Pharmacologist Trustee on Council, and Niamh McKerr from the Young Pharmacologists Advisory Group, not only drew attention to this very important problem; they made it real by sharing their own experiences. And they appealed to their fellow members, whatever their age or career stage, to help us as a community of members to start a conversation about what can be done to improve the environment for students.

Coincidentally, we are now in the middle of the application period to elect an Early Career Trustee position on Council, which will be vacated by Aidan Seeley at the end of the year. Full details of the role and selection process are available on the website.

If you are eligible, and if you share the Society's appetite for leadership, I hope you choose to apply.

UPDATES FROM: Glasgow Pharmacological Society



ABDULLAH ALZAHRANI

Abdullah Alzahrani gained his Master of Pharmacy (MPharm) from Liverpool John Moores University and then moved to the University of Birmingham and obtained his MSc in Toxicology. Abdullah is now a PhD student at Strathclyde Institute of Pharmacy and Biomedical Sciences (SIPBS) funded by the Saudi Arabian government. Abdullah's current research is focusing on finding new anti-diabetic and anti-obesity drugs from natural sources such as plants.

CHARLES KENNEDY

Charles obtained a B.Sc. (Honours) in Pharmacology from Aberdeen University, and then a PhD from University College London, where he worked with Professor Geoffrey Burnstock, on the division of P2 receptors into the P2X and P2Y subtypes. Following a postdoctoral position at Michigan State University, he was a Beit Research Memorial Fellow at Cambridge University, working with Graeme Henderson, before joining Strathclyde University, where he is a Reader.

His research focuses on the pharmacological properties and physiological and pathophysiological functions of P2X and P2Y receptors, with particular reference at present to the pulmonary circulation and to P2Y heteromultimer formation.

Charles is a past editor of the *British Journal of Pharmacology*, chairs the IUPHAR P2X receptor nomenclature sub-committee and sits on the P2Y receptor sub-committee.

The GPS group and some early career members with Professor Steve Hill.

We were delighted to be part of the team which formed the Glasgow Pharmacological Society (GPS) in 2016, with funding from the British Pharmacological Society's Ambassadors scheme. The idea behind the GPS was to bring together students and staff with an interest in pharmacology from Glasgow Caledonian University (GCU), the University of Glasgow (UoG), and the University of Strathclyde (UoS). We hoped to showcase pharmacology and inspire current and future scientists.

We have been lucky to attract some of the biggest names in pharmacology to speak at our annual events. We were absolutely delighted that Professor Humphrey Rang agreed to speak at our first event in June 2016, as Professor Rang is a co-author of the famous textbook that every undergraduate pharmacologist relies upon during their degree! Professor Rang's impressive career, expertise and eminence in the field attracted many undergraduates, postgraduates and academic staff to fully pack the lecture theatre at GCU. Lively Q&A and networking sessions followed, and students had the opportunity to meet Professor Rang and have their textbooks signed.

In March of 2017, we were thrilled and honoured to host the current President of the British Pharmacological Society, Professor Stephen Hill. His talk, which took place at the UoG, focused on his research on ligand binding to cell surface receptors using fluorescent ligands and bioluminescence energy transfer. The students enjoyed the talk and took full advantage of the following networking session, to speak to

Professor Hill and other academic staff and ask for advice about their future careers. This was a fantastic opportunity to learn about the research that takes place in other highly regarded institutions in the UK. We also got a 'feel' for how pharmacology is progressing due to the arrival of high-resolution techniques like bioluminescence resonance energy transfer (BRET), which can detect receptor-ligand interactions.

We welcomed Professor David Nutt of Imperial College London to speak at our 3rd annual event at UoS in March this year. Professor Nutt drew a large audience of over 200 attendees for his talk entitled *'Why Pharmacologists Should Also Be Revolutionaries'*. Speaking to a captivated audience, he began by describing how scientists have revolutionised our understanding of our world and continue to do so. He then explained how in the 1950s and 1960s, psychedelic drugs, such as lysergic acid diethylamide (LSD) and psilocybin (the active ingredient in 'magic mushrooms'), were legal, obtainable and used to treat a wide array of mood disorders including anxiety, alcoholism, schizophrenia and depression. Social factors led to these drugs being made illegal and thus, barriers were introduced that severely impeded further research. Professor Nutt presented his own recent data from 12 patients with 'resistant' depression, who had been given a single dose of psilocybin. Half went into remission for several months, demonstrating the untapped therapeutic potential of this 'illegal' drug[1]. The lecture was followed by a lively Q&A session and then, filled with revolutionary zeal, the audience stormed the departmental social area, where the discussion continued over drinks and snacks. Vive la révolution.

The GPS also had the fantastic opportunity of hosting the Bill Bowman Prize Lectureship in February 2018. Dr Aisah Aubdool spoke about *'Calcitonin Gene-Related Peptide: A Neuropeptide of Many Talents in the Cardiovascular System'*. Almost 200 people were present in the lecture to learn about Dr Aubdool and the impressive work she conducted in Professor Susan Brain's laboratory, which is cutting-edge in the field of cardiovascular pharmacology. As with all other GPS talks, this lecture was followed by drinks and a networking session. A comment by a postgraduate student in the GPS Facebook page epitomised what we are trying to achieve with these events: 'Incredible lecture. I went there with a very superficial interest, but I came out with a hunger for more'.

> "Incredible lecture. I went there with a very superficial interest, but I came out with a hunger for more"

What does the future look like for the GPS?

We are very proud that following the successes of our events so far, the British Pharmacological Society has asked us to host the Bill Bowman Prize Lectureship for a second time in 2019. We are looking forward to hosting the event and inspiring the next batch of pharmacology undergraduates! As a Society, we aim to expand our event repertoire beyond inviting speakers, to include events such as poster presentations and debates. We also promote the work of British Pharmacological Society at large. The GPS logo, designed by a member of the Society is inspired by the British Pharmacological Society's logo, pointing to the link with the 'mother' Society – we are one of its hexagons. The future is looking bright and exciting for the GPS! If you would like to find out more, please follow us on Facebook (Glasgow Pharmacological Society) or Twitter @glasgowpharmsoc.

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ACKNOWLEDGEMENTS

Eleanna Kritikaki, Abdullah Alzaharani, Charles Kennedy and Yvonne Dempsie on behalf of the GPS.

ELEANNA KRITIKAKI

Eleanna completed her BSc (Hons) Pharmacology at Glasgow Caledonian University and is currently studying towards an MRes in Biomedical Science at the University of Glasgow. She is due to start a PhD in Neuroscience in the University of Sussex in September. Eleanna was one of the founding members of the Glasgow Pharmacological Society. She is an active member of the British Pharmacological Society and has contributed to the 'How do Drugs Work?' YouTube video series.

YVONNE DEMPSIE

Yvonne graduated from the University of Glasgow with a BSc (Hons) Pharmacology before gaining her PhD from the University of Nottingham. Yvonne then moved back to Glasgow to work as post-doctoral researcher in the lab of Professor Mandy MacLean before taking up a lectureship at Glasgow Caledonian University. Yvonne's research focuses on finding novel therapeutic targets for the treatment of pulmonary arterial hypertension.

Yvonne is the British Pharmacological Society's Ambassador for the Glasgow area and started the Glasgow Pharmacological Society with funding from the Ambassadors scheme.

THE 1618 *PHARMACOPOEIA LONDINENSIS*

JEFF ARONSON

Jeff Aronson is a Consultant Physician and Clinical Pharmacologist in the Centre for Evidence Based Medicine in Oxford's Nuffield Department of Primary Care Health Sciences. He is a President Emeritus of the British Pharmacological Society and currently Vice President Publications. He was Editor-in-Chief of the *British Journal of Clinical Pharmacology* 2002–2007, Editor of Meyler's Side Effects of Drugs – The International Encyclopedia of Adverse Drug Reactions and Interactions, 16th edition (seven volumes and online, 2015), and co-editor with John Talbot of Stephens' Detection and Evaluation of Adverse Drug Reactions: Principles and Practice, 6th edition (2011). He is an Associate Editor of BMJ Evidence Based Medicine. His weekly blog on medical words appears at blogs.bmj.com/bmj/category/jeff-aronsons-words.

This year we celebrate the 400th anniversary of the publication of the first edition of the *Pharmacopoeia Londinensis* in 1618 (Figure 1).

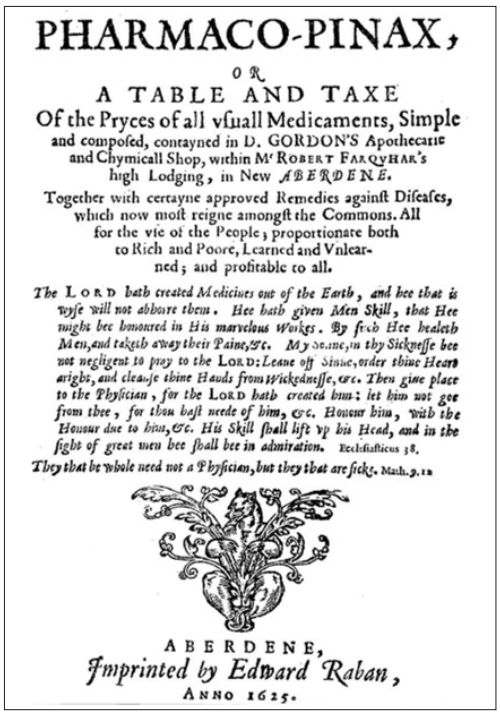
Figure 1. The title page of the Pharmacopoeia Londinensis

Early pharmacopoeias

The earliest English word for a medical treatise that described drug treatments was the Anglo-Saxon "laeceboc", or leechbook[1]. The best known, Bald's *Laeceboc*, was probably compiled in the early tenth century, soon after the death of King Alfred. Terms such as "dispensatory" and "receipt-book" were also in currency from the 16th and 17th centuries. The word "pharmacopoeia" comes from the Greek word φαρμακοποιία (pharmacopoiia), literally "drug-making", which was found in the post-classical (Hellenistic) dialect called Koinē (ἡ κοινὴ διάλεκτος). Instances in mediaeval Latin include the titles of books such as *Pharmacopoeia seu de medicamentorum simplicium delectu: praeparationibus, mistionis modo* by Jacques Dubois (Basel, 1552), *Pharmacopoeia, medicamentorum omnium, quae hodie ad publica medentium munia in officinis extant* by Anutius Foesius (Basel, 1561), *Augstburgensis Pharmacopoeiis* (Augsburg, 1564), and *Dispensatorium usuale pro Pharmacopoeis inclytae Reipublicae Coloniensis* (Cologne, 1565). Texts that were pharmacopoeias, but called by other names, were also published in Florence (*Antidotarium Florentinum*, 1498), Barcelona (*Concordia Pharmacolorum Barcelonensium*, 1535), Nuremberg (*Dispensatorium Valerii Cordis*, 1546), and Saragosa (*Concordia Aromatorium Cesaraugustae Saragosa*, 1546), as well as Mantua (1559), Bologna (1574), Bergamo (1580), and Rome (1583). All of these served individual municipalities or city states; the *Pharmacopoeia Londinensis* was the first to serve a whole country.

Two mediaeval medical treatises, the *Old English Herbarium* and *Medicina de Quadrupedibus*, translations of Latin texts, have been described as together forming "the common pharmacopoeia of the early Middle Ages". However, the first recorded use of the word "pharmacopoeia" in English is, coincidentally, also from 1618—a reference to a "Pharmacopaea" by Querketanus in a translation by Thomas Bretnor of a Latin text by Angelus Sala Vincentinus Venitus (1576–1637) called *Opiologia: or, A treatise concerning the nature, properties, true preparation and safe use and administration of opium. For the comfort and ease of all such persons as are inwardly afflicted with any extreame grief, or languishing pain, especially such as deprive the body of all natural rest, and can be cured by no other means or medicine whatsoever.*

An alternative word for a pharmacopoeia was "pharmacopinax". "Pinax" the Greek word for a writing-tablet, appears in several Latin titles, such as *Pinax iconicus antiquorum ac variorum in sepulturis rituum* by Lilius Gregorius Giraldus (Lyon, 1556), *Pinax theatri botanici* by Caspar Bauhin (Basel, 1623), and *Pinax rerum naturalium Britannicarum*, by Christopher Merrett (London, 1666). It also appears in the Latin titles of later formularies issued by the College, such as *Pharmacopoeiæ Collegii Regalis Londini. Remedia Omnia Succinctè descripta: Unà cum Catalogo Simplicium Ordine Alphabetico digestorum: Quibus annexum est Manuale ad Forum: Nec-non Pinax Posographicus* (1689), in which it referred to a table of dosages. However, the only English pharmacological instance of which I am aware is *Pharmaco-Pinax, or a Table and Taxe of the Pryces of all vsuall Medicaments, Simple and composed, contayned in D. Gordon's Apothecarie and Chymicall Shop*, published in Aberdeen in 1625 (Figure 2).



PHARMACO-PINAX,

OR

A TABLE AND TAXE

Of the Pryces of all vſuall Medicaments, Simple and compoſed, contayned in D. GORDON'S Apothecarie and Chymicall Shop, within Mr ROBERT FARQVHAR's high Lodging, in New ABERDENE.

Together with certayne approved Remedies againſt Diſeaſes, which now moſt reigne amongſt the Commons. All for the vſe of the People; proportionate both to Rich and Poore, Learned and Vnlearned; and profitable to all.

The LORD hath created Medicines out of the Earth, and hee that is wyſe will not abhorre them. Hee hath given Men Skill, that Hee might bee honoured in His marvelous Workes. By ſuch Hee healeth Men, and taketh away their Paine, &c. My ſonne, in thy Sickneſſe bee not negligent to pray to the LORD: Leane off Sinne, order thine Heart aright, and cleanſe thine Hands from Wickedneſſe, &c. Then give place to the Phyſician, for the LORD hath created him: let him not goe from thee, for thou haſt neede of him, &c. Honour him, with the Honour due to him, &c. His Skill ſhall lift vp his Head, and in the ſight of great men hee ſhall bee in admiration. Eccleſiaſticus 38.

They that be whole need not a Phyſician, but they that are ſicke. Matth. 9. 12

ABERDENE,
Imprinted by Edward Raban,
ANNO 1625.

Figure 2. The title page of the Aberdeen Pharmacopinax of 1625

The *Pharmacopoeia Londinensis*

The story of the 1618 *Pharmacopoeia Londinensis* starts with another anniversary, the foundation in 1518 of the College of Physicians, as it then was, by Henry VIII. Although the College was given a Royal Charter, formalized by an Act of Parliament in 1523, it was not originally known as the Royal College of Physicians, as it is today. The College received a new charter from Charles II in 1663, which referred to "the King's College of Physitians in the Cittie of London", and in 1674 Daniel Whistler referred to himself as "Registrar of the Royal College of Physicians"[2]. However, the name was not legally confirmed until promulgation of the 1960 Royal College of Physicians of London Act.

When the College was founded, medicines could be prescribed by apothecaries as well as physicians. Indeed, later, in 1543, "An Act That Persons Being No Common Surgeons May Minister Outward Medicines" stated that "every person being the King's subject, having knowledge and experience of the nature of herbs, roots and waters, [may] use and minister [them], according to their cunning, experience and knowledge." Apothecaries originally purveyed non-perishable commodities—spices, drugs, comfits, preserves, and the like. They were members of the Guild of Grocers, classed with pepperers and spicers, but they gradually focussed on medicines, and by about the middle of the 14th century they were practitioners who prepared and sold drugs for medicinal purposes. However, in 1540 Henry VIII promulgated The Pharmacy Wares, Drugs, and Stuffs Act, empowering the physicians to inspect apothecaries' wares and destroy them if defective.

Although the apothecaries were keen to be recognized as independent practitioners, their requests were refused until 1617, when The Worshipful Society of the Art and Mistery of Apothecaries was founded under James I. The title of the Society implied, no doubt, that a little hocus-pocus did not go amiss when your remedies had little or no efficacy.

The College of Physicians had first discussed the possibility of publishing a pharmacopoeia ("una aliqua, certa, publica, ac uniformi Pharmacopoeia ...", as the College Annals put it) in 1585, intending it to be adopted by all apothecaries, but the task was considered too burdensome ("Sed quoniam res videbatur operosa ...")[3]. However, the idea was revived in 1589 when it was "proposed, considered, and resolved that one definitive public and uniform dispensatory or formulary of medical prescriptions, obligatory for apothecaries' shops, should be prepared." Preparation of the *Pharmacopoeia* began, but its gestation was slow and indeed ceased after 1594, until it was revived in June 1614.

The foundation of the Society of Apothecaries in December 1617 had been supported by two Fellows of the Royal College of Physicians, Dr Henry Atkins and Sir Théodore Turquet de Mayerne, both of whom had been working on the College's pharmacopoeia. Since the pharmacopoeia had always been intended to be used by all apothecaries, this concentrated

> "Every person being the King's subject, may use and minister herbs, roots, and waters, according to their cunning, experience, and knowledge"

> "follow this Pharmacopoeia upon paine of our high displeasure"

the physicians' efforts and led to the publication of the *Pharmacopoeia Londinensis* in Latin on 7 May 1781. Its publication was preceded by a royal proclamation that "all Apothecaries of this Realme [should] follow this Pharmacopoeia ... upon paine of our high displeasure".

However, the first edition was botched at the printers' shop. The College withdrew it and issued a revised version, which they designated the first edition, on 7 December 1618, claiming in an epilogue that the printer of the earlier version had "snatched away from our hands this little work not yet finished off, without consulting the President [of the College, Sir William Paddy] ... who ... was out of town"[4]. Which is why the *Pharmacopoeia Londinensis* had two first editions.

The groups of simples, medicines composed of a single ingredient, 1190 items in the second version compared with 680 in the first, as listed in the first index of the Pharmacopoeia, are shown in Table 1. They are discussed in detail by Brockbank[3]. The second index listed the types of formulations available, with 20 main headings, including vina medicata (medicated wines), decocta (decoctions, extracts made by boiling in water), sirupi (syrups), electuaria alterantia corroborantia sine opio (electuaries, medicines mixed with honey, preserves, or syrups, prepared without opium), pilulae purgantes leniores sine scammonio aut colocynthide &c (mild purgative pills), olea simplicia (simple oils), unguenta simpliciora (ointments), and emplastra et cerata (emplastra, sticky pastes, usually applied to the skin on linen or leather, and waxed plasters, ointments, or liniments).

The *British Pharmacopoeia*

The *Pharmacopoeia Londinensis* was not widely used when it first appeared, and many physicians kept their own personal formularies. However, further editions continued to appear, laying the foundations for other national pharmacopoeias. The *Edinburgh Pharmacopoeia* first appeared in 1699, the *Dublin Pharmacopoeia* in 1807, and the last edition of the *London Pharmacopoeia*, the 11th, in 1851. By then the need for harmonization had become clear, particularly since the Poor Law Amendment Act of 1834, with the institution of infirmaries and dispensaries, had resulted in increasing demands for medicines. The *British Pharmacopoeia* (*Pharmacopoeia Britannica*), recommended and announced in the Medical Acts of 1858 and 1862 respectively, appeared in 1864 and is still in use today.

Table 1. The main headings in the list of simples in the first index of the 1618 *Pharmacopoeia Londinensis*, with English translations; the heading in the first line is from the May version, the heading in the second from the December version

Catalogus simplicium quae ad pharmacopoeae huius compositiones requiruntur	Catalogue of simples required for preparing the formulations in this pharmacopoeia
Catalogus simplicium quae ad pharmacopoeam conducentium	**Catalogue of simples suitable for a pharmacopoeia**
Radices	Roots
Cortices	Barks
Ligna	Woods
Folia	Leaves
Flores	Flowers
Fructus et germina	Fruits and buds
Semina sive grana	Seeds or grains
Lachrimae	Tears
Succi	Juices
Plantarum excrementa	Plant extracts
Animalia	Animals
Animalium partes, excrementa & opera	Animal parts, extracts, and tissues
Marina	Things from the sea
Sales	Salts
Metallica	Metals

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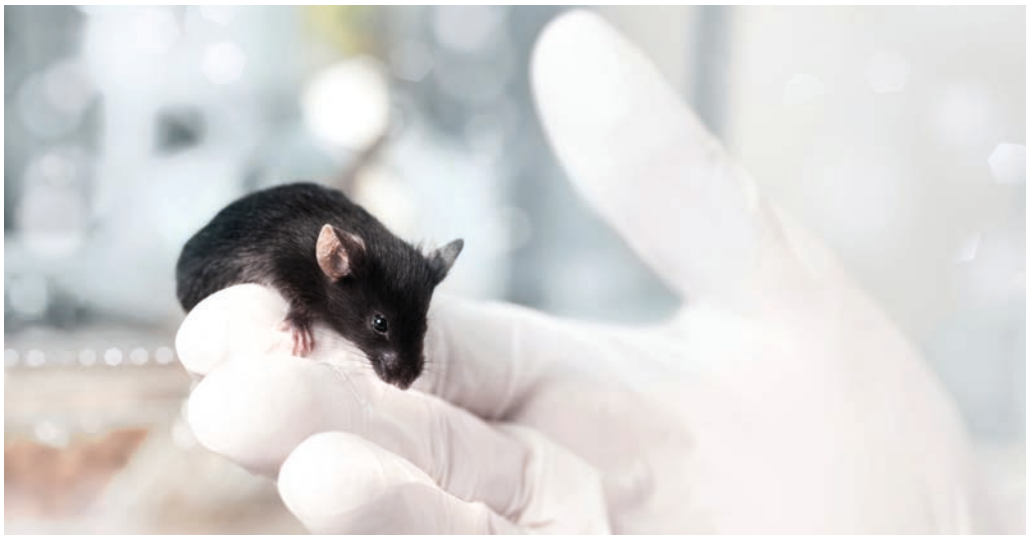
USING ANIMALS IN BIOMEDICAL RESEARCH: WHY EDUCATION HOLDS THE KEY

This article was first published by Times Higher Education on 13 June 2018



Animal (or *in vivo*) experiments play an important role in biomedical research. They are essential to support the development of innovative medicines which can ultimately improve human and animal health.

But for these studies to be scientifically valid, laboratory animals must be used appropriately by researchers. Similarly, researchers must be able to meaningfully interpret and critique published data, discriminating between well-designed and flawed *in vivo* experiments. Improving this knowledge base within the biomedical workforce improves reproducibility of research which in turn supports biomedical innovation.

Building this broad skillset requires extensive specialist training. To support this, the British Pharmacological Society and partner organisations have just launched a new curriculum for undergraduate and taught Masters education on the use of research animals.

A new curriculum for the use of research animals

The new curriculum is the culmination of a year-long collaboration between academics, industry scientists and animal welfare experts. It has been designed to:

1. help students understand when research requires the use of animals, and when it doesn't
2. provide education in the skills needed to interpret and critique reported data obtained from research animals
3. share good practice on how to design animal experiments and to integrate animal welfare as part of that process
4. foster openness about the use of research animals

MIKE COLLIS

Mike Collis (FPS) is a member of the Society's' Animal Welfare & *In Vivo* Pharmacology Sub-Committee. After post-doctoral research in Antwerp with Paul Vanhoutte and at the Mayo clinic with John Shepherd, Mike joined ICI pharmaceuticals studying hypertension. He moved to Pfizer in 1991 as Manager of Cardiovascular Research and subsequently established a new therapeutic team working on tissue repair. With the closure of Pfizer in Sandwich, he was appointed as Chief Executive of The Physiological Society. Mike established and chaired the Society's Integrative Pharmacology Fund (2004-2015) and continues to take a keen interest in the training of scientists who perform *in vivo* research.

DAVE LEWIS

Dave Lewis is a Senior Lecturer in Pharmacology and Scientific Ethics at the University of Leeds, and currently a Project Leader at the Leeds Institute of Teaching Excellence. His research interests were the physiological and pharmacological characterisation of the Central pathways underlying the regulation of the cardio-respiratory and gastrointestinal systems. More recently, Dave has focused on educational research; undergraduate Capstone research experiences and the creation and delivery of education, training and CPD in research animal sciences, nationally and internationally. He Chairs the British Pharmacological Society's Animal Welfare & *In Vivo* Pharmacology Sub-Committee and IUPHAR's Integrative and Organ Systems Pharmacology initiative.

MANASI NANDI

Manasi Nandi is a Senior Lecturer in Integrative Pharmacology, King's College London. Her research focuses on cardiovascular regulation in disorders including pulmonary hypertension and septic shock. She has extensive experience of preclinical animal models - coupling pharmacologically and genetically modified systems to characterise novel therapeutic targets. More recently, her focus has been in data sciences to identify earlier biomarkers for sepsis. Her teaching activities include post-graduate education around the use of animals in research (providing both theoretical and practical training). Her undergraduate teaching focuses on the drug discovery and development pathway. She incorporates blended learning approaches, coupling lectures with e-learning resources and active learning workshops. She received the Society's Rang prize for excellence in teaching in 2015.

ANNA ZECHARIA

Anna is the British Pharmacological Society's Director of Policy & Research. Anna was awarded a BSc in Pharmacology from Guy's, King's and St Thomas' School of Biomedical Science, with time spent at Pfizer (UK) and Cel-Sci (USA). She went on to complete her PhD and postdoctoral training in cellular and *in vivo* neuroscience at Imperial College London where she used genetic mouse models to study how natural sleep pathways interact with sedatives and general anaesthetics. She co-founded ScienceGrrl in 2012, a Not for Profit organisation supporting and showcasing women and girls in science - leading on organisational strategy, policy work and social media.

The curriculum focuses on knowledge and understanding, experimental design and how to interpret the data. It highlights issues around ethics, animal welfare, regulation and the 3Rs, and invites students to consider wider social attitudes towards this type of research. It does not require all students to have hands-on contact with animals, as observation or video simulations may be enough to convey the intended learning outcomes. For those students who do want practical exposure to research animals, the curriculum advises educators on a range of appropriate techniques to achieve the desired learning outcomes.

Rebuilding the animal research skills base

In addition to supporting the knowledge and skills of the next generation, in the long term we hope that this new curriculum will help maintain UK strengths in the life sciences and drive innovation. Today, the UK is a world leader in the appropriate and ethical use of animals in research and is committed to maintaining the highest standards in education and training for *in vivo* researchers. But this strong position was only achieved thanks to the efforts of educators and funders. Following reports of an acute skills shortage among UK researchers they worked together to rebuild the animal research skills base.

Public-private partnerships are essential to this process. Indeed from 2004 to 2015 the government- and industry-backed Integrative Pharmacology Fund (IPF) successfully helped to increase the capacity and quality of *in vivo* education, training and research in higher education. It also helped to foster improvements in animal welfare, research outcomes, and the 3Rs.

As a result, a lack of technical *in vivo* skills is no longer a clear and present danger – but we cannot be complacent. Indications are that many skilled scientists are due to retire in the next ten years. Furthermore, the UK's ability to continue to easily recruit from the European Union is uncertain. Therefore, the new curriculum is designed to help educators maintain the UK's hard-earned, world-leading position.

> "Delivery of the curriculum will be simple for some institutions and more challenging for others"

Cross-sector support is crucial

Delivery of the curriculum will be simple for some institutions and more challenging for others. We recognise that resources can be limited and that not every educator has direct experience of working with research animals.

Therefore the British Pharmacological Society and The Physiological Society are pleased to announce a joint funding commitment to supporting implementation of the curriculum. We will work closely with educators to understand how this funding could achieve the greatest impact for students. The fund will be used to support the development of complementary online resources aimed to help students engage with the curriculum. It will also be used to fund educators' professional development. We especially want to support those who may be less experienced in teaching these – often challenging – topics.

This new curriculum for animal research is the first to be supported and endorsed by a significant number of organisations. These include research organisations, national and international learned societies (including the Royal Society of Biology), UK universities, the NC3Rs, and industry (including the Association of the British Pharmaceutical Industry). Its wide adoption should help students to understand the appropriate use of animals in research; interpret and critique data acquired from them; improve the quality, reproducibility and welfare of such studies; and lay the foundations for a highly skilled and well informed next generation of researchers.

To express interest in the implementation fund contact education@bps.ac.uk

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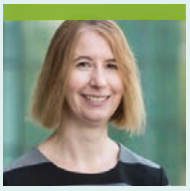
Dr Michael Collis, Dr Dave Lewis, Dr Manasi Nandi and Dr Anna Zecharia are members of the British Pharmacological Society's curriculum development team.

DAVID KENDALL

David Kendall is the Chief Scientific Officer of PharmNovo AB/UK, a small drug discovery company focused on the development of chronic pain medicines. He is Professor Emeritus of Pharmacology at the University of Nottingham and Visiting Professor at Liverpool John Moores University School of Pharmacy and Biomolecular Sciences.



SARAH NICKOLLS

Sarah Nickolls is a group leader in the Screening Profiling and Mechanistic Biology department at GlaxoSmithKline. She has a strong background in drug discovery having previously worked at Pfizer and Neurocrine Biosciences and has both clinical and preclinical experience. Her PhD on GPCR agonist bias was supervised by Professor Philip Strange.

DRUG DISCOVERY, DEVELOPMENT & EVALUATION

THE OPIOID EPIDEMIC: NEW APPROACHES TO AN OLD PROBLEM

Opioid analgesics have been a mainstay of pain treatment for centuries but over the past few decades, their overuse for both medical and non-medical reasons has led to what has been described in the popular press as a worldwide opioid epidemic, and by the USA Department of Health and Human Services as a public health emergency. The USA statistics are staggering; since 1999, the amount of prescription opioids sold to pharmacies, hospitals and doctor's offices has quadrupled with no overall change in the amount of pain that American patients reported. Deaths from overdoses of prescription opioids such as oxycodone, hydrocodone and morphine have also quadrupled since 1999, with over 42,000 fatalities in 2016 alone[1]. Opioid dependency is an important associated social and medical problem with 2.1 million people in the USA reporting an opioid use disorder in the same year.

Opioids are clearly efficacious and appropriately prescribed for acute pain but their use in chronic non-cancer pain is controversial with recent meta-analyses concluding that opioids alone are ineffective[2]. NICE guidance for chronic pain states such as neuropathic pain indicates that opioids should not be used unless patients are individually advised by a pain specialist[3]. The provision by the NHS of universally accessible pain management services with non-opioid strategies perhaps explains, in part, why opioid over-prescribing in the UK is not at the level of that in the USA.

The commonly used opioid analgesics are poorly selective agonists of all three opioid receptors (μ, κ and δ)[4] although, morphine, for example, is about 50 fold more potent at μ vs δ receptors[5]. The well-known unwanted effects of morphine-like agonists including constipation, nausea, itching and potentially fatal respiratory depression are largely μ receptor-mediated as is the tendency to induce analgesic tolerance and physical/psychological dependence[6,7]. Thus, maintaining a clinical balance between effective analgesia and adverse side effects with conventional opioids is extremely difficult.

One developmental approach for the opioid analgesic family is to design drugs that are selective for the κ and δ receptors and, indeed, there is excellent preclinical evidence that δ receptor agonists are effective analgesics in chronic pain states, although their effects on acute pain are limited[8]. Early δ-selective compounds such as SNC80 were reported to be proconvulsant and this limited pharma companies' enthusiasm for this approach. However, this property has since been found to be structurally dependent and not a universal class feature and newer agents such as JNJ-20788560, TAN-67 and KNT-127 are free from proconvulsant activity and are also devoid of the adverse μ receptor-mediated side effects[9]. There is also evidence of δ-mediated anxiolytic and antidepressant activity which would be beneficial to patients suffering from chronic pain[10]. κ-receptor agonists are also analgesic in preclinical models but compounds that enter the brain cause hallucination, dysphoric effects and aversion. However, the development of peripherally restricted agonists is a realistic research focus[11]. At the present time, although they have considerable potential, very few clinical studies of κ or δ agonists have been conducted and none are currently marketed.

Perhaps an ideal situation would be to have opioids that retain the very effective analgesic properties of μ receptor agonists without their adverse effects. Recently, efforts have been made to achieve this by taking advantage of the potential for biased agonist signalling.

Agonists for the μ receptor can activate Gi/Go protein signalling and also arrestin-associated transduction pathways. Based largely on knockout studies, it is thought that G protein biased signalling is crucial for analgesia whilst arrestin-3 (β-arrestin 2) recruitment is related to unwanted side effects[13]. Based on this hypothesis, Trevena

UPDATES FROM OUR AFFINITY GROUPS

Inc developed oliceridine (TRV130), a μ receptor agonist reported to be selective for G protein over arrestin signalling and this has been shown to be as effective as morphine with fewer opioid-like side effects in patients with moderate to severe pain following abdominoplasty[14]. Manglik *et al*.[15] reported the development of another G protein-biased μ receptor agonist, PZM21, which they reported to be as effective an analgesic as morphine but devoid of respiratory depression and Schmid *et al*. have recently described some other G protein-biased μ receptor agonists that induce less respiratory depression than morphine at equi-antinociceptive doses[16]. However, Hill *et al*.[17] have carefully re-examined the properties of PZM21 and reported that it is a partial agonist for both G protein activation and arrestin recruitment, induces respiratory depression and rapid tolerance to analgesia, but not respiratory depression, similar to equi-antinociceptive doses of morphine. The reasons for the disparity between the studies of Manglik and Hill are unclear but the potential for exploitation of signalling bias to optimise agonist function is clearly worth further development.

Given the problems associated with existing opioid analgesic therapy it is perhaps attractive to consider completely different drug development targets. For example, considerable attention is being paid to the potential of ligands interacting with the NaV1.7 ion channels that are key players in controlling activity in pain pathways[18]. Various strategies for inhibiting Nerve Growth Factor (NGF), particularly with regard to osteoarthritis pain, are also being pursued[19], although there are some concerns about the long-term safety of anti-NGF antibodies. Whatever new targets emerge, the centuries' long dependence on opioid analgesic drugs is unlikely to diminish significantly in the near future and clinicians and drug discoverers must continue to focus on safe and effective alternatives.

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UPDATES FROM OUR AFFINITY GROUPS

STEVE SAFRANY

Steve Safrany is an Associate Professor of Pharmacology at RCSI-Bahrain. His research interests include inositol phosphates and lipids, and sigma receptors. Prior appointments include Universities of Wolverhampton, Bath, Dundee and Leicester plus a five-year stint at the National Institute of Environmental Health Sciences. Steve studied at Loughborough University (BSc(Hons)DIS) and Leicester University Medical School (PhD).

GARY STEPHENS

Gary Stephens is an *in vitro* electrophysiologist with an interest in modulation of ion channels and receptors and their role in presynaptic function, with a focus on models of disease, namely ataxia, pain and epilepsy. For the latter, he is interested in mechanisms of action of plant derived cannabinoids.

MOLECULAR & CELLULAR PHARMACOLOGY

The Molecular & Cellular Pharmacology Affinity Group supported three symposia at *Pharmacology 2017* which, respectively, focused on rational drug design through fragment-based drug discovery, drug targets in membrane trafficking, and pharmacologically targeting protein-protein interactions.

Alongside this contribution to the main meeting, the group also had input into a very successful 8th European Workshop on Cannabinoid Research at the University of Roehampton on 31 August–2 September 2017. We, alongside other Affinity Groups, also supported the recent 7th Focused Meeting on Cell Signalling at University of Nottingham 16-17 April 2018.

Speakers at the "Small molecule inhibitors of ion channels in chronic pain states" at EPHAR 2016, Istanbul enjoy a post-symposium trip on the Bosphorus. Left to right: Eddy Stevens (Metrion Biosciences), Damian Bell (IONTAS), Nikita Gamper (University of Leeds) and Wendy Imlach (Monash University).

The Molecular & Cellular Pharmacology Affinity Group would like to highlight some areas of interest and expertise within the broader Affinity Group. There has been significant activity to support ion channel pharmacology. This support has included a Society-sponsored symposium "Small molecule inhibitors of ion channels in chronic pain states" at the Federation of European Pharmacological Societies' (EPHAR)'s 2016 meeting in Istanbul, and the recent Society-sponsored symposium "Ca2+ signaling in health and disease" at the World Congress in Basic and Clinical Pharmacology 2018 in Kyoto, Japan. We will also support a symposium "Targeting voltage-gated calcium ion channels in disease" at *Pharmacology 2018*. Activity in this area has also included a Themed Issue "Targeting ion channels to treat chronic pain" which is currently being finalised. The Themed Issue has collated contemporary review articles and original articles by leading experts in the pain field detailing recent pharmacological advances in the pharmaceutical industry and academia. Notable molecular ion channel targets that were highlighted in the Themed Issue include the voltage-gated sodium channel NaV1.7, voltage-gated calcium channels CaV2.2 and CaV3.2, two-pore potassium TREK channels, as well as specific transient receptor potential and acid-sensitive ion channels. The issue highlights that translation of some impressive *in vitro* and *in vivo* data to the human condition via successful clinical trials is the next key challenge.

UPDATES FROM OUR AFFINITY GROUPS

One of our Affinity Group members and PhD student at the University of Glasgow, Sarah Hesse, attended the Cell Signalling meeting. Sarah gives us an account of her experiences from this meeting.

For more than a decade the Cell Signalling meeting has been held in Leicester, but for this year's 7th Focused Meeting on Cell Signalling, the University of Nottingham became the new host. The organising committee, comprising some old and some new members, put together a great programme with talks ranging from GPCR signalling and structures to receptors and their drugability in various disorders. These talks were complemented by many posters showcasing the interesting science different attendees from near and far were working on. Plenty of coffee and lunch breaks as well as the designated poster sessions provided abundant opportunities to grab a drink, have a chat, and learn more about what else goes on in the field. Of course, the conversations were not always strictly about science and even as a newbie to the Cell Signalling meetings I was made to feel very welcome - a feeling that was shared by all attendees. I also very much enjoyed the treasure hunt and raffle, which encouraged conversation with all of the different sponsors of the events resulting in helpful insights and advice on different techniques and assays to assess GPCR signalling. Despite not winning any prizes in the raffle myself, I made many new connections with other scientists, which is most likely a bigger win in the grand scheme of things.

Being the topic of many a joke, I was part of the Glasgow group that braved the 6-hour trip down to Nottingham by bus. As Graeme Milligan jokingly pointed out during his conference dinner speech, this was an attempt to keep up the boundaries between less senior staff on the bus and the principal investigators flying in from Glasgow. However, to me, the 7th Focused Meeting on Cell Signalling was a great example of how the existing boundaries can be broken down one at a time: half of the speakers were female and many early career scientists and PhD students had the opportunity to present their research as part of the oral presentations, to a supportive audience ranging from PhD students, such as myself, to professors who were well-known and established in their fields.

As I am very much still at the beginning of my PhD project, this meeting gave me the opportunity to appreciate the breadth of the GPCR field more as well as to put some faces

Members of the Tobin and Milligan groups from the University of Glasgow.

to names printed on the papers I had been pouring over for the last couple of months. One talk that stood out to me was Dr Madan Babu's talk about pharmacogenomics of GPCR drug targets, which really brought out how much of an effect genetic variation could have on drug responsiveness between individuals and the economic burden associated with this. Going by the data presented, researchers should consider GPCR variants when performing *in vitro* and *in vivo* studies as well as clinical trials.

Finally, I would like to congratulate the organisers of the 7th Focused Meeting on Cell Signalling on hosting a very engaging meeting fostering early-career as well as female researchers in the field, which will be beneficial to ensure high-quality, diverse and collaborative research efforts in the field of cell signalling in the future. If somebody had told me five years ago, that I would be where I am now attending conferences like the Cell Signalling meeting alongside so many bright and exciting people, I would have doubted them. Today, I am curious to see where I, and all of the interesting and smart people that I met, will be in another couple of years. Will we be meeting again at the 12th Cell Signalling Meeting in 10 years' time? All I can say is that I for sure will be back – whether the event is being held in Nottingham or elsewhere.

SARAH HESSE

Sarah graduated with an Integrated MSci (Hon) in Neuroscience from the University of Glasgow in 2017. She then started as a PhD student in Andrew Tobin's and Sophie Bradley's lab in the Institute of Molecular, Cell & Systems Biology at the University of Glasgow. Her project ranges from advanced neuroimaging using CLARITY in combination with confocal and light-sheet microscopy to molecular pharmacology studies.

NITRIC OXIDE: FROM POLLUTANT TO NOBEL PRIZE WINNING DISCOVERY

Despite its presence being known to the scientific community for over two centuries, nitric oxide (NO) is still a relative newcomer to pharmacology. Identified in 1772 by Joseph Priestly, for the next two hundred years it was solely considered to be an atmospheric pollutant. It wasn't until the 1970s and 80s that preliminary research was undertaken[1] and eventually led to the identification of NO's signalling role in both the cardiovascular and nervous systems.

In 1980, Robert F. Furchgott, and John V. Zawadzki first identified that the relaxation of blood vessels by acetylcholine (ACh) requires the presence of endothelial cells, wherein ACh stimulates the release of an unknown substance[2]. The release of this substance – coined endothelium-derived relaxing factor (EDRF)– was suggested to be the cause of the vascular smooth muscle relaxation process.

In 1977, Ferid Murad was carrying out unrelated research to decipher the mechanism of action of nitroglycerin, amongst other compounds. Despite being used as a potent explosive, nitroglycerin was also given to patients with recurring bouts of angina pectoris. The mechanism by which the key ingredient of dynamite provided these patients with pain relief was unknown.

Finally, in 1987, Louis J. Ignarro provided the last pieces of the puzzle. Following from previous findings that vasodilator drugs utilise the release of NO to carry out their pharmacological effects[2], Ignarro suggested that EDRF and NO were one

Image: Adam Baker/Flickr

EDWARD WICKSTEAD

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, alongside being a blogger, writer and advocate for mental health awareness.

and the same. He was indeed correct, and ascertained their identical biological and chemical properties[4]. This was the first time that a gas had been shown to play an important role in physiological regulation in humans.

> "This was the first time that a gas had been shown to play an important role in physiological regulation in humans"

Likely as a direct consequence of these three seminal pieces of work, NO was named "Molecule of the Year" in 1992 by the journal Science. However, it wasn't until six years later that Murrad, Furchgott and Ignarro shared the Nobel Prize for Physiology or Medicine[5]. 20 years on, and the physiological roles of NO have diversified extensively. Considered to be an unconventional neurotransmitter, NO has been identified to be involved in neural communication in both the peripheral and central nervous systems[6,7]. Roles for NO in preventing cellular apoptosis[8], stimulating cellular migration[9], and regulation of cell division[10] have also been recognised.

It was within the important roles of NO within the immune system where its pathological potential was identified. Produced in high quantities both in peripheral macrophages and central nervous system microglia, NO is toxic to invading bacteria, and assists with their degradation. However, further research into its immunological functioning has identified that excessive production of NO may not only be implicated in auto-immune diseases such as arthritis, but also in neurodegenerative conditions including Alexander disease[11]. These pathophysiological roles of NO are directly related to its free radical activity, which can cause cellular damage through a process known as nitrosative stress[12].

With these findings, drugs have been manufactured to modulate NO signalling for a wide variety of disease states. Perhaps most infamously however, sildenafil is used to overcome erectile dysfunction[13] – Pfizer patented sildenafil as 'Viagra', and it remains one of their best-selling products. However, it is also used to treat pulmonary arterial hypertension[14], and there is hope that further research will provide novel insights into both homeostatic physiology, and the pathogenesis of several diseases.

December of this year marks the 20th anniversary of Murrad, Furchgott and Ignarro receiving the Nobel Prize for their ground-breaking research into NO. Today, there are over 150,000 journal articles on NO published and available through PubMed.

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HEART FAILURE: GETTING TO THE 'ROOT' OF THE PROBLEM

Dr Christopher Primus and Professor Amrita Ahluwalia of the William Harvey Research Institute and Barts Heart Centre in London are running a trial investigating the benefits of inorganic nitrate in patients with heart failure. They are using crowdfunding to raise the final funds for their Phase 2 study.

Heart failure is a huge problem in the UK: the British Heart Foundation estimate that 900,000 people are living with the disease, with levels of morbidity and mortality comparable to those with cancer[1]. Traditional treatment with prognostic therapies like angiotensin-converting enzyme inhibitors (ACEi) and beta-adrenoreceptor blockers (β-blockers) have revolutionised treatment, but we have seen only two successful phase 3 studies resulting in new therapeutics in the last decade[2,3]. The management of heart failure is a challenging task, and so a multi-faceted approach tackling multiple dysfunctional pathways is key.

Nitric oxide (NO) is critical to maintaining our heart and blood vessel health, and its beneficial effects are well established[4]. All forms of heart failure are associated with reduced bioavailable NO [5], and so finding some way to restore NO levels and its beneficial effects may help to improve outcomes in those with the disease. Excitingly, the human body has developed a way to do this, and this underpins the health-related benefits of a diet rich in green-leafy vegetables[6]. Through utilisation of this alternative pathway of NO generation, the enterosalivary circuit can take the *inorganic nitrate* naturally present in green-leafy vegetables and beetroot, and convert it to NO using both the healthy bacteria in our mouths, as well as our own mammalian enzymes – Professor Ahluwalia and Dr Primus explain this in their crowdfunding video at bartshealth.hubbub.net/p/beetroothearts. The Ahluwalia Lab have already shown the benefit of nitrate-rich beetroot juice in hypertension[7] and hypercholesterolaemia[8], as well as benefits of the downstream product, *nitrite*, in acute heart attacks[9], but they now need your support to do this in patients with heart failure.

The team have already managed to raise £230,000 in charitable funds, and have now set up a crowdfunding campaign to raise the additional funds needed to complete the research with:

- Measures of heart function using state-of-the-art cardiac magnetic resonance imaging
- Sensitive measures of natriuretic peptides [and uric acid] to see how the juice is working and provide proof-of-concept as a result.

Barts Charity have already agreed to match every pound raised up to a total of £10,000, so please support them in their venture by interacting with them on Twitter and Instagram **@beetroothearts** or sharing their mission and donating to the cause at bartshealth.hubbub.net/p/beetroothearts.

CHRIS PRIMUS

Chris graduated with distinction in clinical practice from Imperial College London in 2008, having been awarded first class honours for his intercalated BSc. Having undertaken his junior training at both Oxford and University College London Hospitals, he took up a training post as a specialist registrar in cardiology in North East and Central London. Since then he has continued to develop his interest in both heart failure and infective endocarditis with the Barts Heart Centre team. He joined the Ahluwalia Lab in 2016, investigating the key role of inflammation in heart failure with a doctoral fellowship from the Derek Willoughby Trust, with support from Barts Charity.

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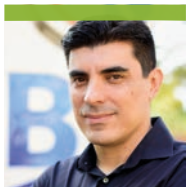
SOLVING PUZZLES IN NANOTECHNOLOGY: HOW TO TRANSFORM AN ARTIFACT INTO AN ANTIDOTE



MARCELO BISPO DE JESUS

Marcelo Bispo de Jesus is Group Leader of Nano-cell Interactions Lab at University of Campinas, Brazil. He received his PhD in cell biology at the University of Groningen. Dr de Jesus was granted the São Paulo Research Foundation's Young Investigator award, before taking up a position at the University of Campinas. In his current position, Dr de Jesus leads a multidisciplinary team working in the field of nanotechnology, focusing on gene delivery and nanotoxicology.

de Jesus lab group members at the University of Campinas, Brazil

The idea of a magic bullet is very compelling and attractive. Curing diseases with the precise delivery of therapeutics to the target cell or microorganism has received the attention of many laboratories around the world and has captured the imagination of writers and film directors for many years[1].

The possibility of engineering nanotherapeutics capable of effectively achieving these goals is the daydream of researchers everywhere. Nanomaterials are not only used in medicine; their use expands to electronics, agriculture, textile production, and many other industries[2,3]. Many nanomedicine products have reached the shelves, being used to either treat or diagnose diseases[4]. But one limitation of their use in medicine is their toxicity. For this reason, many efforts are under way to understand the mechanisms of nanotoxicity[5].

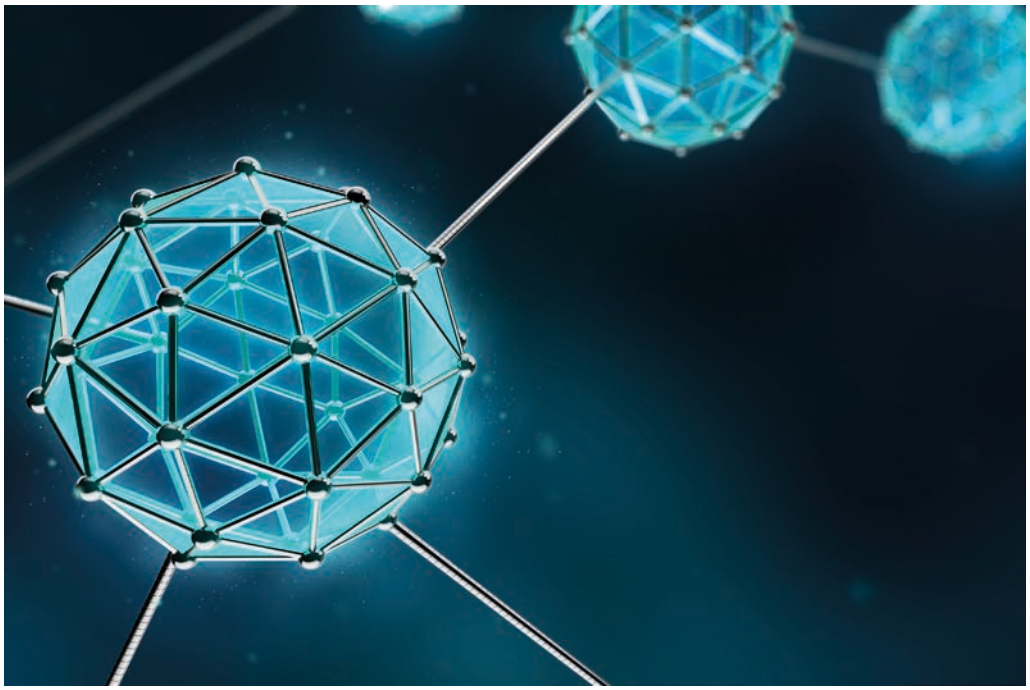
My laboratory is multidisciplinary and highly collaborative, and we focus on how nanoparticles interact with cells. One of the areas of interest in my lab includes investigating the mechanisms through which nanomaterials interact with cells in the body. This puzzle requires the knowledge of the nanoparticle's properties and how the biological media interact with the nanomaterial. Obviously, cells play an important role in taking up the particles and processing them. For these reasons, we are firstly interested in how nanomaterials interact with cells[6,7], how they are taken up by cells,

and what they do with nanomaterials such as carrying oligonucleotides[8]. Secondly, we are interested in investigating the risks involved in the use of nanoparticles and the events they may trigger in different cells of the body. One of the risks they present relates to their small size and the way through which they can travel in the body and reach cells in many vital organs, potentially inducing toxicity.

Through the study of silver nanoparticles, we have found that they induce oxidative stress in hepatocytes[9]. Previous studies have also found that cell death is induced by silver nanoparticles[10] and therefore we wanted to investigate the connection between oxidative stress and cell death. In our studies we found that whilst the presence of some antioxidants mitigated silver nanoparticle-induced oxidative stress, other antioxidants didn't. Then things started to become more interesting. Digging deeper, we found that some antioxidants can bind with silver nanoparticles. This was somewhat unexpected and a potential game changer. This finding led us to wonder, if specific antioxidants can bind directly to the nanoparticles *in vitro*, how does this translate *in vivo*? Could the binding of antioxidants to silver nanoparticles prevent toxicity? We know that silver nanoparticles lead to hepatotoxicity so, we treated rats with silver nanoparticles, one hour later we injected the antioxidant and after 24 hours we checked for the toxic effects. The result was astonishing: all signs of toxicity related to nanoparticle liver accumulation were gone[11]. After antioxidant treatment, they were excreted in the urine. The good news was that this antioxidant is approved for human use and has been for decades.

Our work continues but is just one example of how we were able to transform an artifact into an antidote.

> "Then things started to become more interesting. Digging deeper, we found that some antioxidants can bind with silver nanoparticles"



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THE MEDICINES ACT 1968 – 50 YEARS ON

MARY JOAN MACLEOD

Mary Joan MacLeod is a Clinical Senior Lecturer in Clinical Pharmacology at the University of Aberdeen. Her main clinical area is Stroke Medicine, and her research interests are aligned clinical trials, stroke imaging and data science using national datasets to look at the factors affecting stroke outcomes. She also chairs the University of Aberdeen Clinical Studies Oversight Group and serves on Scotland A Research Ethics Committee. She also has a significant input into Clinical Pharmacology teaching in the medical curriculum and MSc Clinical Pharmacology MSc course.

2018 marks the 50th anniversary of the Medicines Act, a comprehensive piece of legislation initiating statutory regulation of the manufacture, marketing, labelling and importing of medicines for human use in the UK. While modifications have considerably altered the original legislation, the underlying principles remain. The Act has helped to shape the pharmaceutical industry and supply chains, and with oversight ranging from over the counter medicines to complex treatments for rare diseases, affected the lives of almost every man, woman and child in the UK.

Regulation of medicines in the British Isles dates back as far as the 16th Century, to the Apothecaries Wares, Drugs and Stuffs Act, which in 1540 brought the manufacture of mithradatium and other medicines under the supervision of four appointed inspectors. With the identification of new chemical entities in the 19th and early 20th Century, regulations governing pharmaceuticals were developed, but dealt mostly with quality control rather than prescribing or administration[1]. While regulation occurred earlier in the US following deaths caused by improperly prepared sulphanilamide, it was only after the thalidomide tragedy (1957-61) that formalised medicines control was introduced in the UK. In January 1964, the Committee of Safety of Drugs (CSD) was created, comprising experts responsible for reviewing data on new drugs[2]. Their remit covered both drug safety and drug efficacy. The consequence was a voluntary set of controls, based on an agreement between the ABPI (Association of the British Pharmaceutical Industry) and the Pharmaceutical Association of Great Britain (PAGB) to consult with the CSD prior to initiating large-scale clinical trials or marketing new drugs[2]. This relationship set the basis for continuing good communication between government and industry, reflected in the significant contribution of pharmaceuticals to the UK economy over the years.

In 1971, twenty years after the inception of the National Health Service, the Medicines Act 1968 reached the statute books and was implemented. The Act was initially administered by the Medicines Division within the Department of Health. This had executive function and thus a degree of autonomy from government, which also served to increase confidence in decision making[2]. The Medicines and Healthcare products Regulatory Agency (MHRA) has emerged through various iterations and through close cooperation with the European Medicines Agency (EMA) has maintained a vital role in European drug evaluation and pharmacovigilance.

As a result of the complicated nature of the original Act and frequent amendments, as well as closer integration with EU structures, the Human Medicines Regulations (HMR) 2012 largely repealed or revoked most of the Medicines Act 1968 and about 200 further statutory instruments[3]. This legislation aimed to simplify the law to make it easier to understand and apply, with the hope this would reduce time and costs for businesses and the public sector. The HMR aimed for improved harmonisation of processes, and more pragmatic targeting of regulator and pharmaceutical pharmacovigilance resource towards areas of greatest risk to patients. The intended effect was to alleviate burdens upon industry, whilst at the same time maintaining public health and reducing the numbers of adverse drug reactions in the general population. The general perception is that the 2012 regulations were a successful consolidation, but did not go far enough, particularly to recognise the roles of health care professionals other than doctors in diagnosis and treatment of disease[4]. The current NHS staffing crisis with remodelling of roles and responsibilities means that this remains an urgent area for revision. Other areas identified as requiring further change include simplifying market entry for generic Marketing Authorisation holders, and reviewing wholesale licensing for pharmacies[4]. More important recent amendments to improve harmonisation across Europe include recognition of Cross Border Prescriptions and implementation of the Falsified Medicines Directive.

What has the Medicines Act 1968 achieved? The initial impact of the Medicines Act was to significantly reduce the number of new

drugs coming to market: from about 50 drugs per year in the early 1960s, to about 20 in 1980[5]. This raised ongoing concern that the regulatory burden was stymying product development, and to a certain extent this influenced the revision in 2012[4]. The cost of getting a new product to market is heavily influenced by regulatory requirements, and is now approximately £1.15 billion and takes around 12.5 years[6]. From a public health and patient perspective, however, effective new drugs have been developed and approved with a remarkably small number of drug withdrawals or high profile adverse events in the post-marketing phase. Between 1953 and 2013, 462 drugs were withdrawn from the market worldwide. 53 of these were in the UK after 1971, including high profile cases such as flosequinan or mibefradil. A further 45 were withdrawn across Europe[7]. These reflect approximately 2% of approved drugs during the same period, suggesting that pharmacovigilance systems have generally been highly effective. Each high profile withdrawal has been followed by a review of systems, and the close working between international regulatory agencies has been beneficial in identifying issues either before licensing or in the early post-licensing phase.

> "Of the top 20 drugs prescribed in 2017 in England, only five were available prior to 1968, reflecting huge changes in health care"

Of the top 20 drugs prescribed in 2017 in England, only five were available prior to 1968, reflecting the huge changes in health care as a result of the development of new drug classes (particularly cardiovascular and respiratory) over this time period. In 2017, £9.17 billion's worth of prescriptions were dispensed in the community in England and Wales, composing 1.11 billion prescription items[8]. The underlying economic value of drug research, development and implementation within the regulatory framework which has underpinned the current UK prescribing landscape is hard to determine, but clearly highly significant.

What about the next 50 years?

While the number of new entities coming to market may not have dramatically increased over the past few years, advances in technology have increased the range and complexity of pharmaceutical and medical device products. Increasing globalisation, the application of artificial intelligence and machine learning in development and diagnostics, the internet and data protection legislation, changing patient populations and expectations all contribute to a need for proactive review of legislation.

Clearly the UK vote to leave the European Union will impact on future harmonisation. It will alter the UK's parallel pharmaceutical distribution market, and may affect access to some specialist drugs or have an impact on the drug supply chain in other areas. How the new EU Clinical Trials Regulation which comes into force in 2019 will be translated into the UK legal framework is unclear, but may give opportunity for specific modification to maintain the UK's lead in Phase I studies. As the UK accounts for 22.7% of the total EU market in pharmaceutical distribution, significant effort is now being concentrated on minimising the potential impact of regulatory divergence on development, manufacture, distribution and administration of drugs[9]. Despite the fact that the MHRA has been responsible for around 40% of drug evaluation on behalf of the EMA, the MHRA will lose involvement in evaluating medicines for the EU from March 2019. Thus, it is likely that regulatory divergence will become apparent quite quickly. Mutual Recognition Agreements (MRAs) exist with countries outwith the European Economic Area such as Turkey, Switzerland and Canada. A future MRA between the UK and the EMA could involve recognition of Good Manufacturing Practice, Good Distribution Practice and medical devices assessment. However, change is also a time of opportunity, and we hope that recommendations from service users, industry and health professional bodies can be incorporated into new legislation. It is essential that the UK maintains its position at the forefront of drug development and clinical trial design and delivery.

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OCTOBER
Clinical Pharmacology Month

CLINICAL PHARMACOLOGY MONTH

Clinical pharmacologists work in healthcare, academia, drug discovery, and regulation. They were instrumental to the development of the Medicines Act in 1968. For example, Sir Derrick Dunlop became the first chairman of the Medicines Commission following implementation of Act.

Today clinical pharmacologists continue to lead on new drug development, regulation and the safety monitoring of healthcare products in the UK. In October the British Pharmacological Society will be celebrating clinical pharmacology month to increase awareness of the value of clinical pharmacology. A series of national and local activities will be organised including our medical student competition and grand rounds and lectures from members taking place in hospitals and universities.

For more information or to get involved, please contact Lisa Hevey, Clinical Education, Training and Policy Manager (lisa.hevey@bps.ac.uk) or visit our website www.bps.ac.uk/clinical-pharmacology-month.

BAP
British Association for Psychopharmacology

summer meeting 2018

Featuring a range of non-clinical and clinical presentations across of range of neuropsychiatric conditions

- Towards a mechanistic understanding of anxiety disorders: translational, pharmacological, neural and computational perspectives
- Microglia role in neuropsychiatric disease and its potential as a treatment target
- New concepts in the co-morbidity of psychiatric disorders, eating disorders and obesity
- Bridging the translational gap in psychiatry: a role for neuronal oscillations?
- Mineralocorticoid/ glucocorticoid receptor imbalance and early life stress as risk factors for affective disorders

King's College London, Exhibition Road, London
Sunday 22nd to Wednesday 25th July

A Guest Lecture by Daniel R. Weinberger, MD (John Hopkins University)
Genomic insights into the neurodevelopmental origins of Schizophrenia

Preclinical Workshop hosted by Understanding Animal Research:
How to ... engage with public audiences on animal research

Trainees' Workshop
Public engagement for early career scientists: What? Why? And How?

A Public Lecture presented by Professor David Nutt

PLUS bursaries, prizes and poster sessions

Welcome Reception and Disco
Conference Dinner at the Royal Garden Hotel including presentation of the 2018 Prizes and Awards

For full details of the meeting go to www.bap.org.uk/BAP2018

PERSPECTIVES IN PHARMACOLOGY

DRUG DISCOVERY CHALLENGES NOW THE LOW HANGING FRUIT HAS BEEN HARVESTED

Photo by Liana Mikah on Unsplash

Up until the late 70s, pharmacological discovery was a process exemplified by increasing technical expertise in surgery and bioassay, and was associated with a series of important discoveries. However we tend to view this 'golden era' through rose tinted spectacles. The reality is that the vast majority of research, as will be evident from a perusal of old volumes of pharmacology journals, was unimportant and anodyne. We remember only the 'good bits'.

Moreover, the great discoveries such as the mechanism of action of aspirin were, to a large extent, the plucking of low hanging fruit. Much of the discovery, such as the antiarrhythmic action of amiodarone, was by chance. And some, such as the discovery of the mechanism of action of digitalis, was far from immediate, taking (in this example) several hundred lugubrious years in a process littered with wishful thinking and the invention of catch-all concepts such as 'multifactorial mechanisms' (a euphemism for 'it does lots of things but we don't know how this leads to the primary beneficial effect').

The main purpose of pharmacology is drug discovery. One of the problems in pharmacology is that when the low hanging fruit were plucked, or serendipity delivered a new medicine, we took inordinate encouragement from these great successes, and have tended to imagine this reflects the excellence of our knowhow and the sophistication of our discipline. Unfortunately, in more recent years, the truth is beginning to dawn on some of us: progress is slow and translation commonly fails, and the drug discovery process is more haphazard than one would expect if driven by genuine expertise and knowhow. Consider the

> "Progress is slow and translation commonly fails"

MIKE CURTIS

Mike graduated with a BSc in Pharmacology from Chelsea College in 1979, and a PhD from University of British Columbia in 1986 (under the supervision of Michael Walker). After three years' postdoctoral training at the Rayne Institute (under the supervision of David Hearse), Mike became a lecturer in Pharmacology at King's College London in 1989, and reader in 1996. His research is cardiovascular and his main interest is antiarrhythmic and proarrhythmic drugs. He has published over 100 papers (cited over 5000 times) and has an h index of 34. Mike has supervised 12 PhD students, two of whom were AJ Clark scholars. He has a keen interest in teaching and training, and has published several research guidance articles including the *British Journal of Pharmacology*'s design and analysis guidance (2015) and the Lambeth Conventions arrhythmia guidance (2013). Mike has held several editorial roles including reviews and themed issues editor for the *British Journal of Pharmacology* (to finish a 17 year run on its editorial board) and has been editor in chief of J Pharm Tox Methods since 2001. He served on the executive committee of the Society for three years, and that of the British Society for Cardiovascular research for 17 years (15 as treasurer).

post-Viagra success rate of Pfizer, Sandwich, for example. There is even a perception that we are getting worse at drug discovery.

The reality may be that we are neither better nor worse, but appear worse because the low hanging fruit are now largely gone and the hit rate has consequently declined. This means that drug discovery is, and has always been, intrinsically a low yield activity, characterized by false discovery and failed translation.

The emergent 'dry pipeline' has allowed those opposed to animal research to argue that animal models are misleading and outcomes will not accurately predict the human response. This may be true in cases where there are no drugs effective in humans (positive controls) with which to validate a model, meaning the model is unvalidated and potentially invalid. However, it cannot be the main reason for failed translation of treatment of conditions where it is easy to validate a model with positive and negative controls. Take this explanation for failed translation away and we start to wander into murkier areas.

For example, part of the explanation for the 'dry pipeline' of failing translation, perhaps the larger part, may be that we are not (and never were) very good at experimental design, with non-blinded non-randomized studies yielding false positives. Early legendary observations, such as when ACh is injected into a dog it had profound and obvious effects, did not require a great deal of experimental design to reveal themselves.

These early observations, also, came about from the pursuit of curiosity, often by comfortably-off men (in the main) not reliant on their research for their primary income. There was also no need to publish regularly in high journal impact factor (JIF) journals, no 'publish or perish' tyranny, and no need to put a positive spin on every trivial finding. As time progressed, the workplace environment has changed, becoming highly competitive. The primary measure of success is no longer an impactful discovery and a new medicine, but a 'high impact' paper and citations.

With rewards based on 'impactfulness', findings need only be positive and exciting. *Reproducible* (i.e., correct) findings are no longer necessary for a 'successful' career in preclinical (especially academia-based) research. Moreover, all the while the work stays preclinical, if the findings are incorrect this is likely to go unchallenged, partly because people work in silos, with replication of other people's work regarded as an unoriginal (and largely unfundable) pursuit.

In the meantime, knowhow about experimental design has not improved. If I say that most if not all pharmacology journals publish in almost every issue papers with n=3/group, and report 'highly significant' effects (P<0.001) even with small samples, the tragedy is that many reading this statement will think 'so what?'. Indeed, far too many pharmacologists (sometimes cheerfully) admit they know nothing about design and statistical analysis.

> "We are polluting the literature with an increasing preponderance of findings that are likely to be false"

Unfortunately this has always been so. But today, with the low hanging fruit gone, and the pressure to publish so great, the effect is that we are polluting the literature with an increasing preponderance of findings that are likely to be false. Indeed, there are some individuals who are doing this knowingly. How many? It is hard to tell, and it is widely regarded as distasteful to broach the topic. Regardless of the relative contribution of ignorance versus deliberate fraud, unless things change, eventually the funders will begin to realise that the 'breakthrough' promises are not forthcoming and start to speculate that their investment may not be good value for money.

That said, given that members of the public are often naïve, and far too willing to put hope before evidence (witness the numbers who believe in space aliens, the investment value of a lottery ticket, ghosts, and god), the processes leading to our being found out will likely be slow. That is no excuse for letting the situation drift, however.

I would like to see pharmacologists applying more rigour to their experimental design. Sadly I suspect that the 'publish or perish' mentality is now so pervasive that attempts to improve standards will be resisted ('don't rock the boat-ism'), and that without a better coordinated effort, with unswerving leadership, nothing much will change. We shall see.

ALLTRIALS: HAVE YOU REPORTED ALL OF YOUR TRIALS?

Randomised clinical trials are by far the best tool we have to assess whether a medicine works or not. Governments and regulators demand to see the results of the highest quality trials to make decisions about treatments. Thousands of trials happen every year, all around the world, and hundreds of thousands of people volunteer to be part of them.

So it's a problem that around half of these clinical trials have never reported results. The evidence base for medicines we use every day is incomplete and because trials that show a medicine works are twice as likely to have reported results than trials that show that a medicine doesn't work, the evidence base is skewed. It means that the thousands of patients who gave up their time to join trials, trusting that what is found out about their condition or the medicine will be shared with doctors, have had their trust betrayed.

The AllTrials campaign[1] is the global movement of 800 organisations and 90,000 people calling for all clinical trials to be registered and results from them to be reported. I help run AllTrials. I wrote here last year[2] recommending that researchers start to publish unreported trials because AllTrials was going to start shining a light on researchers' and organisations' past reporting. Since then support has grown – some of the world's largest funders and regulators have now committed to doing the same. Here's where we are now.

Tracking tools

Over the last year we have launched a suite of public tracking tools that allow anyone to identify which clinical trials have reported results and which haven't, and to see who is responsible for the trials. The TrialsTracker[3] built by the EBMDataLab in University of Oxford is one of these tools. It pulls in information from the world's largest clinical trial register, the US federal ClinicalTrials.gov, for all clinical trials registered there since 2006. Then it automatically searches the register and in the peer reviewed literature for results from the trials and flags each trial as either reported or not. The TrialsTracker currently shows that 45.2% of trials registered on ClinicalTrials.gov since 2006 are missing results.

What about trials that are running today? The new FDAAATracker tool[4] flags trials on the US register in which reporting results are overdue under US law. The FDA Amendment Act is the law that says that trials must be registered when they begin and must report results to the register a year after they end. As I'm writing this piece the FDAAATracker is showing that only 65% of recently ended trials have reported results on time. It shows that the FDA is entitled to have collected fines of over $200 million from parties responsible for trials that have broken the reporting rules. You can see which trial sponsors are reporting the most, and the least, of their trials here fdaaa.trialstracker.net/rankings/. Readers could have a look at how their own institution is performing. If it's not good, let them know you'd like to see them improve.

The Unreported Trial of the Week

AllTrials has started to shine a light on specific unreported trials. We are running the AllTrials Unreported Clinical Trial of the Week[5] – a weekly series of articles in the British Medical Journal on trials the FDAAATracker has flagged as unreported. So far we have written about nine unreported clinical trials including: a trial involving 200 cataract surgery patients, a trial run in New York investigating whether ketamine

SÍLE LANE

Síle is the head of international campaigns and policy at Sense about Science, the UK charity that campaigns around the use and misuse of evidence in public life. Sense about Science runs the AllTrials campaign for clinical trial transparency which the British Pharmacological Society supports.

> "Don't risk getting caught out – make reporting your trials your priority now"

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could treat cocaine dependence, and a trial involving 270 seniors across Europe and the US on strategies to reduce agitation in Alzheimer's patients. Three of those previously unreported trials have gone on to submit results. We know this works!

Audits of funders and institutes

We have been taking a closer at how academic institutes and funders are responding to calls for transparency. A recent paper in *the Journal of the American Medical Association*[6] found that most large charities and government bodies who fund clinical trials don't have a policy to ask that the results from these trials are reported. This audit of the 18 philanthropic and public bodies that spend the most money on clinical research found that most (66%) do not require researchers to report results and that only half ask for clinical trials to be registered. Only two of these global bodies had a policy that reached the gold standard for transparency, the UK's Medical Research Council and Germany's research funding organisation Deutsche Forschungsgemeinscaft. Altogether the 18 funders spend around $40 billion on health research every year. If results from research isn't shared, this money is wasted.

Another recent paper[7] has shown that most academic institutes in the US do not have any publicly stated policy to ensure that clinical trials are registered and their results reported. Under half of them have a policy on registration of clinical trials (43%) and only around a third (35%) have a policy on results reporting.

The results of these two recent papers are shocking. The requirement to register and report trials is moral, ethical, professional and legal (see the box), and institutions should have a policy and a public commitment to compliance. The academic research sector is lagging behind on this. An audit of the world's largest pharmaceutical companies' policies on transparency that we published in the *BMJ* last year[8], found that over 90% of companies have policies to both register their trials and to report summary results. Dr Ben Goldacre of the EBMDataLab at the University of Oxford -a co-founder of the AllTrials campaign, said, "Public funders have fallen well behind and are now doing worse on transparency than the pharmaceutical industry. We need these funders to show leadership, to tell their grant recipients very clearly that all trials must be registered and reported."

In May 2017 the World Health Organisation (WHO) backed this effort when it asked charities and governments worldwide to sign up to its strong standard on transparency[9]. The WHO has long held that registering clinical trials and publicly sharing results from them is an ethical imperative for all researchers. Their statement asked funders of clinical trials to write and implement a new strong policy that will guarantee that all funded researchers register and report their trials. Twenty-one funders, including the Bill & Melinda Gates Foundation, Médecins sans Frontières and the Wellcome Trust have joined the WHO's statement. We will be auditing these funders soon to ensure that they have done what they promised.

I would advise every researcher to get all past trials reported, soon. The FDA said it will focus its sanctioning efforts on trial supporters who have not complied with reporting guidelines in the past. The US federal funder, the National Institutes of Health, has just said that it will no longer fund research if it cannot verify that the researcher registers and reports their trials[10]. Other funders are considering adopting this policy too. The Health Research Authority is going to start asking researchers applying to run a new clinical trial about whether their past trials have been registered and reported. More research regulators around the world are going to adopt this too. Soon, if a researcher wants to get approval to run a trial, to get a trial funded, published and accepted by a regulator, they'll soon be asked not just whether that trial will be registered and reported but whether all other trials they've run in the past have been too. Don't risk getting caught out - make reporting your trials your priority now.

THE OBLIGATIONS ON RESEARCHERS TO REPORT CLINICAL TRIALS ARE...

...ethical

The Declaration of Helsinki, adopted by the World Medical Association in 1964, last amended in 2000, is the internationally agreed ethical standard for clinical researchers. It says that researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports.

It also says that ethical imperative to report includes results of unreported trials conducted in the past. And that: "Negative and inconclusive as well as positive results must be published".

The World Health Organization states: "The registration of all interventional trials is a scientific, ethical and moral responsibility" and: "The key outcomes are to be made publicly available within 12 months of study completion by posting to the results section of the primary clinical trial registry."

...contractual

Many of the world's largest medical funders – including the US National Institutes of Health, the European commission, the Australian National Health and Medical Research Council, foundations and patient non-governmental organisations – mandate that results from trials they fund must be reported.

Funders around the world are signing up to a WHO-led statement committing to audit their grants for compliance. This is one reason institutional reviews boards and other approval bodies are now asking about researchers' reporting histories in new applications.

...legal

All trials registered on the EU clinical trial register since 2004 must have results reported. The new EU regulation 536/2014 from 2019 will make this a legal requirement that can be enforced through fines and other sanctions.

The FDA Amendment Act 2007 requires that trials with a site in the US or forming part of treatment licensing are registered on ClinicalTrials.gov and report results within 12 months of completion.

Fines of up to $10,000 a day can be imposed by the FDA. In 2015 the United Nations began urging every government to ensure it has legal enforcement measures to require researchers to disclose clinical trial results.

...professional

International good clinical practice for running clinical trials includes reporting results.

Many professional registration bodies include this explicitly in their definition of professional standards, or implicitly through reference to the standards above, which means failure to report is professional malpractice.

...decent

Full reporting of results improves medicine and improves research – so it improves lives. People who volunteer for clinical trials trust that the results will contribute to understanding. Researchers who do not report results are choosing to flout the legal, ethical and professional requirements related to their own trials and choosing to damage that trust for all others.

THE FUTURE OF THE AMBASSADORS SCHEME

TEESHA BHURUTH

Teesha works within the Education, Engagement and Policy team at the Society. Teesha works with other staff and members to develop and nurture the Society's relationships with its growing membership, potential members, stakeholders, Ambassadors and members of the public.

Teesha graduated with a First Class BSc in Biomedical Sciences from the University of Southampton. Her Technical Support and Field Sales Representative roles for laboratory specialists Anachem Ltd (Mettler Toledo) were followed by a year as Employment Contracts Officer for University College London. She enjoys, and has experience of, engaging a wide range of audiences in support of the Society's strategic objectives, and acts as the primary contact for groups and networks in the pharmacology community.

Dr Cristina Pérez Ternero speaking to undergraduate and postgraduate students about discrimination in the workplace and other challenges faced by women at the 'Women in Medical Research' event, which was part sponsored by Ambassador funds, in March 2018 at Queen Mary University of London.

In 2017 the Society concluded and reviewed its two-year Ambassadors Scheme pilot, and in December Council agreed to expand the Ambassadors Scheme as a fully-fledged initiative from 2018.

In just two years the Ambassadors have established an invaluable connection between the office and the Society's membership, and with members of neighbouring organisations. In 2017, the Society's 13 UK-based Ambassadors facilitated a range of engagement activities for university students, school children, and pharmacologists in the local community.

Examples include:

- Supporting pharmacological or biomedical student societies through funding speaker travel, networking drinks and prize sponsorship
- Combining funds to sponsor a mini-symposium
- Hosting a pharmacology careers day with sixth form students
- Establishing a specialist network for pharmacologists, pharmacists, primary and secondary school practitioners and social scientists, to establish ways to improve prescribing and use of opioid-based analgesics
- Recruiting student helpers at engagement events and using funds to cover their lunch/ refreshments

"The materials and funds I received from the Ambassadors Scheme allowed me to organise several pharmacological events at both King's College London and Queen Mary University of London, and establish the pharmacology society at the William Harvey Research Institute. Recently we have focussed more on sponsoring prizes, which is a great initiative for increasing the awareness of pharmacology and celebrating outstanding achievements of the pharmacology students."

Aisah Aubdool,
Ambassador, King's College London

It was positive to see in the pilot scheme review that the 13 Ambassadors were resourceful and used their funds in a broad manner across a range of activities, which engaged a variety of audiences including students, schools and the public. The Society is excited to appoint more volunteers into the scheme from different sectors to get involved (NHS, Industry and academia), which will ultimately help to improve the Society's networks and community building – both integral parts of the Society's new 5-year strategy.

The Society would like to say a big thank you to all of the 13 pilot Ambassadors who contributed to making the pilot scheme a success:

- **Alasdair Gibb,** University College London
- **Amos Fatokun,** Liverpool John Moores University
- **Anne Leaver,** University of Edinburgh
- **Anja Mueller,** University of East Anglia
- **Aisah Aubdool,** King's College London & Queen Mary University of London
- **Breandán Kennedy,** UCD Conway Institute
- **Daniel Hawcutt,** University of Liverpool
- **Paul Chazot,** University of Durham
- **Richard Roberts,** University of Nottingham
- **Samir Ayoub,** University of East London
- **Shori Thakur,** University of Hertfordshire
- **Steve Tucker,** University of Aberdeen
- **Yvonne Dempsie,** Glasgow Caledonian University

Flashback: What was the Ambassadors Pilot Scheme?

The British Pharmacological Society's Ambassador pilot scheme was conducted between 2015 and 2017 in order to contribute to the delivery of the Society's strategic objectives by:

- **Promoting pharmacology in organisations at a local level**
- **Providing guidance and support to pharmacologists**
- **Ensuring that the Society's activities represent the interests of members**

Each appointed volunteer received the title of Ambassador, access to a £500 grant per year and Society membership and/or marketing resources to facilitate engagement activities within their network.

Join the Ambassadors Scheme: Coming soon in 2018

- **Do you enjoy getting people together to talk research, policy or diversity in science and are you keen to make this happen in your department?**
- **Would you like to put together small scientific meetings or networking events for your department or do you do this already?**
- **Are you interested in running a public engagement activity that will raise awareness about the importance of pharmacology and raise the Society's profile?**
- **Are you keen on inspiring school students to study pharmacology, and are you willing to spare some time to deliver a careers talk?**

Volunteer with us, be part of the Scheme and make a difference in your network. Watch this space for news of the Scheme's re-launch and expansion and how you can become an Ambassador within your network.

"Pilot Ambassadors were resourceful and used their funds in many creative ways, which engaged a variety of audiences, and helped to build local communities of pharmacologists.

The Society learnt a great deal from the pilot phase, especially that improving the visibility of Ambassadors would improve the visibility of the Society at an organisational level. I look forward to seeing the scheme flourish in 2018 where I believe it will strengthen the networks between the Society and academia, the NHS and Industry."

Alister McNeish,
Vice President Policy & Public Engagement

"The Ambassador title gave me increased legitimacy to make an impact within my university and to engage external audiences through an identifiable link to the Society. Regular contact with the Society kept me up to date with the latest information so that I was appropriately informed to confidently raise awareness and disseminate knowledge about the Society's work."

Alasdair Gibb,
Ambassador, University College London

INCLUSION AT THE BRITISH PHARMACOLOGICAL SOCIETY

TEESHA BHURUTH

For Teesha's biography see page 28.

LISA HEVEY

Lisa graduated from the University of Sheffield with a BA in Sociology before studying for an MA in Sociology (Research) at the Sorbonne (Paris IV). She has worked in the Higher Education sector for several years in addition to teaching English as a foreign language for many years. She previously worked at the Equality Challenge Unit and the Medical Schools Council as a Policy Officer where her work focused on selection methods used for those applying to medicine and widening participation.

The first objective set out in the Society's new five-year strategy for 2018-2022, which launched at the end of 2017, is "To remove barriers to participation and success, while welcoming equality and celebrating diversity, and being inclusive in all we do".

The issue of representation – be it socioeconomic, gender or ethnicity – is an ongoing challenge within pharmacology, and the science community more widely.

Where the Society has been able to redress the balance swiftly, however, it has done so. We now collect much more granular information on gender and identity through our new member database, and that information has helped us to improve our diversity policies. In tandem with Council, where equality and diversity is a standing agenda item, the Women in Pharmacology Advisory Group has worked hard to ensure we have a good gender balance across all of our committees. Where a longer-term commitment is needed we are presently working to identify the challenges and lay the foundations for change. Our report, 'Pharmacology Education and Employment Pathways'[1], identified that:

> "**58%** of pharmacology students are women"

and that this high percentage continues on into the early years of training, PhD and post-doctoral research. However, the subsequent decline in number is a concern. The Society offers bursaries for childcare while members attend our meetings and is also available a bespoke career break membership, but to address the root cause of the problem will take longer.

In light of the Society's new strategic objectives for the next five years, the Society has reviewed its approach to widening participation, equality, diversity and inclusion. The Women in Pharmacology Advisory Group was consulted and supported the investment of resources and time into the establishment of a new mechanism to embed the broader scope of Equality, Diversity and Inclusion (EDI) at the Society.

The Society will be seeking advice externally from an expert individual and/or organisation who has led similar change to guide this process and to ensure that the Society starts from a position of best practice in this area, and the best way to approach monitoring and decision making in the future.

It is an exciting time for the Society as we begin implementing our new EDI strategy. Rest assured that women in pharmacology will remain a significant focus of this new group and a priority for the Society. We will be sharing further details, including how to get involved, in a communication to all members in due course.

Our commitment to improving equality and diversity

- The Society will make every effort to increase diversity within its leadership and governance structures, its membership, and its professional development activities.
- Throughout all of its charitable objectives the Society will articulate gender and ethnic diversity as a core value and highlight its importance to pharmacology at every level.
- Society management and participation in Society initiatives should reflect the gender and ethnic diversity breakdown of the membership.
- The Society will provide opportunities for and support of professional development for women and minorities.

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EVIDENCE FOR GENDER INEQUITY IN PHARMACOLOGY: RAISING AWARENESS AND MOTIVATING CHANGE

The exchange of ideas and knowledge is an essential aspect of being a scientist that enhances our collective progress. As academics our contributions to the field, both as individuals and teams, are measured by our metrics. Peer reviewed publications are the core ingredients we use to demonstrate our productivity and capability. However, the quality and impact of our research relies on a variety of evidence, including peer recognition in the form of invited conference presentations and scientific awards.

I have recently returned from a mini world tour where I gave a departmental seminar, was an invited speaker at the Society's Cell Signalling meeting, attended an Early Career Researcher (ECR) symposium and a large scientific meeting (Experimental Biology, San Diego). The value and impact of these opportunities are at the forefront of my mind.

The immediate positive outcomes from this trip were:

1) opportunities to plan projects and new grant applications with collaborators (both established and new);
2) share my technical expertise and research ideas with new audiences;
3) invitations to speak and to contribute a minireview;
4) meet with potential new recruits.

Undoubtedly, attendance and participation in scientific meetings facilitates development of our networks and allows us to be ahead of the game by immersing ourselves in unpublished and cutting-edge research. These amazing opportunities are overshadowed by my growing awareness that female scientists are often poorly represented within invited speaker ranks at conferences[1-4] or among recipients of scientific honours[5]. In recent years, I can recall attending sessions completely absent of female speakers, suggesting that pharmacology may not be immune to this inequity. Since I am an analytical pharmacologist at heart, I thought of taking a closer look at the data.

Female pharmacologists are overlooked as invited speakers at large scientific conferences

The gender of invited speakers was assessed within programs from three recent pharmacological society annual scientific conferences and the upcoming International Union of Basic and Clinical Pharmacology World Congress in Pharmacology (IUPHAR – WCP; as published online 11/5/2018). Speakers selected from submitted abstracts were excluded from the analysis, as were trainee prize sessions and workshops/satellite meetings. The gender of speakers was assigned by referencing publicly available information: images and biographies from institute websites and social media (researchgate, LinkedIn) or by employing online gender name tools (genderchecker.com or epublishing.nademoya.biz/japan/names_in_japan.php). Speakers without a web presence, with gender-neutral names or listed as 'to be advised' were allocated as unknown. Females represent ~35% of British Pharmacological Society and ~44% of ASCEPT (Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists) total membership (among those that disclosed their gender), but this breakdown is unavailable for ASPET (American Society for Pharmacology and Experimental Therapeutics). The British Pharmacological Society has committed to 30% female representation across all activities in 2015 (www.bps.ac.uk/about/our-public-benefit/championing-women-in-pharmacology). Recent ASCEPT, ASPET and British Pharmacological Society annual scientific meetings have exceeded this aspiration, with female invited speakers representing 35-40% of the total (Figure 1A). In contrast, the recent IUPHAR-WCP, a quadrennial event representing global pharmacological societies including ASPET, ASCEPT and British Pharmacological Society, does not meet this level. Furthermore, analysing the different session types and themes reveals that across the 87 IUPHAR-WCP symposia, 33 have speakers from a single

KAREN GREGORY

Dr Karen J Gregory is an Australian Research Council Future Fellow and lab head of the Class C GPCR Biology laboratory at Monash Institute of Pharmaceutical Sciences, Monash University, Australia. Karen received her PhD in Pharmacology from Monash University in 2009, and spent four years at Vanderbilt Centre for Neuroscience Drug Discovery supported by an National Health and Medical Research Council CJ Martin overseas biomedical postdoctoral training fellowship. Her research program focuses on allosteric modulation of metabotropic glutamate receptors; attractive therapeutic targets for diverse psychiatric and neurological disorders.

gender (all male). There was only one female speaker among the 33 cutting edge lectures and 7 plenary sessions (Figure 1B). Symposia and cutting-edge lectures were grouped into 12 themes; two themes met or exceeded the aspirational target for female speakers. It is worth noting that ASCEPT, ASPET and British Pharmacological Society all have diversity policies for submitting symposium proposals that includes consideration of gender, career stage and institution. Implementation of equal opportunity guidelines in other fields has resulted in an increased proportion of female invited speakers to better align with membership demographics[6].

How do smaller scientific meetings compare?

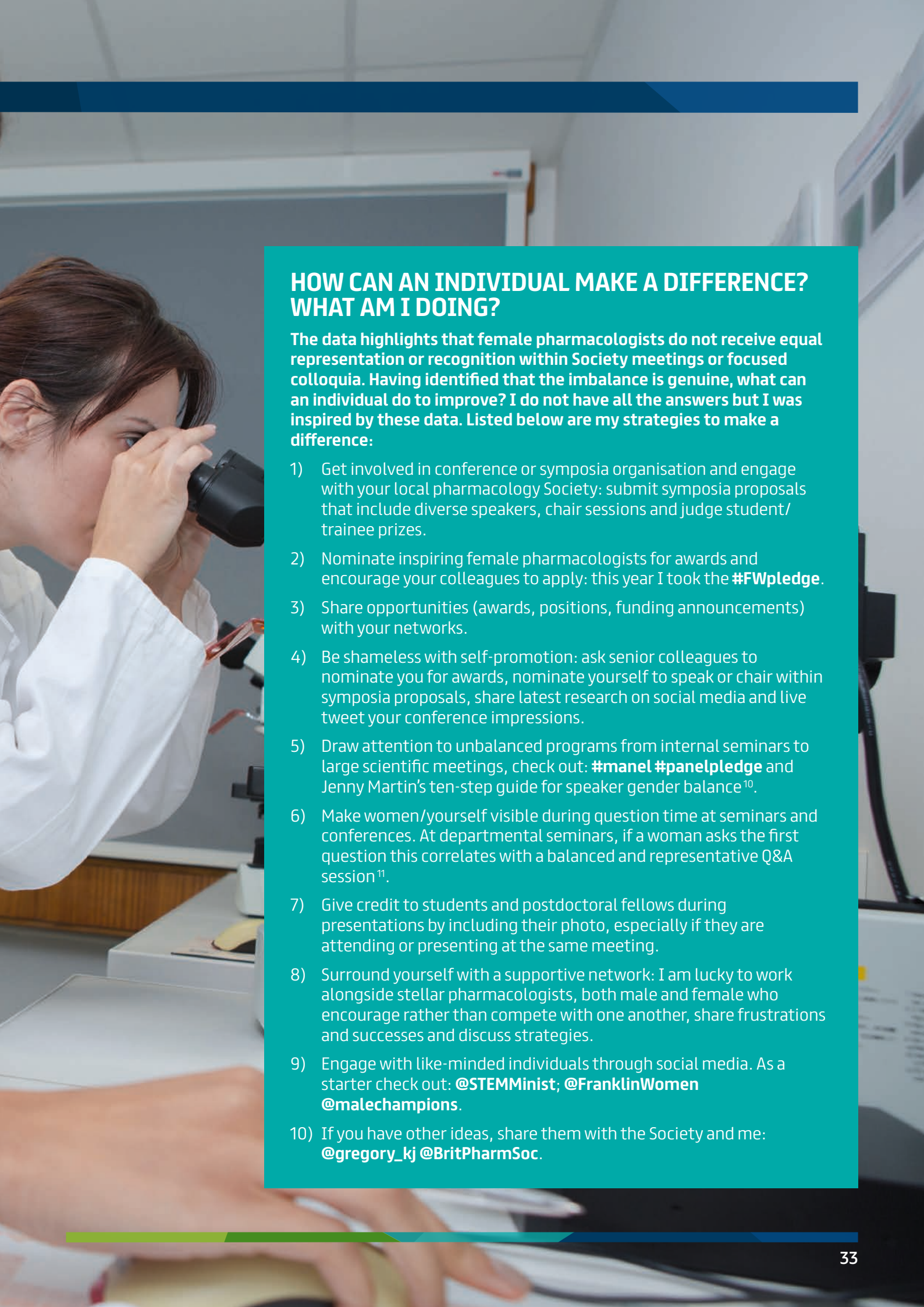
Given the varied performance of different research areas within the IUPHAR-WCP program, I next assessed satellite symposia and focused meetings. For this purpose I analysed G protein-coupled receptor (GPCR)-centric meetings, since this is a field I am most familiar with. Nine meetings were included that have been held in the past six months or are planned before the end of the year. Of the nine meetings, only two have in excess of 30% female speakers (Figure 1D). As co-chair of the upcoming British Pharmacological Society-MPGPCR 2018 meeting, I am proud that we have >40% female invited speakers. Without compromising the scientific quality of the program, this may reflect the composition of the organising committee (four women and three men) and upfront discussions on creating a diverse program (gender, location, career stage and research). Organising committees with female members have demonstrated a propensity to have a higher proportion of female speakers [1,7].

Peer recognition of female pharmacologists – keynote lectures and scientific awards

Keynote lectures and scientific awards recognise an individual's outstanding contributions to the field. Across all society meetings, I analysed the recipients of award/keynote lecture slots, as well as scientific awards, excluding early career awards. Award lectures within the British Pharmacological Society and ASCEPT-APSA programs showed similar levels of recognition of female scientists (Figure 1B), although it should be noted that one British Pharmacological Society award specifically acknowledges female pharmacologists. Within ASPET award lecturers, women were not well represented, nor within scientific prizes receiving only 2 of 11 division-sponsored awards. Since focused meetings generally only have one or two keynote lectures (two had no designated keynote speakers), the gender of keynote lecturers was assessed globally. Among the seven meetings, no women received this distinction (Figure 1D). The paucity of female awardees may be in part attributable to the lower proportion of women within senior academic roles and among nominees, but may also reflect unconscious bias among conference organisers/judging panels.

Why should we address the imbalance?

As scientists, conference presentations and scientific awards are key metrics we use to indicate the excellence and impact of our research programs. The peer recognition and exposure gained from presenting to an international audience has the potential to create a wealth of new opportunities. Indeed, the "Matthew effect" where early success is a strong indicator for future success, applies to science funding[8], and likely also to speaker invitations and awards. Beyond the importance to an individual, a diverse speaker program (where gender is but one factor) benefits the scientific community. Diverse and inclusive teams are known to make better decisions and ask different questions[9], therefore diverse conference programs are likely to push scientific boundaries more effectively, with increased exchange of ideas and knowledge. Within biological sciences >50% of UK PhD students identify as female (www.hesa.ac.uk/data-and-analysis/sfr247/figure-14), therefore increasing the visibility of female pharmacologists provides role models for trainees and changes perceptions around the contribution of women to the field.



HOW CAN AN INDIVIDUAL MAKE A DIFFERENCE? WHAT AM I DOING?

The data highlights that female pharmacologists do not receive equal representation or recognition within Society meetings or focused colloquia. Having identified that the imbalance is genuine, what can an individual do to improve? I do not have all the answers but I was inspired by these data. Listed below are my strategies to make a difference:

1) Get involved in conference or symposia organisation and engage with your local pharmacology Society: submit symposia proposals that include diverse speakers, chair sessions and judge student/ trainee prizes.
2) Nominate inspiring female pharmacologists for awards and encourage your colleagues to apply: this year I took the **#FWpledge**.
3) Share opportunities (awards, positions, funding announcements) with your networks.
4) Be shameless with self-promotion: ask senior colleagues to nominate you for awards, nominate yourself to speak or chair within symposia proposals, share latest research on social media and live tweet your conference impressions.
5) Draw attention to unbalanced programs from internal seminars to large scientific meetings, check out: **#manel #panelpledge** and Jenny Martin's ten-step guide for speaker gender balance[10].
6) Make women/yourself visible during question time at seminars and conferences. At departmental seminars, if a woman asks the first question this correlates with a balanced and representative Q&A session[11].
7) Give credit to students and postdoctoral fellows during presentations by including their photo, especially if they are attending or presenting at the same meeting.
8) Surround yourself with a supportive network: I am lucky to work alongside stellar pharmacologists, both male and female who encourage rather than compete with one another, share frustrations and successes and discuss strategies.
9) Engage with like-minded individuals through social media. As a starter check out: **@STEMMinist**; **@FranklinWomen @malechampions**.
10) If you have other ideas, share them with the Society and me: **@gregory_kj @BritPharmSoc**.

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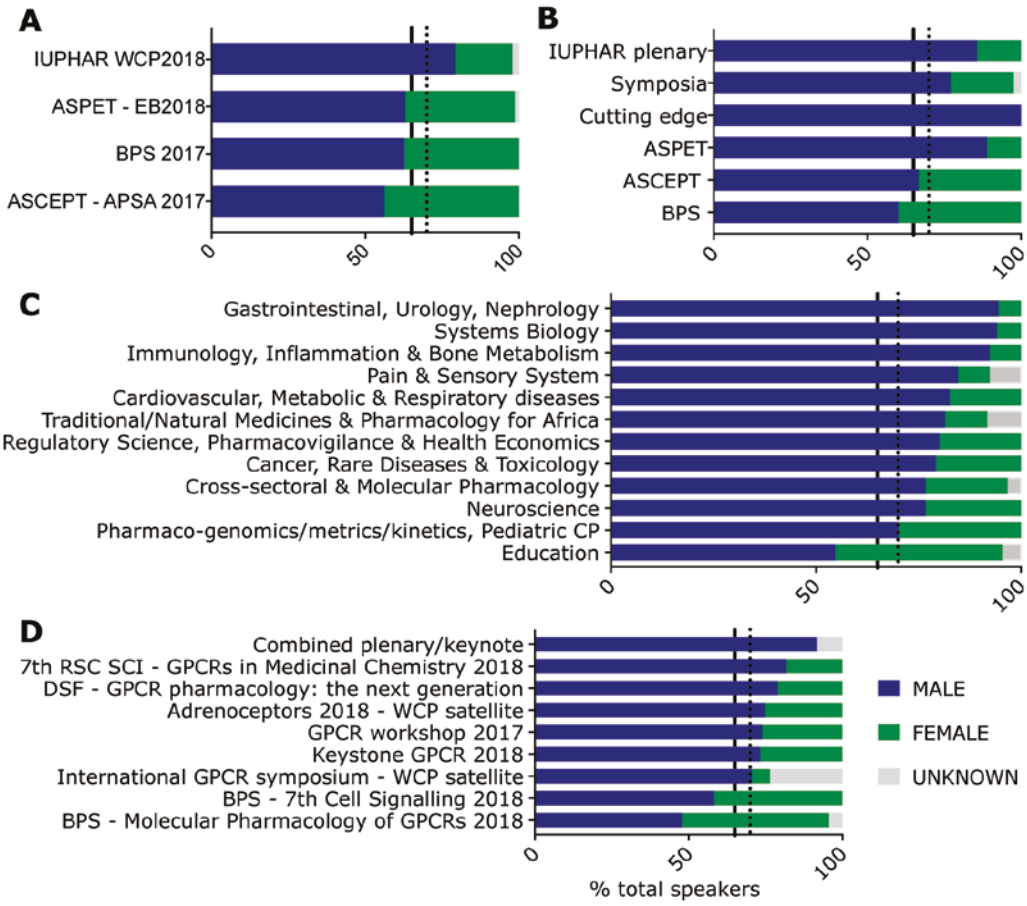

Figure 1. *Assessment of conference speakers based on gender. A) Invited speakers within large society meeting programs: British Pharmacological Society Pharmacology 2017, International Union of Basic and Clinical Pharmacology World Congress in Pharmacology (IUPHAR – WCP), Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) annual scientific meeting 2017 held jointly with Australasian Pharmaceutical Science Association (APSA), and American Society for Pharmacology and Experimental Therapeutics (ASPET) symposia within Experimental Biology 2018. B) Breakdown of invited speakers within IUPHAR-WCP 2018 session types and as award/plenary lectures within society meetings. C) Gender representation across different research themes within IUPHAR-WCP 2018. CP: clinical pharmacology. D) Gender of invited speakers within GPCR focused meetings. In each panel the solid vertical line at 65% provides a reference for male membership levels within the British Pharmacological Society. The dotted line at 70% indicates the British Pharmacological Society aspirational target for 30% minimal female participation across all activities. RSC: Royal Society of Chemistry; DSF: Danish Society for Pharmacology (Dansk Selskab for Farmakologi).*

AN ANTARCTIC EXPEDITION FOR WOMEN IN SCIENCE LEADERSHIP

Antarctica is the coldest, windiest, highest and driest continent on Earth, yet it is the unexplored nature of its landscape that is the defining characteristic. The Antarctic Treaty[1] which protects areas below 60° South latitude, represents 80% of the World's population, yet very few people have experienced Antarctica.

On Sunday 18 February 2018, I departed from the Southern tip of Latin America, set sail through the Beagle Channel and crossed the perilous Southern Ocean to Antarctica. The journey across the Drake Passage was not only the start of a 21-day expedition, but the culmination of a year-long leadership program for women in science.

79 global women in STEM and several thousand penguins, Cuverville Island, Antarctica. Photo credit: Oli Samson http://olisansom.com

KATHERINE DUNCAN

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.

The Gerlache Strait, Antarctica. Photo credit: Katherine Duncan

> "Homeward Bound is a ground-breaking leadership, strategic, and science initiative, set against the backdrop of Antarctica"

Homeward Bound[2] is a ground-breaking leadership, strategic, and science initiative, set against the backdrop of Antarctica. As a scientist, whose career spans three continents and 18 years so far, I was acutely aware of the imbalance of women in science leadership roles. Although improvements have been made in school education to encourage more girls into science, less women than men pursue science degree programs overall. For example, in the UK, the number of women enrolling in higher education science subjects has increased, however they only comprised 37% of the total for 2016/17[3]. It has been documented that socioeconomic, environmental, experiential and educational factors contribute to applicants choosing to study STEM (science, technology, engineering and maths) subjects[4,5]. The imbalance is amplified in leadership positions, with men often holding occupations that confer higher status, power and pay[6]. Homeward Bound seeks to address this, firstly by creating a global 1000-strong network of women STEM leaders and secondly by equipping this network with a strong foundation of leadership skills.

In March 2017, I was selected to join 78 other female scientists chosen from around the world through a rigorous peer-review process. The eleven months prior to Antarctica involved frequent teleconference calls with fellow participants while developing the four emerging components of the leadership program.

These included leadership development; scientific collaboration; strategic capability; visibility and science communication. I achieved these leadership goals using diagnostic tools with the support of life coach sessions to create a personal strategic map and foster new scientific collaborations.

The last four weeks of the program were comprised of a week in Argentina and three on board the MV Ushuaia in Antarctica. On this expedition, every day involved synthesising new collaborations, personal development and strategic direction. For example, a Science Symposium at Sea was held along with science-themed group discussions, my contributions particularly aligned with the oceans and human health group. The group also had the opportunity to visit five Antarctic scientific research stations, to engage with hundreds of scientists, including those at the British Antarctic Survey base of Rothera.

On the ship, there were approximately six hours of leadership program a day in addition to a landing. Photo credit: Oli Samson http://olisansom.com

Blue whale skeleton, leadership discussions and glaciers at Port Lockroy, Wiencke Island, Antarctica. Photo credit: Katherine Duncan

Microbiology at the Argentinian base, Carlini Station. Photo credit: Katherine Duncan

Impactful discussions were often held while sitting amongst penguins, sailing around icebergs or watching killer whales long after the program had ended for the day.

Homeward Bound provided space, time and a supportive network to enable an accelerated leadership strategy and develop a collective impact, all against the inspiring backdrop of the world's most remote continent.

My advice to early career researchers? Align your research career to your values, create a support network and be proactive to be the change you want to see. I have regularly focused on my leadership skills including being selected for the Scottish Crucible and training courses in academic leadership from Barefoot Thinking, MyConsultants and at the University of Strathclyde. Homeward Bound will run for a further six years and welcomes applications from women with a background in STEM. I am currently in the process of writing a blog about this life changing expedition, you can follow along with the journey at www.medicinesfromthesea.com/antarctica or through my tweets @kate_duncan.

Inside the Antarctica circle at the British Antarctic Survey base of Rothera, one of five scientific stations we visited. Photo credit: Ellen Moon

> "Align your research career to your values, create a support network and be proactive"

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RUTH LOWE

Ruth is a programme officer at the Academy of Medical Sciences with responsibility for the SUSTAIN, mentoring and INSPIRE programmes

SUSTAIN – ENABLING FEMALE SCIENTISTS TO THRIVE

> "We believe the programme is building a strong network of women researchers that will last far beyond the end of each cohort"

At the Academy of Medical Sciences, we have a commitment to developing talented researchers. To do this, we have created a range of innovative programmes of tailored support that respond to specific need.

The Academy has been proud to develop SUSTAIN as a response to a mounting evidence base that shows not enough women researchers in science are securing senior leadership posts in the UK. We believe a concerted effort is needed to ensure women are appropriately supported along their career trajectory to enable them to secure those senior positions.

SUSTAIN is a pilot programme, targeted at those researchers who have just transitioned from early career positions to independence, and aims to enable women to thrive in independent research careers. Since it launched in 2015, it has grown into a bespoke programme of training and support to develop participants' leadership and career potential.

It is a year-long programme which brings together a cohort of twenty women across scientific disciplines and institutes, creating a close-knit network where participants are "free from internal politics and competition", as one participant described it. "I found that liberating," she added, because "the group became a safe space, to discuss difficult things about work, and life in general".

An independent evaluation of the first two rounds of SUSTAIN has been completed by Dr Rachel Hallett, Kingston University and St George's University of London/Habe Consulting, and Dr Amy Iversen, King's College London. Dr Hallett worked on both evaluations and Dr Iversen led the first evaluation. It confirmed that after completing the programme, participants had improved in a range of psychosocial and work-related variables, such as burnout, job satisfaction, resilience, and self-compassion in comparison to baseline scores. Work-life balance showed a significant improvement, which is particularly positive, as this was the most common issue mentioned in applications to the programme.

Participants from both cohorts rated SUSTAIN very highly for 'enjoyability' and 'usefulness'. One participant told us that she had put herself forward for SUSTAIN because, "it seemed like the sort of thing I ought to do... and I am so glad I did". She continued "it has been a great year and has provided a confidence boost and support network at a time when I really needed it".

As well as providing support, training and guidance to the women who take part in SUSTAIN, one participant told us that she thinks the programme will affect the scientific community more widely. She commented that SUSTAIN "will have long term impact in creating a better (fairer and more inclusive) culture in science". To begin this culture change, we hope to catalyse the learnings from SUSTAIN and see it implemented in institutions across the country.

So, it's time to share how we did it.

Training

SUSTAIN is made up of several elements which together create a supportive environment where all scientists can flourish.

The cohort attends bespoke training courses to support their transition to independence.

We theme training courses around key challenges that women report when they apply to SUSTAIN: communication skills; resilience; leadership; network building, and career planning. Feedback has shown that participants rank all of the training courses equally highly.

One part of the programme that has been received particularly well is bespoke media training for women, where we take participants into television studios for a fully immersive experience. This forms part of our commitment to increase the number of women experts commenting in the news media – currently, men outnumber women experts 3:1 on news and current affairs programmes.

Support and networking

The programme puts a strong emphasis on the value of supportive networks, and each participant is matched with both a mentor from the Academy's Fellowship and a peer coach. They are encouraged to meet regularly, to build strong bonds and discuss the challenges they experience as women in science. Many of the mentoring relationships continue past the programme's end.

The success of the mentoring relationships hinges on the impartiality of the mentor – having someone senior, a Fellow of the Academy of Medical Sciences, from outside the mentee's institution and research area - allows for an objective and seasoned reflection of the mentee's situation and options.

One participant said she was apprehensive at first, as her mentor is "terrifyingly brilliant on paper", but said that "in person [the mentor] has been kind, generous with her time and gives the sort of no-nonsense responses that made me think rationally about where I am and what I need to do".

One theme that came out of the evaluation is that SUSTAIN creates a safe space, where participants are able to try new things, talk about challenges and work together to find solutions.

One participant commented, "I am so grateful, SUSTAIN has been a very valuable investment in me as a person and will strengthen me, help me find coping strategies and confidence to make and mark my way". Another added, "SUSTAIN has given me the self-belief and skills to put myself forward and make progress in my career. I think it will have a long lasting impact on my outlook, and I would highly recommend it to colleagues."

Our SUSTAIN mentors have a similarly positive view of the programme. Professor Moira Whyte FMedSci, University of Edinburgh, who chaired the reference group and is a SUSTAIN mentor, found it "a privilege and pleasure to be involved in the programme".

We believe the programme is building a strong network of women researchers that will last far beyond the end of each cohort. Please get in touch if you would like to learn more about how to embed elements of SUSTAIN into your institution, or to discuss our programme further.

> "The group became a safe space, to discuss difficult things about work, and life in general"

WEB LINK

acmedsci.ac.uk/grants-and-schemes/mentoring-and-other-schemes/sustain

MAILBOX

sustain@acmedsci.ac.uk

STEVE TUCKER

Steve Tucker is a senior lecturer in Pharmacology and Medical Science at the University of Aberdeen, where he heads the undergraduate Pharmacology programmes and the post-graduate Clinical Pharmacology programmes. As a current member of the British Pharmacological Society's education and training committee and a British Pharmacological Society Ambassador, one of Steve's interests is advancing teaching methods and approaches in pharmacology and in particular pharmacokinetics, which he teaches at both undergraduate and postgraduate levels. Music is a vital part of keeping his work and life balanced, and has been part of his life for as long as he can remember.

MUSIC, THE MEDICINE FOR MY MIND

I had reached the second verse of "Yesterday" when it started... My examiners, unable to contain their smirking, actually started laughing! Outraged, angry and upset, I stopped playing, stood up and walked out, all the while glowering as my mockers tried to regain their composure and professionalism.

I have never been a naturally talented musician, and had started playing the drums a few years earlier as a hobby and a stress outlet, but for higher music, I was required to play another instrument...the electronic keyboard. It was my preliminary exam performance on this instrument that brought such mirth to my examiners, and where I solemnly swore I would overcome my shortfall in talent through hard work, dedication (and a keyboard tutor). I was determined to prove my deriders wrong.

I formed my first band "SMS" when I was 13 with two close friends, where I played drums and we laboured through random songs ranging from "Flower of Scotland" to our own original material. Our intended first single "Debut" was a five minute long instrumental electronic chord progression, which varied depending on how much of it our keyboard player could remember! Maturity brought influence and inspiration from the 90s grunge scene, where my next band "Karma" played cover versions, primarily of Nirvana, and I tried very hard to emulate their drummer Dave Grohl's ferocity and metronomic timing. I grew and dyed my hair as a further attempt to be like my hero! Regrettably, my family always seem to find these photos to embarrass me with at gatherings, in particular those where I had the left half of my hair yellow and the other half pink. Hindsight suggests I looked less like a famous drummer and more like the famous drumstick lollypop!

In the remainder of my school years I was the drummer for "The Jellystone Bears" and we performed various gigs in the school and other local venues. We also did some recording in a local studio, and my fascination for this very experimental, scientific process was seeded. Having started University, I was invited to join a band called "9 o'clock shot" named after a Friday night ritual offered at a local bar, and in all honesty, we were amazing! As a group made up of 5 very different characters, our musical talents, influences and ideas combined with synergistic potency, and we all still firmly

9 o'clock shot promotional photoshoot 1996

believe we were ahead of our time. For most of my time as an undergraduate we played (at least) weekly across different venues in and around Aberdeen, enjoyed radio play and did some recording sessions in more professional, advanced and expensive studios (the latter continuing to fascinate me on account of its experimental methodology). Our mix of varied cover versions and ever growing catalogue of original songs attracted a small fan base, who would turn out religiously to watch us on our usual Sunday night slot, a marathon three hour set in the basement of a bar in Aberdeen city centre. Alas, all great things must come to an end, and sadly our momentum was lost

as members moved away for work, family, and real life, leaving us all to lament that we were the best band ever never to be discovered. I will always be thankful for my time with 9 o'clock shot, for the shared experiences, camaraderie and the dreaming, but also because the money earned allowed me to buy my first copy of Rang and Dale's "Pharmacology"! In the ensuing years, I was part of a few other bands, notably "Superstar" (an indie rock band), "The Beaker People" (a folk band) and "Permanent State of Arousal" (a heavy rock band), but gradually the time for such indulgences became restricted and my passion for a certain discipline studying drugs and how they work began to take precedence.

With drums not being the most portable instrument, or the easiest to practice without drawing complaints from the neighbours, I decided I would turn my very limited musical talent towards learning other instruments (guitar and bass). This was also a slap-back at those who had spent years tormenting me with the joke "what do you call a person that hangs about with a group of musicians?...A drummer".

While I can now play bass guitar to a reasonable level, I can only muddle along on its six-string relative, clearly proving the limits of my musicianship, which involves rhythm and percussion but little else besides. Indeed, some of the earliest forms of musical production are likely to have arisen from percussive striking of objects by early man, and that's about as far as my musical talents evolved. However, from the Stone Age to the modern age, I discovered the most amazing studio software package that transformed my laptop into a recording studio, which has transformed my approach to music and meant that I could make my mediocre guitar parts sound quite good. It allows me to lay down and mix vocals, chord progressions, loops, bass lines and drum rhythms and then go wild with effects, sequencers and synthesizers, transforming them from initial ideas and fumblings on the guitar to songs that I barely recognise I wrote. With all of the available options, each project becomes an infinite experiment, but differs from pharmacology as these are vast uncontrolled experiments with no requirement for n numbers, validation or peer-review, no funding pressure, time constraints nor budgeting; they are trial and error efforts and the results can be easily undone or altered with no consequence! For me, such process is the perfect foil for the strict

Makeshift home studio recording 2018

constraints of scientific research and the two complement each other harmoniously (pun intended). Interestingly, there is a certain mirroring between work and my musical output where stressful times tend to drive a darker and more introspective musical product, and this definitively shows the importance of music to my work-life balance by providing something different that I enjoy, and acting as a channel for stress or frustration. Currently, I am in the midst of finishing my first complete album recorded on my own, under the working title "Divisive Incitive", a 12-track demo of my musical musings on life, work and their associated pressures. So, while the days of complimentary drinks for the band, local pseudostardom/ notoriety and transporting my precious drum kit around may have gone, I am able to indulge my love for music in the comfort of my own home (more precisely my kitchen, where I won't disturb my wife and kids)!

As far as the conclusion of the opening story goes, inspired by the appalling attitude of the examiners, and after much grit and determination, I was awarded an A for higher music, something I took great pleasure in sharing with them whilst exaggeratedly laughing at them. That done, I headed off to study science.

> "It's the perfect foil for the strict constraints of scientific research and the two complement each other harmoniously"

ON PARLIAMENT, POLICY AND PHARMACOLOGY

> "I have often thought there are too few scientifically trained people in Government, it is clear that there would be challenges in increasing the quota"

Left to right: Michael Edward Preedy, Postgraduate student, William Harvey Research Institute, Queen Mary University of London; Maria Tsalenchuk, Undergraduate student, University of Leeds; Cai Read, Postgraduate student, University of Cambridge; Ajay Shah, Early Career student, University of Nottingham; Harriette Brennan, Undergraduate student, St George's University of London

WHAT IS VOICE OF THE FUTURE?

Voice of the Future is one of the most engaging Parliamentary events of the year where young scientists and engineers quiz key political figures at the Houses of Parliament about the science policy issues that matter to them. This event offers young scientists and engineers the chance to put their burning science policy questions to key political figures, through a unique opportunity in Westminster. Organised by the Royal Society of Biology on behalf of the science and engineering community, the annual event reverses the format of a Parliamentary Select Committee, giving a panel of early career scientists the opportunity to question senior figures from Parliament and Government on issues that matter to them[1].

The British Pharmacological Society called to its wider membership seeking volunteers from undergraduate, postgraduate, early career categories to come forward and take part in the event, and we were delighted to have five members get involved on the day! We hear from two of them here.

REFERENCES

1. https://www.rsb.org.uk/policy/policy-events/voice-of-the-future
2. CaSE | MPs to Watch [Internet]. [cited 2018 Mar 21]. Available from: http://www.sciencecampaign.org.uk/engaging-with-policy/science-in-westminster/mps-to-watch.html

I was privileged to attend "The Voice of the Future" event at Portcullis House on 13th March 2018, organised by the Royal Society of Biology. This event offered a meaningful platform for a diverse range of young scientists to question senior figures on issues at the heart of our professions.

As an early-career medical professional and pharmacologist, I take an interest in politics and policy because I appreciate the material role it plays in medicines and their development.

For me, attending this event afforded the opportunity to experience politics and politicians on a real level, removed from high-profile news stories picked up by the media. There are few opportunities in life where pharmacologists are able to scrutinise those that we elect to represent us face-to-face, particularly on matters relating to science. Though many anecdotally report that there are too few scientifically or medically trained MPs in parliament, recent data indicate that 103 MPs are from a science, technology, engineering, maths or medicine (STEMM) background[2]. Indeed, I took this as an opportunity to better understand the potential role of scientific thought in science policy making, something which was often encouraged during my time at King's.

Brexit and its impact on the biopharmaceutical industry was a recurring theme of the morning and it was interesting to gain a government perspective on the matter. The Minister of State for Universities, Science, Research and Innovation was keen to champion the UK government's industrial strategy. He highlighted the recent successful investments made by a plethora of biopharmaceutical companies, despite the UK's decision to leave the European Union.

To my surprise, I was humbled by the role of the MP. Facing a committee eager to ask difficult questions is clearly a daunting ordeal and I am certainly more appreciative of the work of MPs as a result of this event. Though I am both a pharmacologist and a medic in training, I am certainly not abreast of all matters relating to science. Whether it be on the regulation of medicines or rare minerals use in technology, it was rather impressive to see that the Minister was so well versed across the board, despite having no formal scientific training.

Although, I have often thought there are too few scientifically trained people in Government, it is clear that there would be challenges in increasing the quota. Realistically, scientists are absorbed in evidence-based decisions, and the reality of policy is that the views of the public may conflict with the data. Members of Parliament are elected to represent the views of their constituents, not drive decisions purely on evidence. For this reason, scientists may struggle in such a setting – a view that was corroborated by Members of the Science and Technology Committee.

I thoroughly enjoyed my morning at Parliament; the Speaker of the House of Commons introduced the event and spoke with great force and reminded us that there needs to be dialogue between those interested in science and our Government. This sentiment echoes my personal desire to continue to be involved in scientific policy. Though there are challenges for scientists, being able to advocate an evidence-based view on matters may help fuel a narrative where members of public are more attune to evidence too. ***–Ajay***

AJAY SHAH

Ajay graduated from King's College London in 2015 with a BSc in Pharmacology with an extra-mural year spent at the Wolfson Centre for-Age Related Disease where he investigated TRP channels. Having completed his degree, he went on to join inVentiv Health Commercial as a Graduate Consultant working with a range of biopharmaceutical companies. He is currently a second year medical student at the University of Nottingham, where he is continuing to develop his interest in pharmacology.

I thoroughly enjoyed the Voice of the Future 2018 event, held at Portcullis House. It was exciting to be able to sit in Parliament and hear from various MPs and scientific advisers, and to witness the engagement from a wide range of scientific Societies.

One of the things that I enjoyed the most about the day was being able to hear about the different areas of interest and concern from these different Societies and organisations, and people at different stages in their scientific careers, ranging from ethical implication of artificial intelligence, to mental health concerns and diversity in science.

I was lucky enough to be able to ask a question about depression in early-career researchers. I received a response from Dr Rupert Lewis (Director of Government Office for Science) about the worrying statistics of mental health problems in academics, and information from the foresight report into mental wellbeing and mental capital.

I learnt quite a few new things from the discussion topics, especially with regards to current areas of scientific focus for the Government. A particular question posed was about the Science and Technology select committee and whether they should have a scientific background, and also whether it is important to encourage science graduates to enter politics. The answers from the representatives there revolved around scientist's choices to enter politics and the need for research to establish why they don't. My experience at this event has most definitely motivated me to engage more with policy, where possible. ***– Harriette***

HARRIETTE BRENNAN

Harriette completed her BSc in Biomedical Science at St George's University and is now transferring into the second year of Graduate Entry Medicine at St George's. Harriette has a particular interest in neurology and completed neuroscience modules in the final year of her BSc as well as a research project in neuropharmacology. Following Harriette's research into tramadol-related deaths, under the guidance of Dr Caroline Copeland, she received a Young Pharmacologist Award from the Society during *Pharmacology 2017*. Harriette intends to continue research into opioid polypharmacy alongside her medical studies.

AN UPDATE FROM OUR MEETINGS TEAM

JOHN CHALLISS

Dr (R.A.) John Challiss is Professor of Molecular and Cellular Pharmacology at the University of Leicester and head of the Department of Molecular and Cell Biology. Although a biochemist by training, he is very much a pharmacologist by inclination and has been an active British Pharmacological Society member since 1988 (elected to Fellowship, 2016). His research has focused on aspects of G protein-coupled receptor regulation and signal transduction for >30 years. He has co-organised the seven British Pharmacological Society focused Cell Signalling meetings that have taken place to date (2005-2018) and is very much looking forward to welcoming colleagues old and new back to the 8th meeting in 2020.

LINDSAY MCCLENAGHAN

Lindsay joined the British Pharmacological Society in January 2018 following five years organising conferences and exhibitions at the British Society for Rheumatology. Prior to that, Lindsay organised awards shows, networking events and meetings for a publishing company, working with a range of association and corporate clients. Lindsay studied Events and Cultural management at the University of Ulster and spent the first few years of her career working in venues and at sporting events before moving to London. Her role at the Society is to oversee the events team and to deliver the Society's meetings strategy.

THE 7TH BRITISH PHARMACOLOGICAL SOCIETY FOCUSED CELL SIGNALLING MEETING

This event took place in Nottingham for the first time and was a huge success, welcoming 221 attendees – more than ever before. Professor John Challiss, one of the meeting organisers has offered his highlights of the meeting.

The meeting illustrated how incredibly dynamic our field is, with lots of new impetus and opportunities from the application of structural, imaging, and pharmacogenomic insights to pharmacology. A key takeaway message from the conference was that pharmacology as a discipline has to embrace everything that new technologies which provide structural details have to tell us about how receptors work and how drugs interact with receptors.

A number of the talks, including Patrick Sexton's Vane Medal Lecture, showed how structural information can really provide novel pharmacological insights. The true potential of these methods (crystallography, cryo-EM, NMR, molecular dynamics, etc.) is just being realised and pharmacologists need to continue to play a leading role in shaping their application. It was exciting to see how studies using the latest technologies, for example in high end imaging and ligand design, thrive on a bedrock of rigorous pharmacology – with the trusty organ bath still making an appearance at one point.

We were delighted by the consistently high quality of the speakers, both invited and selected for short communications. Patrick Sexton provided a tour-de-force on structure-function relationships at the GLP-1 receptor, Martha Sommer presented her beautiful work on understanding receptor-arrestin interactions, Sophie Bradley, Lora Heisler and Laura Bohn led the way on translation to *in vivo* models, while Graeme Henderson gave a fantastic perspective on opioid receptor tolerance, effortlessly bridging the clinical context and molecular mechanisms.

Two excellent short communications, from Laura Kilpatrick and Sam Groom, showed the quality of our past and present British Pharmacological Society AJ Clark students. The vibrant poster session was another reminder that our field is in good hands with the emergence of the next generation of Principle Investigators, many of whom are from (or have adopted) a UK pharmacology base. Finally, the meeting continues to provide a friendly meeting space to share excellent science. We are especially proud of the inclusivity of the meeting, where every delegate can feel they are making a contribution.

The British Pharmacological Society would like to thank Professor Challis and the scientific organising committee for their hard work and support of the meeting. If you would like to organise a meeting with the Society, contact meetings@bps.ac.uk.

A tweet from poster prize winner Patricia Centeno.

BILL BOWMAN PRIZE LECTURESHIP

Dr Aisah Aubdool was recently awarded the Bill Bowman Prize Lectureship for 2018. Following presentation of her work in Glasgow and London for the Society, Dr Aubdool took time to reflect on the award and lectureship.

Winning the prize was a magnificent honour! I was totally surprised, especially as I am one of the youngest basic pharmacologists to have been awarded this prize. It is a great privilege that the British Pharmacological Society has recognised the research I conducted in Professor Susan Brain's lab at King's College London over the last six years. I see this prize as encouragement for me to work harder, with a step closer to those academic dreams.

In this lecture series, I presented the work I conducted during my PhD where we discovered that the neuronal ion channel TRPA1 acts as a primary vascular cold sensor. We identified that TRPA1 activation is essential in initiating the local cooling response and subsequently, in the vasodilator response which is important to protect against local cold-induced injury. The activation of sensory nerves releases the neuropeptide CGRP, which is a potent vasodilator in the microvasculature. Whilst the activity of TRPA1 to release CGRP from sensory nerves appears to be site and stimulus specific, the role of CGRP, more generally when released endogenously or administered exogenously, appears to be pivotal in cardiovascular disease.

Further work in my postdoctoral project in collaboration with Novo Nordisk has revealed that the chronic delivery of a long lasting CGRP analogue protects against hypertension, reducing blood pressure, vascular, renal and cardiac hypertrophy, fibrosis and oxidative stress. These protective effects are consistent with further experiments in a model of heart failure where the CGRP agonist preserves cardiac

function, and prevents cardiac remodelling and limits damage associated with the progression of heart failure. My current findings provide evidence for a potential novel therapeutic strategy, with the concept that CGRP agonists are anti-hypertensive and cardioprotective, with limited adverse effects when treatment starts early onset of hypertension or heart failure.

I would like to thank the person who nominated me and I am deeply grateful to the British Pharmacological Society for giving me a platform to be able to share my research on the role of sensory nerves in the cardiovascular system. I also had the opportunity to visit several research groups, networked with both undergraduate and postgraduate students and met some amazing scientists who made this award an unforgettable experience. Thanks to the added interest in my work resulting from this opportunity, I was invited to present my work at other meetings.

I strongly recommend applying for Society prizes. Winning the Bill Bowman Travelling Lectureship Prize has been hugely satisfying and an inspirational journey, one which I will look back on fondly in the years to come.

If you would like to apply for, or nominate a colleague for an award, visit www.bps.ac.uk/membership-awards.

AISAH AUBDOOL

Aisah is a postdoctoral researcher at the William Harvey Research Institute, where she studies the role of endothelial C-type natriuretic peptide in angiogenesis and vascular remodelling in the lab of Professor Adrian Hobbs. Prior to this, she graduated with a BSc (Hons) in Pharmacology and completed her MRes and PhD studies in Cardiovascular Medical Research under the supervision of Professor Susan Brain at King's College London. Aisah has been a British Pharmacological Society Ambassador since 2015 and is a member of the Society's *Pharmacology Matters* Editorial Board.

ABSTRACT REVIEWERS REQUIRED

We are looking for volunteers to support in the abstract review for *Pharmacology 2018*

Enthusiastic Society members with an interest in any area of pharmacology are encouraged to apply. Applications are accepted for the following two review opportunities:

- Initial abstract review in September 2018
- To chair and review abstracts at the conference for publication and prizes

Please note you must have reached the early career level (two years post-PhD) to be eligible to apply. Guidance on how to assess abstracts will be provided.

Benefits to you

- Opportunity to shape the annual meeting programme
- Insight into current research undertaken in your field
- Recognition as a reviewer in the conference programme booklet
- Growing your involvement in the Society

To apply, please email meetings@bps.ac.uk

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