PN
Physiology News
Issue 109 / Winter 2017

Future physiologists

Early career special issue

Experimental models in physiology

27 – 29 June 2018 | University of Exeter, UK

The Mighty Mouse and the might of other models

- Why is the mouse not so mighty?
- Complementary models

Pathophysiological models: Cells to complex systems

- Insights from animal models of human disease
- Towards human models

Future directions: Opportunities and challenges

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The Physiological Society

Physiology News

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Please email Julia Turan at **magazine@physoc.org**

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Welcome to the Winter 2017 edition of *Physiology News*

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News & views

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Cover image: Cover design by Matteo Farinella

Physiology 2019

The Society's Annual Conference

Aberdeen Exhibition and Conference Centre, UK

8–10 July 2019

www.physoc.org/physiology2019

The Physiological Society

Hannah Marie Kirton

Cardiovascular Research Fellow,
University of Leeds, UK

Affiliate Working Group,
The Physiological Society

It has finally arrived! No not Christmas, but a special Early Career Researcher edition of your favourite magazine! The Affiliate Working Group has had the enviable pleasure of guest editing the Winter 2017 edition of *Physiology News*. I've been thrilled to lead on this endeavour.

As our front cover illustrates, the road to academic success is challenging. For those pursuing a career in academia, the linear path from PhD to postdoc to lectureship now exists only for a select few. In a turbulent time of declining funds, Brexit negotiations and debates over metrics (namely impact factors and citation rates), early career researchers face more time in their glorious white lab coats. One thing however is certain, early career researchers must clear their own path to success, and whilst there may be disheartening stumbles, fame (but not fortune) for those remaining in academia can be achieved.

In this edition, we've chosen to highlight early career research success, including a feature interview from a L'Oréal UNESCO Fellowship awardee, Dr Annie Curtis. Annie shares her journey, providing realistic tips and advice on fellowship applications and how to be optimistic in your approach. Furthermore, Jo Edward Lewis compiled an article that details how there is no 'one size fits all' for scientists, demonstrating the diversity within scientific careers from undergraduate to lecturer. In 'The postdoc problem', I highlight the good, the bad and the ugly of academia and what it is like to be an early career researcher, outlining what is required of academia to recognise and facilitate talented, thirsty researchers in their pursuit of success. Kim Barrett, Editor-in-Chief of *The Journal of Physiology*, also lends her insight on the key factors leading to publication success.

Despite the challenges ahead, I see outstanding, inspiring early career research that is highly recognised in physiology. In this issue, we display several examples - Jessica Piasecki, at Manchester Metropolitan University, emphasises the importance for elite female athletes to lead healthy lifestyles, and the importance of balancing training needs whilst maintaining bodily health and a regular menstrual cycle. Emmanuel Amabebe, at the University of Sheffield highlights how C-section impacts on the early-life microbiome and immune system, and influences disease susceptibility. We also have a revealing article explaining the key questions about blood sampling sites. This is important in terms of experimental design, and influences data interpretation, so do watch where you put that cannula!

The Affiliate Working Group would like to thank The Physiological Society for providing the opportunity to guest-edit and share our thoughts with Members. Although being early career researchers is a challenge, it has never been a more exciting time to be the future generation of science. Physiology offers a multitude of opportunities, exciting prospects, cutting edge research tools, and a great foundation for collaboration and outstanding research.

So go find yourself somewhere quiet, and enjoy reading this issue over a warm cup of coffee, hopefully while you're at our Leeds conference, *Future Physiology*.

'Although being early career researchers is a challenge, it has never been a more exciting time to be the future generation of science'

Ensuring physiology flourishes

David Eisner

President, The Physiological Society

'It goes without saying that the future success of physiology lies entirely within the hands of today's early career researchers'

It seems difficult to believe that I am more than halfway through my term as President. I have been persuaded by the powers that be at *Physiology News* that it would be good to institute a Presidential column. The deadline is now only a few days away and I feel like a vicar on a Saturday night desperately thinking of something to write.

A major thing that has exercised me, not just in my role at The Society but also in my own laboratory, is the question of 'What is Physiology?' The Society has begun to develop a new five-year strategy, and the first meeting of its steering group was devoted to trying to agree a definition. When I began my academic career, physiology could be defined, perhaps circularly, as 'that which is done in Physiology Departments'. In the subsequent 30 or so years, departments of Physiology have virtually disappeared. Many, possibly even more, people are doing physiology now but do not always realise it. My own university, like others, has reorganised into organ- and disease-based Divisions, and members of The Society can be found in 10 of these Divisions.

There are, of course, arguments in favour of an organ-based structure. As someone who works on the heart, I benefit from mixing with colleagues who are biochemists, pharmacologists, geneticists, etc. On the other hand, I still feel that I have much more in common with other physiologists even if they do work on the kidney, brain or whatever other body system. Not only do we share a conceptual approach, but the experimental techniques are often very similar. Because of the structure, my own PhD students naturally gravitate to cardiovascular meetings but, gratifyingly, are always pleasantly surprised by how much they get out of meetings of our Society.

There is nothing new, of course, about a concern for the fragmentation of physiology. Ole Petersen, a previous President, wrote in 2000 (Petersen; *Eur J Physiol* **441**, 725–725), at a time when the loss of separate physiology departments was already underway, 'Physiologists should live in their own house, but collaborate extensively with other disciplines'. He also pointed out that physiologists, for a variety of reasons, suffer from a lack of self-confidence compared with their molecular colleagues. Another of my predecessors, Denis Noble (Committee Secretary, before the post of President was established), has argued consistently that our physiology should not simply be regarded as being slavishly controlled by genes (Noble *et al.*, 2014; *J Physiol* **592**, 2237–2244).

A lack of identity in the physiological community is also of concern to our Society. At a time when most physiologists worked in physiology departments, it was natural to become a member of The Society. Indeed, when I joined the staff of the Department of Physiology at UCL, an item on the agenda of staff meetings was always what was happening at The Society. With departmental reorganisations, there is a danger that the organ- and disease-based societies and their meetings are becoming the new defaults. Whatever the cause, The Physiological Society realises that it cannot afford to be complacent about attracting and retaining members.

It goes without saying that the future success of physiology lies entirely within the hands of today's early career researchers. Affiliate Members of The Society contribute greatly to the life of The Society and its meetings. I am delighted to see that they have organised a two-day *Future Physiology* meeting to be held in Leeds, which might be occurring as you read this issue.

The loss of separate departments of physiology has occurred to a much smaller extent in Germany. This may be a consequence of the fact that physiology has a defined identity in the medical curriculum there. This, in turn, contrasts with the situation in the UK where the adoption of problem-based learning and integrated courses has taken responsibility for the medical curriculum away from the practitioners of individual subjects.

I end with a shameless advertisement. There will be time to discuss differences across Europe as well as enjoy first-class physiology when we join with our colleagues from the German and Scandinavian Societies as well as the Federation of European Physiology Societies in the first of a series of *Europhysiology* meetings in London (14–16 September 2018). This meeting will be like one of our usual Annual Meetings but with the bonus participation of many of our European colleagues. See you there!

Henry Lovett

Policy and Public Affairs Officer, The Physiological Society

Brexit already causing problems – Policy team highlights the issue to politicians

As the negotiating process around Brexit grinds on, both between the United Kingdom and the European Union, and domestically throughout British politics, the level of uncertainty around the outcome only seems to be rising. While we have not left the bloc, and will not do so until March 2019 (at the earliest), this uncertainty is already impacting upon people and industries in the UK. The science sector was fairly united in wishing to remain in the EU. However, the vote was to leave, so now the aims of the sector are to make both the process and outcome of leaving the EU as smooth and trouble-free as possible, and to benefit from the opportunities presented by a new regulatory regime.

It is heartening that the government has recognised the importance of science, technology and innovation to the UK, and statements put out show the intention to make the UK one of the world's brightest science hotspots. This support is welcome, but has not translated into definitive reassurances about the nature of the future working relationship with the EU, and the rights of foreign scientists in the UK. It is understandable that the government cannot prejudice negotiations by making unilateral promises, but they must also be aware of the impact of their drip-feed of information on the situation back home.

Scientists, universities and companies are already feeling the effects of the Brexit vote. The Society has reached out to its Members to hear their stories of problems faced due to Brexit uncertainty. These case studies, along with supporting information on the views of scientists and the public, have been published in a booklet, available on our website, which highlights the negative effects of this uncertainty with real stories and real faces.

Some of the problems that Society members have been facing include:

- Having to cancel EU funding applications as the term of the grant would go past our EU leaving date.
- Job offers being turned down by EU researchers, including one describing the UK as 'not truly open for scientific business'.
- The weak pound making purchases from overseas much more expensive.
- EU researchers not seeking new jobs or contract extensions in the UK.
- Cross-border collaborations between Northern Ireland and the Republic of Ireland being cancelled over the particular uncertainty of the Irish situation.

The principal cause of the worries felt by EU citizens over the viability of their future life and work in the UK is the impression given by our government of a likely 'hard Brexit' outcome, or even no deal being reached.

We have been using these case studies to underline their message to politicians. The recent party conferences provided the perfect opportunity to reach out to MPs and explain the difficulties being faced by scientists. We have met with politicians from all parties to put across our message, and have given the booklet of case studies to the science minister, Rt Hon Jo Johnson MP. Other organisations from across the science sector are reporting similar situations faced within their disciplines. Hopefully the strength of these united messages will catalyse the efforts of the government to give tangible reassurance to scientists about the support they will receive over the course of the Brexit process, and to EU nationals about Britain's desire for them to stay in the UK. This would be a positive way to help one of the UK's key sectors and display some good faith to the valued foreign nationals who contribute their efforts to it.

Bringing you snippets of the latest intriguing research

Needle-covered patch dissolves excess body fat wherever you stick it

A patch of microneedles that dissolved body fat locally by converting energy storing white fat into energy burning brown fat has been trialled in mice. The patch delivers 'browning' drugs via nanoparticles to reduce whole-body side effects, and has reduced fat by as much as 20 percent.

DOI: 10.1021/acsnano.7b04348

Evidence shows natural selection is working right now to cull bad genes in humans

In a genomic study using data from 170,000 people, researchers are looking at evolution in action. They have found that genes related to Alzheimer's disease, and to a stronger nicotine addiction, were less prevalent in the older population – showing a negative association with lifespan. This indicates that these traits may be slowly selected out of our modern human population.

DOI: 10.1371/journal.pbio.2002458

Gut microbes could be triggering relapses of multiple sclerosis

Gut bacteria that are four times more abundant in MS sufferers could be triggering relapses by interacting with the immune system, triggering the appearance of inflammatory cells and reducing the number of regulatory, protective cells. Two separate studies found that mice transplanted with the microbiome of MS sufferers were more likely to develop brain inflammation.

DOI: 10.1073/pnas.1711233114
DOI: 10.1073/pnas.1711235114

New type of diabetes being misdiagnosed as type 2

Type 3c Diabetes occurs when pancreatic function is disrupted after a pancreatic injury such as a tumour, or inflammation. Looking at 2 million records from patients in England, researchers have found Type 3c Diabetes to be more common than Type 1, and often misdiagnosed as Type 2, which could impair treatment.

DOI: 10.2337/dc17-0542

Physiology Feed continues on page 11

Getting your first paper published – shedding light on unwritten rules

Kim E Barrett

Editor-in-Chief of *The Journal of Physiology*, University of California, San Diego

Authorship

Writing a paper can be intimidating, but there is no 'one way' to do this. Start by deciding the authors of the paper as early as possible - this is important to avoid clashes or disagreements in the future. Authors should always be notified of any submission on which they are an author, as they are accountable for what is being published and will be contacted if ethical issues arise. Issues about patents and copyright should also be considered, as certain stakeholders may legally need to check your paper before it is published.

Choosing the right journal

A journal is like a community, so choosing the right journal is important. You want your work to be appreciated by the right editors, referees and target audience. Decide on the journal before beginning the write up, as this can help the manuscript comply with certain journal guidelines and formats (e.g., some journals may prefer a more translational style of writing, and others are much more focused on basic research). Be sure to read the journal guidelines and scope to make sure your paper is appropriate for submission and that you have conformed to their policies on animal/human ethics and study design.

Writing your paper

A good paper should tell a story – it should have a well thought-out hypothesis, a sound experimental design, clear tables and figures, and should contribute to the understanding of the subject area. The essential parts of a manuscript are the introduction, methods, results and discussion.

You should write up the methods section as soon as possible and start writing up the results as you obtain them throughout your research. Some journals, such as *The Journal of Physiology*, have no page limits or charges, so you won't have to limit what is written in this section. The methods should describe the study design and be detailed enough for others to repeat the experiment. It is also compulsory to include, in all reputable journals, the appropriate approvals for animal or human studies. Adding the results should then tell the story of what your research has found.

The discussion is the hardest section for new researchers to write. This section is to 'discuss' what has been found, rather than repeat what was presented in the results. The most important thing to write is whether you have proved or disproved your hypothesis. The phrase 'We are the first to show...' should be avoided, as it's already assumed that the paper is showing novel research (and you can never be completely sure). The discussion should link the hypothesis from the introduction to the conclusion as well as be speculative and look at the wider significance of the findings.

The introduction should be written last and has the aim of getting the reader interested in the topic. This section gives the readers the chance to familiarise themselves with the subject area and gives a good overview of the research. To encourage readers to read on, avoid a summary of results in this section. Writing this section last will also ensure that you only introduce the area of the field on which the results build - not your entire knowledge of the subject as a whole.

Once you have finished the paper, a good title and abstract must be written - these elements are what the majority of readers will see first, and may be the only parts they see! Keeping these concise and specific will help with the discoverability of the paper.

Responding to reviewers

After submitting your paper (avoiding any sloppy mistakes) you have the excitement of anticipating the reviews from experts in your field! The major reasons for a submission being rejected include a paper being inappropriate for the journal, a poorly designed study, a poorly written paper, or a paper being merely confirmatory or incremental.

If your paper is returned for revision, be sure to address ALL comments from the reviewers and thank them for their time. Try to understand what the reviewers are really saying - if they did not understand your work, is it because you didn't present it clearly in the first place? Don't argue with the reviewers but stand firm if you truly think this is the right thing to do.

Ethical issues

Ethical cases are increasing in scientific literature, so here are some tips to help avoid ethical pitfalls. Do not beautify blots or images by editing the contrast or removing blemishes, and be sure not to copy exact wording from another publication, even your own.

Common ethical issues which arise are figure manipulation, data fabrication/falsification, plagiarism, and animal and human welfare concerns. Many journals routinely use software to check for duplicate manuscripts and alterations in figures.

Closing thoughts

Getting published is an essential part of a researcher's career. It establishes expertise and is crucial for grant applications and career development. With these tips, you are hopefully a step closer to getting your work published and on the route to success! Note that you can send any pre-submission enquiries to our publications team at *The Journal of Physiology* (**jphysiol@physoc.org**) or *Experimental Physiology* (**ephjournal@physoc.org**).

Journal myth buster: 10 reasons why you should submit to our journals

In the 2017 membership survey, we asked members whether they had submitted to one of The Society's three journals. Although many had, we were interested to hear the reasons why some of our members had not submitted to our journals. Many cited good reasons such as they considered themselves to be at too early a stage in their career, their data were not ready, or they were retired or not research-active in physiology.

However, there were several reasons given which we would like to challenge and urge you to think again! We hope that this will address some of these issues and encourage more members to submit in the future. Email Sally Howells at **showells@physoc.org** with any further questions.

I cannot afford it	*Physiological Reports* does charge an open access fee, but *The Journal of Physiology* and *Experimental Physiology* do not impose any fees for submission or publication.
The Impact Factor isn't high enough	*The Journal of Physiology* has the second highest Impact Factor (IF) for a general physiology research journal. *Experimental Physiology*'s IF has shown growth year on year, and *The Journal of Physiology*'s IF remains stable year on year.
The research I am doing is of too low quality	*Physiological Reports* is likely to accept all papers that are within scope and that show sound scientific physiology research, whether the results are positive or negative. Its philosophy is that all properly conducted research is of real value.
I don't know how	It's easy! Just go to **www.journals.physoc.org** find the journal and follow the 'submit an article' link.
The acceptance rate is too low or rejection rate too high	Statistics are available online. Please check the latest information. While our editorial process is indeed rigorous, we might accept more than you thought!
I prefer to submit to sub-speciality journals	You might think that people in your field are more likely to read them this way. Although this could have been the case in the past, people now use a keyword search to find papers, meaning that a paper in one of our journals is just as likely to be 'found' as one in a specialist journal.
My work is not within the scope of the journals	Whilst some responders highlighted that they work on teaching (which we don't cover) we are concerned that some people thought that their work would not be suitable, when it would be of interest to us. In particular we are concerned that they did not think we cover: • Mathematical studies – *The Journal of Physiology* has a 'computation physiology and modelling' section. • Integrated renal physiology – we don't publish a lot of renal studies, but we are actively seeking new submissions on this topic. • Invertebrate and non-human studies – we recently updated our scope to highlight our interest in non-mammalian model organisms. • Neuroendocrinology – as with renal physiology, this is an area that we are particularly keen to encourage. If your submission is not suitable it will be triaged and you will receive a 'reject' or 'reject with referral to *Physiological Reports*' decision within lfive days (one average). Alternatively, our journals offer a 'pre-submission' service, so if you are unsure, please get in touch with journals staff prior to submission to check suitability.
Due to past experience	Author feedback is generally very positive. If you have had a bad experience, we hope it was an exception and would very much like to know what we can do to improve the process.
I've already submitted my paper to a preprint server	Not to worry! We do not class this as a formal submission, so as long as it has appeared on a not-for-profit, subject-based preprint server (e.g. bioRxiv), you are free to submit to our journals. Just mention this in your submission.
I had not thought of it	We hope you will do now!

Research in action: Vacation Studentship Scheme case study

Renata de Sousa Brites

Great Ormond Street Institute of Child Health, London, UK

The studentship allowed me to appreciate the potential of the scientific process and supported my career aspirations in an unexpected way. It made me more and more curious about new ways of bringing scientific rigor and methodology into the public sphere, for example in the form of informed policy-making, democratisation of science and technology, capacity building for development or cultural and public engagement. I would definitely recommend the studentship to all students who wish to improve their practical lab skills but mostly experience the many stages and challenges of carrying out an independent and more ambitious piece of research. Not only does it gives you the opportunity to start mastering many different transferable lab techniques and see science happening – which is super exciting! It is also an important exercise in agility, rigor, scientific integrity and critical understanding of the experiment itself. It equips you with the capacity to logistically organise and optimise a piece of research, multitask more accurately between distinct procedures, understand the purpose and effect of each technique and ultimately conduct your practical work more intuitively.

Being surrounded by research in action is also a refreshing reminder of how important it is to deliver and work towards science that prioritises validity and purpose, whilst reconciling with its unpredictability and the biases we inevitably carry with us. Furthermore, it is also incredibly rewarding to learn from experienced researchers and discover how much collaboration is necessary to sustain a successful lab and, ultimately, a scientific community. It is definitely a constructive experience, as you become exposed to the different layers of research, expand your scientific curiosity and start to understand how to carefully develop a hypothesis-driven project.

I am truly grateful to my supervisor for the continuous guidance and to The Physiological Society for this opportunity.

Congratulations to our newly-elected Fellow Members

The review panel, members of the Membership & Grants Committee, were impressed with how well the applicants demonstrated wide engagement with The Society's activities. The Trustees of The Society congratulate these members on their achievement. Full details can be found at **www.physoc.org/fellow-membership**

Those elected to Fellowship are as follows:

- Julien Baker, University of the West of Scotland, UK
- Richard Barrett-Jolley, University of Liverpool, UK
- David Bates, University of Nottingham, UK
- George Billman, Ohio State University, USA
- Stuart Bund, University College Dublin, IE
- Ray Carson, Aston University, UK
- Graham Christie, University of Dundee, UK
- Graham Collingridge, University of Toronto, CA
- Roger Dampney, University of Sydney, AU
- Dirk Feldmeyer, Research Centre Jülich, DE
- Valerie Gladwell, University of Essex, UK
- Barry Hirst, Newcastle University, UK
- Christopher Huang, University of Cambridge, UK
- Malcolm Jackson, University of Liverpool, UK
- Roland Jones, University of Bath, UK
- Sandra Jones, University of Hull, UK
- Cornelis Kros, University of Sussex, UK
- Rohan Lewis, University of Southampton, UK
- Mike Ludwig, University of Edinburgh, UK
- Walter Marcotti, University of Sheffield, UK
- Richard Martin, The University of Iowa, USA
- Lars McNaughton, Edge Hill University, UK
- Toby Mundel, Massey University, NZ
- Myra Nimmo, University of Birmingham, UK
- Ibiyemi Olatunji-Bello, Lagos State University, NG
- Ole Paulson, University of Cambridge, UK
- Marc Poulin, University of Calgary, CA
- Harry Rossiter, David Geffen School of Medicine at UCLA, USA
- Norman Saunders, University of Melbourne, AU
- Michael Shipston, University of Edinburgh, UK
- Mike Snow, University College Cork, IE
- Paul Squires, University of Lincoln, UK
- M-Saadeh Suleiman, University of Bristol, UK
- Pawel Swietach, University of Oxford, UK
- Paul Thomas, University of East Anglia, UK
- David Thwaites, Newcastle University, UK
- Michael Tipton, University of Portsmouth, UK
- Christopher Torrens, University of Southampton, UK
- Stephen Waxman, Yale University, USA
- Håkan Westerblad, Karolinska Institutet, SE
- Stanley White, Ross University, USA
- William Winlow, NPC Newton, UK

What are your thoughts about the International Union of Physiological Sciences?

Our stand at IUPS 2017: The Rhythms of Life

Sue Wray

University of Liverpool,
Liverpool, UK

Since 1889, the International Union of Physiological Sciences (IUPS) has championed physiology without borders and worked to remove political barriers from physiologists interacting and attending meetings. However, IUPS is about more than attending (or not) an international meeting every four years.

As the recently elected First Vice-President of IUPS, I have been learning more about what else IUPS does. It runs workshops, holds regional meetings, and exchanges of scientific equipment and advice, and provides mentoring. It has a council with an executive committee, a board of The General Assembly which contributes additional participation and The General Assembly, which meets every four years at the quadrennial IUPS meetings, and is the deliberative body of the Union.

I also learned that 'there is no money'. The new Council's plan includes increasing the financial base of IUPS, from which increases in its activities can flow. IUPS co-owns the publication *Physiology* with the American Physiological Society. Establishing a new journal, *The Physiome*, should also contribute to financial security.

Particularly important is that IUPS helps to better communicate the importance of physiology as a subject, and to engage and communicate more efficiently with not just its member societies in 80 or so countries, but also with the members in those societies. This is my reason for writing this piece. I want to know what you like about IUPS, what you think it could do better, what its role should be and what would make you want to attend its next meetings (Beijing 2021 and Munich 2025)?

For me, IUPS congresses have always been something to look forward to. They are not only a great opportunity to talk science, but also to meet other physiologists from across the globe. It is the only meeting I go to where I know I will meet face to face with colleagues from Africa and South America, for example. It also goes some way to decreasing the vast differences in the opportunities to undertake research and teaching in physiology across the world. Collaborations and exchanges can be started, offers of mentoring and support given and differences made. The IUPS team will be building on Denis Noble's legacy and working to 'return physiology to centre stage', as it becomes clearer that despite the mountains of molecular data, only when we appreciate their functional importance, i.e. physiology, will humankind benefit. What's not to like?

Learn more at **www.iups.org**

Over 30,000 published studies could be wrong due to contaminated cells

Immortalised cell lines can contaminate exposed cell cultures in labs. Since the 1950s, 451 such contaminated cell lines have been part of 33,00 studies, according to a search in the research database, Web of Science.

DOI: 10.1371/journal.pone.0186281

A protein has been caught conducting electricity, and scientists are really excited

Using a device that locks individual molecules between electrodes (recognition tunnelling) researchers found that a protein, integrin protein domain alphaVbeta3, conducts electricity. If this is confirmed in other proteins, it would allow researchers to identify single proteins by sensing electricity.

DOI: 10.1088/2399-1984/aa8f91

Mathematical proof that it's impossible to stop ageing

A mathematical model of cellular competition, ageing and cancer has shown ageing to be inevitable. We age because our cell types become 'sluggish' and stop proliferating, but cells that do proliferate well are more likely to cause cancer – leaving us stuck in a catch-22.

DOI: 10.1073/pnas.1618854114

3D map of mouse neurons reveals complex connections

A project is underway to create a 3D map of the mouse brain. Researchers got mouse neurons to express a fluorescent protein and scanned the brains. So far, 300 neurons are in the map which has revealed new structural information. Plans are to add another 700 in the next year.

DOI: 10.1038/nature.2017.22908

Infusions of young blood tested in patients with dementia

In a small, controversial study, researchers infused 18 Alzheimer's patients with plasma, blood from which the red cells have been removed. The participants didn't have any adverse reactions and while there was no significant effect on cognition, daily living skills tests both showed significant improvement.

DOI: 10.1038/nature.2017.22930

Reports of recent Committee meetings

The purpose of these short updates is to keep you informed about the work of our Committees. The following summaries detail the meetings of the past few months.

Council Committee

The main points of business at the September Council meetings included an update from the Property Strategy Working Group, Chaired by President-elect Bridget Lumb. At this meeting, Sue Cleverdon from Cleverdon Associates presented the Phase 2 Report, which was divided into external and internal repairs. The external repairs which are required to preserve the building, a critical asset, include several significant areas of spend such as the replacement of the roof above the fourth floor, the second floor flat roof area and the ill-fitting and incomplete windows across the frontage. The internal works required to optimise income from the building would result in The Society occupying the Basement, Ground Floor and First Floor. This would leave the Second, Third and Fourth Floors, which could be used to generate rental income from tenants. The building work is scheduled to start in the New Year and should be completed by the end of April, with the external and internal works being completed simultaneously.

A proposal was tabled for the development of a new website. Council agreed that in order to support the new Vision of *Physiology Flourishing*, it was essential that The Society developed a modern, dynamic website where discoverable, shareable and interactive content could be published to showcase physiology. The project would be led by an internal Web Project Working Group. A Trustee Focus Group will feedback on the navigation and design. It was also noted that *Physiology News* articles were attractive to a general audience and ought to be showcased on the website as a searchable format - possibly a microsite.

Risk management was also on the agenda. The Board reviewed and signed off the Risk Policy which had been drafted in accordance with the Institute of Risk Management publication *Risk management for charities, Getting started: a supplementary guide* and *The Good Trustee Guide* by Anne Moynihan and reflected the approach to risk management to be as much about taking risk for innovation and opportunity as much as safeguarding.

The 'risk register' was put under the spotlight, and the Trustees reviewed any risks where the residual risk score was red (high), or where the difference between the target risk score and the residual risk score was six or above, and considered the most appropriate action.

A skills audit framework was also approved, and a gap analysis is underway to help inform the most suitable requirements for the recruitment of The Society's first External Trustee.

Membership & Grants Committee

The Membership & Grants Committee met in October for the second of their biannual meetings.

The agenda included a review of membership and travel grant (including lab visits) uptake and reporting, Society Rep activities, the departmental seminar scheme and 2018 plans. The committee dedicated time to consider (i.) the 'member journey' from undergraduate through to retirement, identifying new activities that may enhance engagement of specific membership categories and ensure membership progression, and (ii.) how best to engage A-level students and promote 'physiology' to these future undergraduates. An action plan resulting from this will be developed in collaboration with the Education and Outreach Committee.

Membership numbers were, as always, a focus, and it was noted that there had been a slight decline in the number of Full Members. This is being investigated as some of it may be linked to Members who have not yet logged into the new Member's portal (**www.physoc.org/user**). In terms of Equality and Diversity, The Society is still asking its members to complete this confidential information form on their personal portal page. This will provide anonymised background data on how open and inclusive The Society is, and allow us to benchmark improvements going forward. Society members are encouraged to contact Jen Brammer (**jbrammer@physoc.org** or +44(0)27 7269 5721), Membership Engagement Manager, directly if they have had any difficulties logging in or renewing their membership.

The committee was pleased with the success of the new Fellow membership category and how members were able to demonstrate the many ways they engage with and contribute to The Society. The most recent group of members elected to Fellow membership can be found on page 10.

Affiliate Working Group

The group met for the third time this year, at Hodgkin Huxley House (H^3) in London.

We discussed the forthcoming Future Physiology meeting (**www.physoc.org/futurephysiology/**) taking place in Leeds this December. Along with Society staff, the group have helped organise this early career focused meeting. There was a lively discussion about the social activities; it's set to be an exciting event with three course dinner and DJ until the early hours. The working group hopes to see many of you in Leeds.

We also discussed the bespoke Affiliate newsletter, and how we can ensure the content is relevant and engaging.

Finally, the group discussed ideas and initiatives for 2018; it was a great discussion with lots of ideas to investigate.

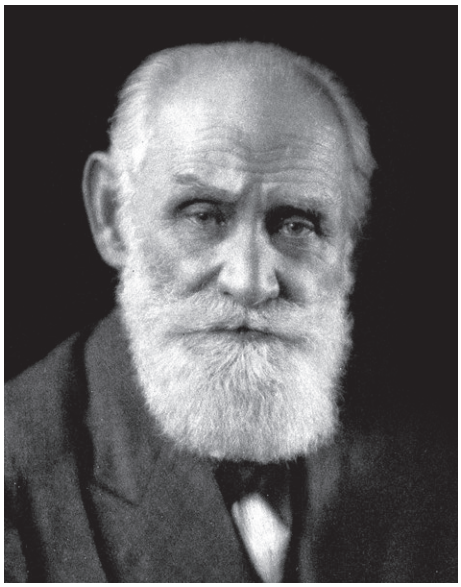
If you have any ideas or suggestions for ways the group should be supporting Affiliate Members and early career researchers, please get in touch. You can provide ideas by getting in touch with Jen Brammer, Membership Engagement Manager, **jbrammer@physoc.org**

Policy & Communications Committee

Policy & Communicationss Committee met in September. Discussion covered the planning of policy projects and their interaction with the forthcoming Society strategy. The Committee received the case studies covered in our latest booklet on Brexit, and reflected upon the recent launch of the report on worldwide physiology with IUPS. Reports were received from the *Physiology News* editorial board and the *in vivo* Sub-Committee.

From the archives: Pavlov's bequest

Ivan P Pavlov (1849–1936) was awarded a Nobel Prize in 1904 for his work on digestion, but is more famous for his later work on conditioned reflexes. Dogs can be conditioned to salivate at the sound of a bell if the bell has been rung just before food is delivered. In honour of our early career conference, *Future Physiology*, his letter to young scientists, *the academic youth of his country*, is reproduced below.



'What can I wish to the youth of my country who devote themselves to Science?

Firstly, gradualness. About this most important condition of fruitful scientific work I can never speak without emotion. Gradualness, gradualness and gradualness. From the very beginning of your work school yourselves to severe gradualness in the accumulation of knowledge.

Learn the ABC of science before you try to ascend to its summit. Never begin the subsequent without mastering the preceding. Never attempt to screen an insufficiency of knowledge even by the most audacious surmise and hypothesis. Howsoever this soap-bubble will rejoice your eyes by its play it inevitably will burst and you will have nothing except shame.

School yourselves to demureness and patience. Learn to inure yourselves to drudgery in science. Learn, compare, collect the facts.

Perfect as is the wing of a bird, it never could raise the bird up without resting on air. Facts are the air of a scientist. Without them you can never fly. Without them your theories are vain efforts.

By learning, experimenting, observing, try not to stay on the surface of the facts. Do not become the archivists of facts. Try to penetrate to the secret of their occurrence, persistently searching for the laws which govern them.

Secondly, modesty. Never think that you already know all.

However highly you are appraised, always have the courage to say of yourself – I am ignorant.

Do not allow haughtiness to take you in possession. Due to that you will be obstinate where it is necessary to agree, you will refuse useful advice and friendly help, you will lose the standard of objectiveness.

Thirdly, passion. Remember that science demands from a man all his life.

If you had two lives that would not be enough for you. Be passionate in your work and your searchings.'

Pavlov's bequest was written just before his death, at the age of 87 on 27 February, 1936, and was translated from the Russian by Professor P Kupalov, chief assistant in the Pavlov Institute at Leningrad.

2018 *Forthcoming events*

22 January

H³ Symposium: Purinergic signalling in obesity and renal pathophysiology
The Hatton, London, UK

www.physoc.org/purinergicsignalling

27-29 June

Experimental models in physiology
University of Exeter,
Exeter, UK

http://www.physoc.org/models/

13 September

Early Career Physiologists' Symposium (ECPS 2018)
QEII Centre,
London, UK

www.europhysiology2018.org/ECPS2016

14-16 Sept.

Europhysiology 2018 – Main Meeting
The QEII Centre,
London, UK

www.europhysiology2018.org

Meeting Notes

IUPS 2017: The Rhythms of Life

1–5 August 2017,
Riocentro,
Rio de Janeiro, Brazil

David Eisner

President, The Physiological Society

The International Union of Physiological Science (IUPS) meeting was held from 1-5 August at a conference centre near the Olympic Village in Rio de Janeiro. The main meeting was preceded by the IUPS General Assembly. This received updates from the various IUPS officers including our very own Denis Noble who was stepping down after serving two four-year terms as President. There was then an update on plans for the 2021 meeting to be held in Beijing. This was followed by the usual presentation of bids for the following (2025) meeting. Given that the 2017 meeting was in Rio and the 2021 meeting will be in China, there had been a view that a European venue would be desirable for 2025. To that end, Markus Hecker, the President of FEPS (The Federation of European Physiological Societies) got together a consortium including the Austrian, German, Scandinavian, Slovenian, Spanish and Swiss Societies to hold the meeting in Munich. This bid was duly approved. The new slate of officers and Council members was approved. Julie Chan was elected as President, and a member of our Society, Susan Wray as First Vice President. This was followed by a contested election for the position on Council of a representative from the Americas. According to Denis Noble, this was the first time in 30 years that there had been more than one candidate for a post!

Members may remember that The Society had produced a report entitled The Health of Physiology, which was launched at Physiology 2016 in Dublin. The Board of the General Assembly of IUPS has now published its own report, Physiology – Current Trends and Future Challenges, about physiology around the world. This was produced by Jayasree Sengupta and Susan Barman together with Henry Lovett (The Society's Policy and Public Affairs Officer). This report formed the basis for a well-attended discussion and interesting meeting which highlighted the commonality of many of the issues facing physiologists worldwide.

The meeting proper began with the opening ceremony followed by Denis Noble's Presidential Lecture in which, with characteristic elegance and energy, he persuaded his audience that it is naïve to think of a one-way system where genes control our cells and tissues.

IUPS attendees listening attentively

This was followed by a lecture from Ada Yonath, who received the 2009 Nobel Prize in Chemistry for her work on the structure of ribosomes. Her spellbinding presentation was highlighted by videos showing protein synthesis on ribosomes and how this can be interrupted by antibiotics. A major strand in her lecture was how antibiotic resistance occurs, how it can be overcome and the effects of antibiotics on the microbiome. In some ways the inclusion of this subject took IUPS back to its early days when physiology was synonymous with the totality of biomedical science. She also ended her talk pointing out that doing science and having a family is possible for women as well as men.

The other plenary and keynote lectures in the meeting provided a wonderful overview of the breadth and dynamism of modern physiology. Daniel Martin told us about the relevance of his research passion (high altitude physiology) to his 'day job' as an anaesthetist. It may have been my imagination but the odd member of the audience seemed a little queasy when Daniel described taking arterial blood samples from the groin area, while situated near the top of Everest! Amira Klip showed us how the immune system is involved in glucose metabolism and diabetes. Yusushi Miyashita gave a lovely overview of his research into memory and, in particular, the localisation of what he called the 'feeling of knowing'. The final plenary was the IUPS Fenn Lecture delivered by Nobel Laureate Roger Kornberg. The Society's Annual Review lecture was given by one David Eisner. As well as the plenary lectures, there were 21 keynote lectures including the following Prize Lectures of our Society: Bayliss-Starling, Helen Raybould; Joan Mott Lecture, Rhian Touyz; Paton, Tom Kirkwood. Tom's review lecture Why and how we are living longer? has been published in *Experimental Physiology*. I couldn't get to all the lectures as some were on at the same time as others but I particularly enjoyed Jack Feldman's Hodgkin-Huxley Prize Lecture in which he described the generation of respiratory rhythm complete with pauses for members of the audience to yawn and refresh themselves!

IUPS 2017 was truly an international conference attracting 1547 attendees from 64 countries. There was a total of 60 symposia covering most scientific areas in physiology. Some also dealt with broader issues. A particularly thought-provoking one was entitled The Two-way Physiology Street: Mutual Benefits of Volunteering Expertise. One of the presentations was from a member of our staff, Anisha Tailor, who described the time she had spent enthusing Ghanaian school children about science and finding out that teaching wasn't for her! Another was given by Olusoga Sofola from Nigeria who had received equipment grants totalling a few thousand pounds from The Society in the early 1990s. He had used the equipment not only for his own research but also to support that of many other Nigerian scientists, including a Fellow of our Society, Frank Mojiminiyi. The Society also sponsored a workshop on Getting Your Work Published in Physiology Journals, in collaboration with Editors from the American Physiological Society.

Of the 1028 abstracts submitted, 60 (6%) were from the UK.

The Society had a stand at the conference which had good footfall, with the majority of the visitors being interested in The Society's journals, meetings programme and new Massive Open Online Course in physiology. There were also 'meet the editor' sessions with the Editor-in-Chief of each of our three journals which again proved to be very popular.

The dates of the IUPS meeting would have been very close to those of The Society's normal annual meeting and in 2015 it was decided (with the support of a poll of members) to not hold a 'home' meeting and, instead make IUPS the annual meeting. Consequently, additional funding to support Members' attendance at the IUPS was ring-fenced. In this context, it was disappointing that fewer than 100 people from the UK were at IUPS; a pity that more could not have the pleasure of enjoying such a stimulating meeting.

Overall, I thought that the meeting was a great success and look forward to seeing everyone again in Beijing.

Top words used by IUPS attendees to describe physiology

Meeting Notes

YLS 2017: planning your first symposium – a pilot study

25 November 2017
MRC-ARUK Centre for Musculoskeletal Ageing Research, Royal Derby Hospital, Derby, UK

www.yls2017.co.uk

Colleen Deane

Department of Sport and Health Sciences, College of Life and Environmental Sciences, University of Exeter, UK

Amelia Pollard & Jessica Cegielski

MRC-ARUK Centre for Musculoskeletal Ageing Research, Clinical, Metabolic and Molecular Physiology, University of Nottingham, Royal Derby Hospital, Derby, UK

Joseph Bass

Faculty of Education & Health Sciences, University of Limerick, Ireland

Scientific symposia are designed to enhance scientific understanding, encourage the exploration of novel ideas, develop presentation skills and facilitate networking. It is therefore important that regular conferences are organised, particularly for postgraduates and early career researchers to support their career development.

The aim of this article is to describe the processes that were applied to plan the Young Life Scientists' symposium 2017 (YLS 2017) and highlight the key points to consider when planning a similar event.

Method

Four (26.4±0.6y, 3:1 female:male, (mean±SEM)) PhD students and postdoctoral researchers (pictured below) collaborated on the YLS 2017 proposal. All members provided verbal consent to take part in the YLS project. Written consent was provided on behalf of the supervisor through their letters of support.

Initially, meetings were held to discuss a potential: 1) scientific theme, 2) programme and 3) date and location. Sections of the proposal were delegated to each committee member to write. The proposal structure can be seen in Figure 1.

After confirmation that our application was successful, regular committee meetings were required to ensure the outlined proposal was delivered. Additional aspects had to be added such as creating and continually updating a website and social media pages, setting up a project code for finance, risk assessments, health and safety meetings and gathering external sponsorship. A Gantt chart (See Figure 2) was used to ensure the most significant tasks ($p<0.05$) for the meeting were kept to time.

Section	Title
1	Background
2	Aim
3	Venue
4	Accommodation
5	Programme outline (including proposed keynote speakers)
6	Proposed workshops
7	Preliminary timeline
8	Costings
9	Committee members' CV
10	References
11	Individual letters of support

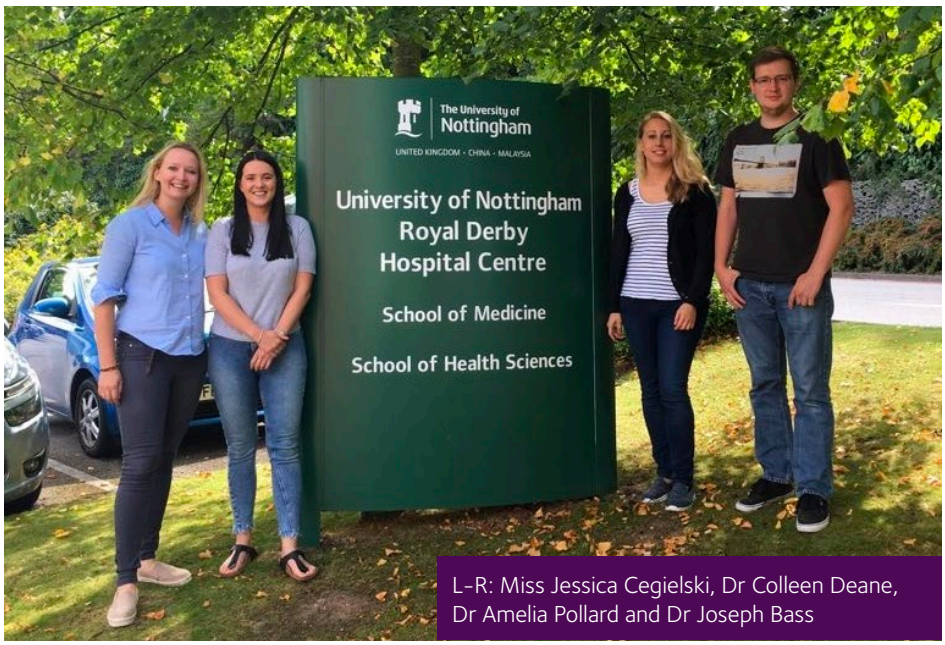
Figure 1. YLS 2017 proposal structure.

Results

The most important considerations for organising a symposium are:

- **Select a diligent organising committee**
  Organising a symposium is very demanding, with some of the tasks being unfamiliar and requiring additional training. The committee was made up of four diligent individuals, all from different undergraduate backgrounds; thus, the collective skills and interests were similar, but also contained unique attributes. Additionally, the collaboration across three different institutions provided greater interest in the event since it was promoted through three universities.

- **Allow plenty of time to organise the symposium**
  Planning a symposium during an early career stage means that a lot of the tasks are unfamiliar and, therefore, thorough planning should be undertaken early on. Importantly, reserving the venue, confirming the speakers and announcing the symposium should occur as a priority, so that the venue and speakers are guaranteed. Furthermore, having these confirmed initially aids approaching sponsors for additional funding. An important aspect that was collectively designed was a Gantt chart with all the key planning milestones as a reference for progress. Planning began in June, allowing ~five and a half months to organise the whole symposium.



L-R: Miss Jessica Cegielski, Dr Colleen Deane, Dr Amelia Pollard and Dr Joseph Bass

- **Organise a great scientific programme**
  Many things make a great scientific programme including the keynote speakers, the topic of the symposium and the relevance of the workshops. When planning the programme, it is important to consider the target audience of the symposium and organise sessions accordingly so that they will be of interest and benefit to those attending. Therefore, keynote speakers should be selected foremost based on the relevance of their research to the symposium. Speakers that are world-renowned and well-respected will entice the scientific community to attend the conference. For YLS 2017, eminent academics were chosen. It was important to host keynote speakers that would encourage and initiate interactions between students and researchers alike, developing future collaborative links. In addition to keynote presentations, workshops were also included in the YLS 2017 programme. Workshops titled 'Life Post PhD' and 'Successful Grant Applications', aimed specifically at postgraduate students and early career researchers, were selected. The workshop 'Life Post PhD' highlighted the variety of scientific career routes after a PhD that are available to postgraduates in addition to careers within academia. For this session, three speakers were invited, all of whom have chosen a different route after their PhD, to discuss their current role and how they secured that position. Showcasing the different career options post-PhD particularly appealed to the postgraduate delegates. The parallel workshop 'Successful Grant Applications' was chosen to support professional development given the limited training during PhD programmes; this workshop enabled early career researchers to gain tips from the experts.

- **Provide informal opportunities for networking**
  Networking is one of the key reasons researchers attend conferences. Therefore, it was essential the programme included plenty of coffee breaks (i.e. during poster sessions) so that networking could happen. Additionally, an evening meal was arranged, which was heavily subsidised by obtaining external funding, so that delegates could continue the discussion of their ideas into the evening and have some delicious food.

Conclusion

Organising a symposium as a postgraduate or postdoctoral researcher is a fantastic, eye-opening experience. For those thinking of applying to host further YLS symposiums, the best advice is: be prepared for the hard work, and enjoy it!

'It is important to consider the target audience of the symposium and organise sessions accordingly so that they will be of interest and benefit to those attending'

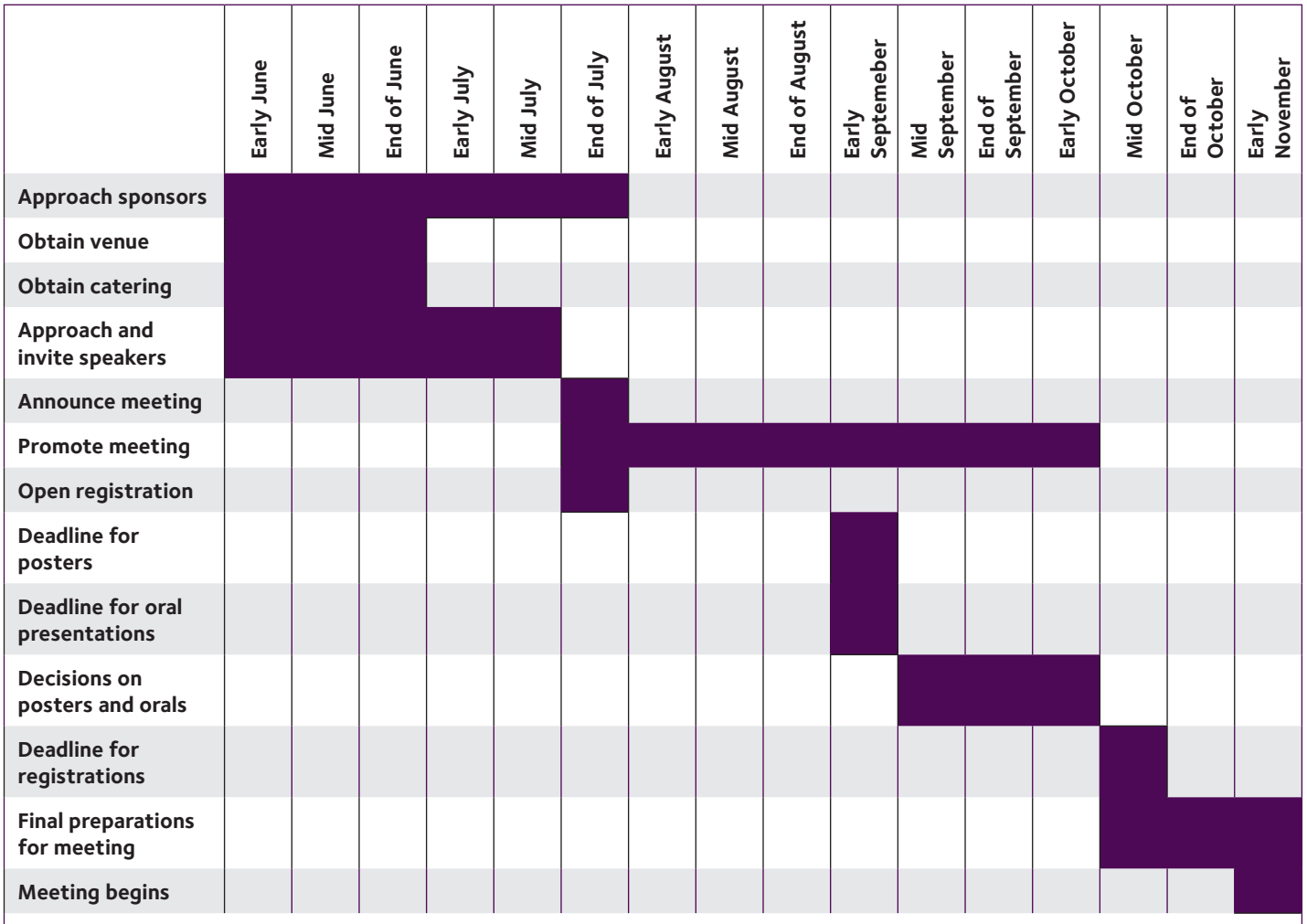


Figure 2. Original Gantt chart outlining our main tasks for organising YLS 2017.

Meeting Preview

Future Physiology 2017: ignite your networking at conferences

13–14 December 2017,
University of Leeds,
Leeds, UK

www.physoc.org/futurephysiology/

Hannah Marie Kirton

Faculty of Biological Sciences,
University of Leeds, UK

Networking at the 2017 Annual General Meeting

Future Physiology

'It's also just as important to talk and network with PhD students, postdocs, and other early career researchers'

We hear it all the time: networking, networking, networking is so important for us. It's true! Never underestimate the power of networking. However, for some of us, it's not that easy. Do you find it daunting? Difficult to initiate? Or do you just need a motivational boost to start building new and existing relationships? Amidst the inhibitions to just get out there and network, it's important to realise the true potential of networking and how it impacts career success. In this article, I have compiled a 'Mini Journal' of networking tips and advice, but more importantly, explain its importance.

What is networking?

Networking is an interaction that exchanges information and ideas, in order to develop productive and professional relationships. Networking is best, and easiest, at conferences and meetings, where there are a multitude of professionals in and related to your field of interest. But remember, networking is not just about speaking with key leaders in your field. It's also just as important to talk and network with PhD students, postdocs and other early career researchers. If anything, forming new contacts with early career researchers is more beneficial, since you will grow together in your field and may regularly contact each other throughout. Plus, they are a direct contact to the group leaders who you may be interested in working with and therefore, a good way to understand how that lab or institute works and supports early career researchers.

Why is networking important?

Put simply, networking with PhD students, postdocs and group leaders can benefit both your research and recognition, which, if performed correctly, will boost your career.

- **Research**
  Communicating with researchers and experts in your field can open up new questions and ideas for your research. This will enable you to view your research from a different point of view, both technically and theoretically. Collectively, this helps to shape and strengthen your research. This also forms the basis of collaborations, which generates a multidisciplinary approach to research and facilitates publications in high-impact journals.

- **Recognition**
  Networking is also an excellent platform to increase visibility within your research field, and visibility to prospective future employers. It also enables you to communicate with PhDs and postdocs you may later work with, who are equally key to your future.

How to network?

Try to break away from your comfort zone at conferences and meetings. It is so easy to stick to your lab team and supervisor, but remember, you have already formed professional relationships with them and see them every day! Challenge yourself. Be curious and open your mind.

Beginners top tips

- If networking is not your strongpoint, start by speaking to early career researchers in your field. Attend early career breakout meetings such as the postgrad, postdoc breakfasts and career sessions, and talk to the people around you, i.e. talk about their poster and research, or even their career. It's amazing how quickly people let their guard down once you talk about or compliment their research.

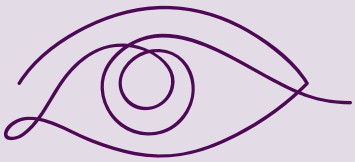
- Attend poster sessions. These are generally more informal and relaxed, helping you to ask your question and engage in conversation over research.
- Add your e-mail address to your posters, this will help people to get in touch with you. Remember, you are not the only one networking.
- Simple ways to interact with researchers at conferences can include striking a friendly conversation at a dinner or coffee queue or sitting next to someone at lunch. This is an easy way to build your confidence and get used to introducing yourself at conferences.
- Alternatively, utilising a familiar point of reference helps to build relationships, i.e. mentioning a work colleague you both know.
- If you're not ready to ask a question at the end of oral presentations, approach the presenter after the session. Be confident, but think carefully about your question!

Advanced top tips

- If you aim to speak with team leaders in your field and don't quite have the courage to walk over and introduce yourself, look out for them at the conference reception or dinner. An easy icebreaker is to smile, introduce yourself, and talk about your lab and research. Try to follow that up with an easy question about their research, or yours!
- Be specific when you approach people. If you admire their work then demonstrate it, by saying something like: 'I really enjoyed your recent paper in *Neuron* about sodium channels'.
- If there is a particular person you would like to speak with, email them a few days before the conference and let them know you'd like to meet up. This cuts out any awkward introductions, and forces you to follow your plans to meet.
- Alternatively, plan ahead prior to a conference or meeting. Read about their research and publications before approaching them with your questions. This will help you articulate questions specifically, clearly and with confidence.
- Once you have developed a network, make a strong effort to maintain that link. Promptly reply to emails or make regular contact when possible. It is very hard to make connections, but very easy to lose them.

Future Physiology 2017

At this year's Future Physiology conference, I have a 'Future Physiology Postcard' stand, where I invite you to write a 'future' task for yourself. Encourage yourself to talk to a particular professor or leading researcher in your field, improve your networking ability, or set a particular goal that could impact your career or research. I will post these to you, as a little reminder of your goal, aspiration or task to fulfil in 2018.



Your networking checklist for Future Physiology

- ☐ Challenge yourself to speak to a particular person or group of people
- ☐ Keep in contact with new networks and friends
- ☐ Add new and relevant contacts to LinkedIn and/or ResearchGate
- ☐ Retrieve a contact email address and follow up once you return
- ☐ Practice writing questions in presentations, even if you do not ask them
- ☐ Go to Early Career social events (i.e. lunches and breakfasts)

Physiologists, watch where you place that cannula!

Physiologists often sample blood during their research, but are we guilty of failing to question why we draw blood from a given vein? The most appropriate site to sample blood from will depend primarily on the study design and outcome measures, and this decision can influence the interpretation of the data generated.

Left, Co-author Harry Smith, and right, lead author Rob Edinburgh

Rob Edinburgh, James Betts, Dylan Thompson & Javier Gonzalez

Department for Health, University of Bath, UK

It is common in physiology research to sample blood for the assessment of the concentration and/or activity of an array of metabolites (e.g. glucose), hormones (e.g. insulin), enzymes (e.g. creatine kinase) or specific cell types (e.g. immune cells). These measures are also taken under a wide variety of conditions such as in the fasted versus fed state, or after rest versus after exercise. However, we often come across research studies asking similar questions, but where different blood sampling methodologies have been used. This can not only influence the concentrations of the measured metabolite or hormone, but in instances where different sampling methods are used, also make comparisons between studies more challenging. When designing research, blood sampling methods are a key consideration and physiologists should always *'watch where they place their cannula!'*

As physiologists, we regularly measure metabolites (e.g. glucose, fatty acids) or hormones (e.g. insulin) in blood samples, sometimes when our participants are fasted, and/or after a physiological challenge, such as the oral glucose tolerance test (OGTT) or a more appetising mixed macronutrient meal (such as a milkshake!). However, when comparing studies that attempt to answer similar questions, it is not uncommon to find that blood might be sampled from an antecubital (elbow) vein, a heated hand vein, interstitial fluid, a finger, or even the earlobe! Therefore, the key question to ask is, *does the blood sampling site matter?*

We spend a lot of time perfecting pipetting skills to ensure that at the measurement stage our results are accurate, and go to great lengths to make sure that blood samples are collected at specific time points, depending on the outcome measures of the research. Even before we get started with data collection, many hours are spent refining study designs. However, do we always give sufficient attention to the most appropriate blood sampling methods? How does this decision influence the measured concentrations of metabolites or hormones? How can we compare data from studies where different sampling methods are used? These are questions which may sometimes be overlooked.

The worrying prevalence and current trends regarding type 2 diabetes are well documented, and we have also known for a long time that blood glucose levels after a meal can predict risk of metabolic disease. As a consequence, glucose tolerance and indices of insulin sensitivity are frequently used in research to assess disease risk and responses to interventions. These measures will therefore be used as our example for exploring the importance of sampling methods.

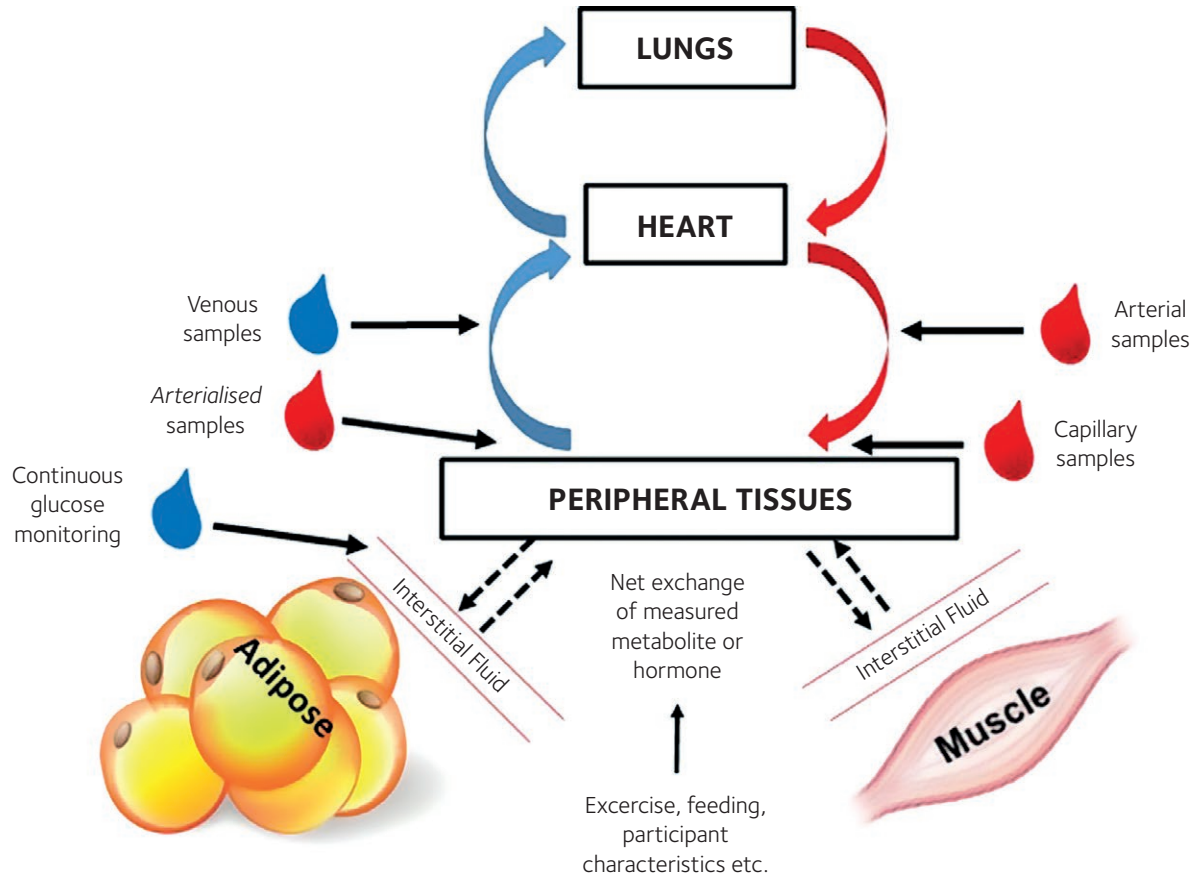


Figure 1. Different blood sampling methods will produce different concentrations of metabolites and hormones due to the location of the sample site in relation to peripheral tissues. The magnitude of this difference between sample methods will depend on factors such as the metabolic or feeding status, and characteristics of participants, as these influence the interaction of peripheral tissues with blood.

Insulin-resistance in skeletal muscle is one of the first defects in the onset of metabolic disease. Whilst arteries are the preferred site for determining peripheral (e.g. muscle) exposure to metabolites such as glucose, or hormones such as insulin (Figure 1), antecubital veins are a more common blood sample site, partly due to the increased risks associated with arterial cannulation, such as greater bleeding from the sampling (puncture) site and blood clots. These risks also make investigating artery-venous differences across a tissue a more difficult procedure.

However, heating the hand to around 37°C causes our capillaries to vasodilate and disperse heat, and since the 1920s we have had evidence that this produces venous blood samples that have a similar oxygen and carbon dioxide composition to arterial blood (Goldschmidt and Light, 1925). These samples are often referred to as *arterialised* or *arterialised-venous* blood. It has also been shown that the veins of a heated hand provide concentrations of many metabolites including glucose, fatty acids and amino acids as well as hormones including insulin, that are consistent with concentrations measured in arteries. Even increasing the air temperature of a room can increase venous concentrations of glucose and insulin.

Although some studies use the heated-hand technique to provide arterialised blood for measures of glucose tolerance, many derive these outcomes from non-arterialised venous blood, interstitial fluid or finger prick samples. This is perhaps because there is no clear consensus or justification in the literature of the most appropriate blood sampling method for an OGTT (or meal challenges).

The chosen blood sample method may be determined by availability of equipment or specialist staff and the measurement period. For example, finger prick samples can be more easily done in a field setting and without the need for cannulation or venepuncture. However, sometimes an explanation for the chosen method is not clear and one method (e.g. antecubital venous cannulation) is chosen over another (e.g. the heated hand technique), when either could have been implemented.

‘Do we always give sufficient attention to the most appropriate blood sampling method?’

This inconsistency raises important questions:

i. How does the sample method influence the concentration of the metabolite/ hormone being measured?

ii. How easy is it to compare between studies where different sampling methodologies are used?

'If differences between blood sample methods were similar under all conditions or populations simple correction factors could be applied... However, this is not the case'

If we remind ourselves of some basic physiology, it is unsurprising that the sample method can alter the measured concentrations of many metabolites and hormones. To better demonstrate this, we will continue with our example for glucose, but this principle applies to many constituents of blood.

If humans are fasted, blood glucose concentrations are maintained at around 4 to 5 mmol/L, with the extracted glucose (primarily by the brain, muscle and other tissues) mostly replaced by the liver. Upon ingesting carbohydrates, blood glucose concentrations rise. Insulin is then produced to lower blood glucose concentrations by supressing glucose appearance from the liver and increasing glucose clearance into (mostly) skeletal muscle. The glucose and insulin are transported to the peripheral tissues via arteries where they interact with the tissues, with insulin binding to its receptors to trigger a process which results in greater glucose transport into insulin-sensitive cells. Veins then carry the blood back to the lungs after this interaction has taken place.

As a consequence, concentrations of glucose and insulin are typically higher when measured in arterial (or arterialised) *versus* venous blood due to the removal of glucose for metabolism and/or storage in peripheral tissues, and some binding of insulin to the cell membranes. For similar reasons, glucose concentrations are higher in capillary plasma (finger prick or earlobe samples) *versus* veins (Figure 1).

Continuous monitoring of glucose over a longer time (weeks) is increasingly common, typically in interstitial fluid of adipose tissue. This allows for assessment of patterns of glucose levels in a free-living setting. However, plasma and interstitial fluid are distinct compartments, with glucose transferred from capillaries to the interstitial fluid by movement across the endothelial cell layer of blood vessels at a rate primarily determined by blood flow (Cengiz and Tamborlane, 2009). Under steady-state conditions for glucose (fasting and rest), interstitial fluid and plasma are reasonably well matched. However, under non-steady state conditions, and when blood flow is altered, differences between methods can become increasingly apparent. Moreover, across certain populations, blood flow to adipose tissue may be different (e.g. obese *versus* non-obese individuals), which may also influence any variation between concentrations of metabolites in blood *versus* interstitial fluid.

This brings us to a second and more important consideration. If differences between blood sample methods were similar under all conditions (e.g. rest *versus* exercise or fasting *versus* after a meal) and populations (e.g. people with *versus* without diabetes), simple correction factors could be applied. This would allow for easier comparisons between studies that have investigated similar questions using different sample methods or conditions (e.g. rest *versus* exercise) within a study.

However, this is not the case. Whilst concentrations of metabolites or hormones are normally similar across any artery in the body at a given time, venous concentrations can differ due to a net uptake or release from the tissue beds in proximity to the sampling site. For example, exercise increases insulin sensitivity and glucose uptake in exercised muscle and can impair insulin sensitivity in non-exercised muscle. As such, the difference in metabolite levels in arterialised *versus* venous blood will depend on the nutritional and metabolic status (e.g. rested *versus* exercised) of an individual.

Some guidelines provide corrections for venous to capillary plasma for an OGTT, but only at rest (e.g. + 1.1 mmol/L; [WHO, 1985]). However, the difference between arterial and venous levels for glucose is higher in the fed *versus* fasted state (Glassberg, 1930). The variation in glucose concentrations between venous and arterialised samples is also different after exercise *versus* rest (Figure 2, Edinburgh *et al.,* 2017). Therefore, it appears that simple corrections between sample methods cannot consistently be applied in all scenarios.

The determining factor here is the interaction of the periphery with the blood. When comparing samples collected after a meal (or during a hyperinsulinaemic clamp) *versus* fasting, the arterialised-venous difference for glucose will be larger due to the higher net extraction of glucose from the blood. A similar finding is apparent after exercise, although this will depend on whether the vein used for sampling is draining exercised or non-exercised muscle. The population studied is important, with different arterialised-venous differences detected in people with *versus* without diabetes (Rabinowitch, 1927), likely due to differences in the efficiency of glucose disposal. It should also be mentioned that concentrations of metabolites may not always be higher in arterialised *versus* venous blood. If peripheral tissues are producing a metabolite at a

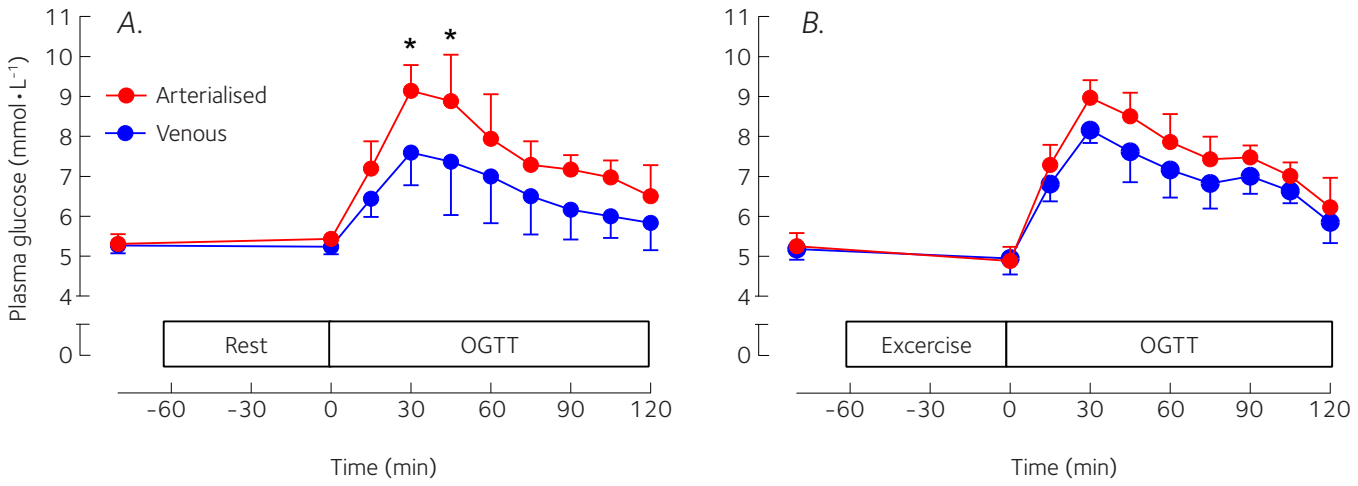


Figure 2. Although plasma glucose concentrations are higher in arterialised compared with venous blood after a period of rest *A.* and after cycling exercise *B.* the arterialised-venous difference is greater after rest *versus* exercise (Edinburgh *et al.*, 2017). This may prevent easy comparisons between studies, as simple correction factors between sampling methods cannot be consistently applied. (OGTT = Oral Glucose Tolerance Test)

rate greater than the extraction from the blood (e.g. lactate from muscle during/after exercise or leptin from adipose tissue) then venous concentrations may be higher than those measured in arterialised blood. The magnitude of this difference will again depend on the conditions in which a sample is collected.

Implications

Given that there are a number of different metabolites/hormones that are routinely measured, and across many different conditions (resting, after a meal, after exercise and so on), how can we develop correction factors for each possible scenario? This is not very practical, so instead we suggest two key points regarding blood sampling methods:

1. *Think carefully about the main outcome measure and this will inform which sample method is most appropriate.*

   The blood sampling method chosen will impact upon the measured concentrations of metabolites and hormones in blood. The most appropriate method for a given study will depend on the outcome measure. For an example of glucose, if you are interested in the exposure of peripheral tissues to circulating concentrations then arterialised blood may be preferable. This is also the preferred method for studying the rate of blood glucose appearance using tracers. However, venous blood may give a better indication of metabolites or hormones released from specific muscles and adipose tissue depots. Continuous glucose monitoring provides useful data, but should be interpreted in the context of the population studied, and conditions in which samples were collected.

2. *Always report the sample method used as this may influence the interpretation of the data, especially when comparing studies.*

Conclusions

Physiology research often involves blood sampling, but a number of different methodologies exist. Decisions made regarding the sampling methods can influence the measured concentrations of metabolites, hormones, enzymes and cell types. The key factor is the interaction of peripheral tissues with the blood and whether there is a net extraction, release or metabolism of a metabolite, hormone, enzyme or cell. This in turn will depend on the population studied and the conditions in which the blood was sampled. Thus, physiologists should always (1) think about the tissues and analytes of interest, (2) report and justify sampling methods and (3) watch where they place their cannula!

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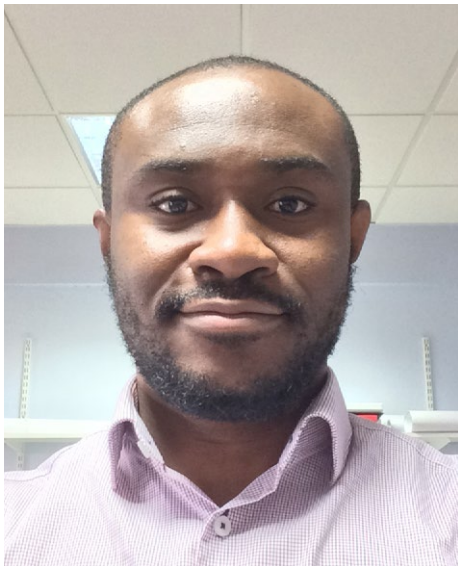
Does C-section impact on the early life microbiome and immune system?

C-section may negatively affect children later in life



Emmanuel Amabebe

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The last two decades have seen a four-fold increase in the incidence of C-section. Over 20% of deliveries in the UK and United States are by C-section. The rate is even higher in Brazil, where up to 80% has been reported. The perception that C-section is life saving and prevents injury to both mother and her baby is rife. This rise is also attributed to increased maternal request due to fear of childbirth, convenience and better control over the timing of delivery. However, a considerable number of C-sections are also medically indicated (Cho & Norman, 2013; Kristensen & Henriksen, 2016).

The influence of the mode of delivery on the infant microbiome and immune system has been topical, with several attempts to elucidate the source(s) of the newborn's microbial colonisation, immune function and risk of certain diseases later in life. This has led to the commercialisation of a vaginal 'seeding' approach to convert C-section infant microbiomes to those of vaginally delivered infants.

Changes in the vaginal microbiome

The human vagina, apart from being a passage for sperm, menstruum and neonates, is a highly versatile organ with a rich diverse microbial landscape. Advances in DNA sequencing techniques have revealed that healthy vaginal microbiota is predominantly characterised by *Lactobacillus* species, i.e. *L. crispatus, L. gasseri, L. iners and L. jensenii.* The protective action of these lactobacilli suppresses other anaerobes including *Gardnerella, Atopobium, Mobiluncus, Streptococcus, Prevotella, Ureaplasma,* etc., which have the potential to cause disease. The distribution of these organisms varies across ethnic groups. For example, it has been reported that Black and Hispanic women harbour more anaerobic species than others (MacIntyre *et al.,* 2015). The reasons behind this are unclear, but a gene-environment interaction has been implicated.

During gestation, there is increased stability and reduced diversity of the vaginal microbiota due to an increase in *Lactobacillus* dominance. This can be explained by the high level of oestrogen, which promotes maturation, proliferation and accumulation of glycogen in the vaginal epithelial cells. Glycogen is catabolised by human α-amylase to smaller glucose polymers, which are then metabolised to lactic acid by a number of *Lactobacillus* species (MacIntyre *et al.,* 2015). Both the vaginal epithelium and lactobacilli (which produce antimicrobial peptides and lactic acid and maintain the vaginal pH at <4.5) form the first line of defence against infection by pathogens. The vaginal microbial composition varies with the gestational age and at late gestation parallels that of non-pregnant women. An aberrant (dysbiotic) vaginal microbiome is associated with adverse pregnancy outcome particularly an increased risk of preterm delivery (MacIntyre *et al.,* 2015).

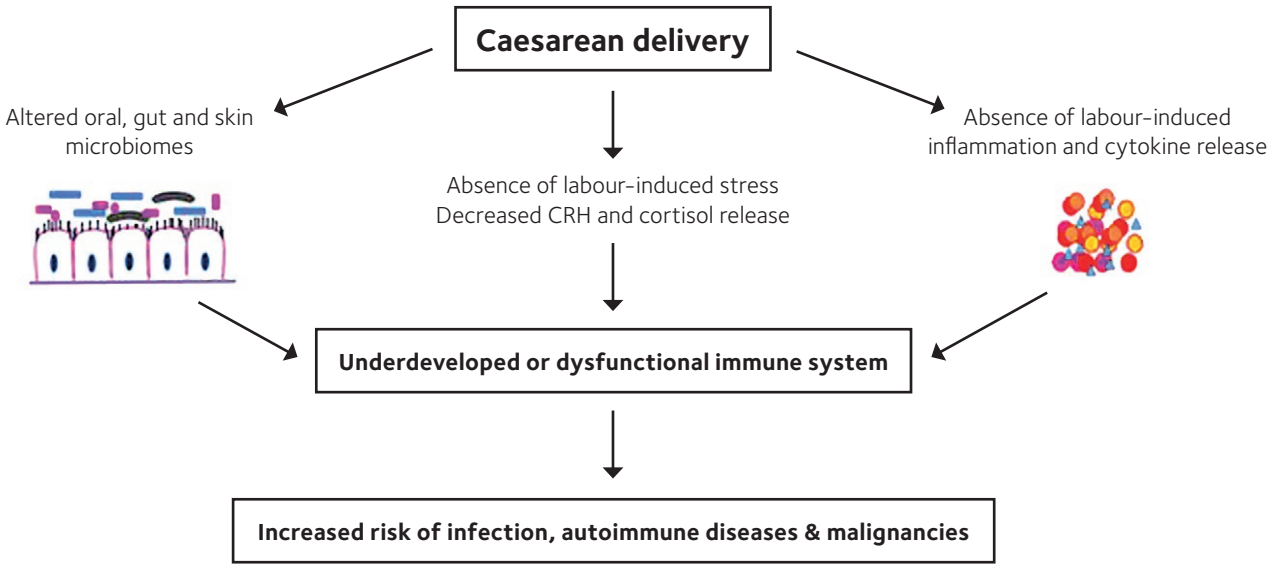

Figure 1. Possible mechanisms by which Caesarean delivery alters the infant microbiome and immune system. Prelabour Caesarean delivery prevents the fetus from traversing the birth canal. Hence, the baby does not acquire the maternal vaginal microbiome leading to an altered microbial colonisation of the oral cavity, gut and skin. Also, there is absence of labour–associated inflammation and cytokine release, as well as inactivation of the hypothalamic-pituitary-adrenal axis resulting in decreased corticotropin releasing hormone (CRH) and cortisol (necessary for maturation of organs, e.g. gut and immune system). Together, these features lead to an underdeveloped or dysfunctional immunity and increased susceptibility to infection, autoimmune diseases and malignancies later in life.

The vaginal microbial composition shifts dramatically shortly after delivery with reduced *Lactobacillus* dominance and increased α-diversity regardless of the community structure during gestation and independent of ethnicity. It can become more similar to the gut microbiome, regardless of gestational age at and mode of delivery, and is maintained for about 12 months. This can be ascribed to the decline in oestrogen levels after pregnancy as the oestrogen-stimulated maturation, proliferation and deposition of glycogen on vaginal epithelium as well as the resultant *Lactobacillus* dominance is diminished. This leads to a reduction in vaginal community stability and resilience characteristic of dysbiosis and subsequently increased susceptibility to post-delivery complications including postpartum endometritis. A persistently altered vaginal microbiome can impact the outcome of subsequent pregnancy especially if conception happens too soon after delivery. An inter-pregnancy interval less than 12 months is associated with preterm delivery (MacIntyre *et al.,* 2015).

Development of the fetal microbiome

In humans, bacterial alterations in the placenta and meconium of neonates were observed after administration of probiotics to their mothers during gestation compared with placebo controls. The placenta was previously described as a sterile environment, required for protecting the fetus against infection. Any microbial colonisation of this organ was most likely due to ascending genital infection. However, it has been proven that the placenta in the absence of any histologic evidence of chorioamnionitis possesses its unique microbiome of aerobic and anaerobic bacteria. Due to its similarity to the gut microbiota, it has been suggested that gut bacteria may gain access to the placenta, and this is supported by the increased risk of pregnancy complications in women with periodontal disease (Nuriel-Ohayon *et al.,* 2016).

These imply that from the early stages of gestation there is *in vivo* transmission of the maternal microbiome to the fetus (Nuriel-Ohayon *et al.,* 2016). Therefore, the fetal microbiome may be established during the gestational period and this amongst other factors may eventually determine the mode of delivery and risk of disease subsequently.

Another possible fetal-microbial exposure could be through swallowing of amniotic fluid contaminated with bacteria. This could prime the immune system of the fetus, which has the capacity to recognise and mount an immune response to pathogens through Toll-like receptor-initiated pathways, production of antimicrobial peptides and lipopolysaccharide-binding protein. This has been termed fetal inflammatory response syndrome and is associated with prematurity.

The effect of mode of delivery on the infant microbiome

Studies have identified distinctions in the microbial composition of various body sites of infants in relation to the mode of their birth. The maternal vaginal microbiome could be an important source of early colonisers of the neonatal gut microbiome, with great impact on the infant's host metabolism and immunity. The guts of infants born by vaginal delivery possess a microbial community similar to the maternal vagina (dominated by *Lactobacillus, Prevotella, Sneathia*) and maternal gut bacteria. Whereas infants born by C-section possess gut microbiota similar to those of their mothers' skin and oral cavity dominated by *Streptococcus, Staphylococcus, Propionibacterium* and *Corynebacterium.* Some C-section neonates were even colonised by nosocomial and nonmaternal skin microbiome (Francino, 2014; Nuriel-Ohayon *et al.,* 2016).

There is a vertical mother-to-infant transmission of the gut microbiome that is circumvented by C-section. This is indicated by lesser exchange of *Bacteroides* and *Bifidobacterium* in C-section-delivered infants.

Anal samples from vaginally delivered babies and neonates swabbed with a maternal vaginal microbiome after C-section were enriched with *Lactobacillus* and *Bacteroides.* In contrast, C-section neonates not exposed

lacked these microbes (Dominguez-Bello *et al.,* 2016) and instead harboured increased amounts of *Clostridium*.

These differences in bacterial colonisation and diversity usually disappear after 6 months of birth but can last up to 7 years in some occasions (Francino, 2014). C-section may also delay the onset of lactation, which is another route of stimulating physiological intestinal microbial colonisation in infants (Nuriel-Ohayon *et al.,* 2016). Together with the absence of vertical transmission of the maternal vaginal microbiome, this can lead to poor immune development with long-lasting sequelae.

Higher proportions of antibiotic resistance genes were also found in the gut microbiome of C-section-delivered infants compared with their vaginally delivered counterparts. Along with abundance of *Staphylococcus* from maternal skin, this was associated with high rate of methicillin-resistant *Staphylococcus aureus* skin infections in infants born by C-section (Nuriel-Ohayon *et al.,* 2016).

Furthermore, the oral microbiome of C-section-delivered infants resembles that of maternal skin shortly after birth, while vaginally delivered infants harbour an oral microbiome similar to the maternal vaginal microbiome. However, similar to vaginally delivered babies, the oral microbiome of babies delivered by C-section but exposed to a maternal vaginal microbiome was supplemented with vaginal bacteria diminished in unexposed C-section babies (Dominguez-Bello *et al.,* 2016). The difference between the oral microbiome of C-section and vaginally delivered infants can last up to 3 months with more bacterial species detected in vaginally delivered babies. Also after exposure to *Streptococcus mutans*, infants delivered vaginally were more resistant to the infection than C-section-delivered infants who were infected nearly a year earlier and harboured a genotype of the bacteria homogenous to that of their mothers (Nuriel-Ohayon *et al.,* 2016). Plausible mechanisms by which C-section alters the newborn's microbiome and immunity are shown in Fig. 1.

The effect of mode of delivery on infant immunity

Despite the widespread perception that C-section averts infant and maternal injury, the infant's poorly developed or aberrant microbiome and dysfunctional immune system may increase its susceptibility to certain diseases (such as neonatal respiratory morbidity, respiratory syncytial virus infection, bronchiolitis, allergies, asthma, laryngitis, gastroenteritis, inflammatory bowel disease, celiac disease, leukaemia, neuroblastoma, atopic dermatitis, juvenile idiopathic arthritis, obesity and type 1 diabetes) (Cho & Norman, 2013; Kristensen & Henriksen, 2016). The risk of these diseases is reduced in infants 'seeded' (swabbing a mother's vagina and transferring it to her baby's mouth, eyes and skin after C-section) with their mother's vaginal microbiome after C-section. The mucosal surfaces have a greater predisposition to the impact of this immune dysfunction, plausibly due to immense immunity-related host–microbial interactions at these sites. For instance, pre- and perinatal intestinal bacterial colonisation stimulates mucosal-associated lymphoid tissue to produce antibodies against pathogens while sparing commensal species, thereby developing immunological tolerance.

Further evidence of a dysfunctional immune function associated with C-section with consequent long-term complications is the observation of reduced concentrations of proinflammatory cytokines (IL-1β, IL-6, IL-8, IFN-γ, TNF-α, etc.) and increased antibody (IgA and IgG) secreting cells compared with vaginal delivery. Also, C-section-delivered infants had reduced cord blood total leukocyte and neutrophil, monocyte and natural killer cell counts. The cord blood leukocytes of such babies also showed reduced *in vitro* transmigration capacity and cell surface adhesion molecule expression levels compared with those of vaginally delivered infants. These hypo-inflammatory state and altered immune responses may predispose C-section children to autoimmune diseases, infection and malignancies. Production of cytokines necessary for induction of labour and neonatal immunity is enhanced by vaginal delivery and impaired in C-section. Again, this can be attributed to the Caesarean-associated altered infant microbial colonisation/composition (Cho & Norman, 2013).

In summary, inadequate microbial exposure during delivery adapts the infant's microbiome and immunity increasing its susceptibility to immune diseases. Neonatal gut microbial colonisation primes the immune system. Children born by C-section may experience delayed postnatal immunological development and priming with potentially deleterious consequences later in life.

Seeding may stimulate microbiome colonisation and immune development similar to vaginally (naturally) born babies and can be a potential 'health boost' in the coming years.

'The influence of the mode of delivery on the infant microbiome and immune system has been topical, with several attempts to elucidate the source(s) of the newborn's microbial colonisation, immune function and risk of certain diseases later in life'

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The female athlete: it's not all about performance

A balancing act between success and health

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Elite athletes train for 365 days a year, only resting when necessary. Each season they will target their major championship, which may last only a month. Their performances are continuously judged and will influence their funding and sponsorship. For the spectators watching at home, they are presented as being at the pinnacle of health and earning a living doing what they love. But some athletes will push their bodies a little too much, resulting in disastrous long-term effects on the body and its systems.

Currently the number of females competing in sport, at all levels, is on the rise, with the nation being pushed to be as healthy as it can be. All too often there is a new regime to follow that is deemed to be the 'healthiest' by some form of social media, a certain food to eat or not to eat, the best exercise to do or avoid. However, most of these regimes posted have very little background and no valid research to back up their claims. They also tend not to highlight the potential ill effects that this restricted lifestyle could lead to.

Female athletes at an elite level tend to follow strict rules when it comes to their diet and lifestyle. They have rigid routines to ensure they meet their daily training and recovery goals to allow them to continually train for months on end. They have set foods that ensure they get the right amount of fuel needed for their training and replenish their muscles after working out. Sometimes an athlete can become so strict and set on their training goals that they lose touch with the social and emotional interactions that make us human!

There is a very fine line for the elite sportsman or -woman between training, competition and recovery (Barnett, 2006). Elite athletes are faced with this challenge on a daily basis. For female athletes, they have an extra balance to take into consideration: the menstrual cycle.

The monthly cycles

The menstrual cycle is a natural process for females, occurring monthly, and is essential to maintain bone health and fertility. It can start from the age of 12 and continues until the onset of menopause around the age of 49-52. The cycle occurs over a period of 28 days. The first 14 days are known as the follicular phase. During this phase, around day 10, the hormones oestrogen, LH (luteinising hormone) and FSH (follicular stimulating hormone) rise, reaching their peak around day 14. LH reaches a level double that of both oestrogen and FSH. After day 14, LH levels rapidly drop off while oestrogen and FSH fall off more slowly, over a 5-day period. The second 14 days are known as the luteal phase, and there is a gradual increase in another hormone, progesterone, which reaches a peak around day 22 and returns to base levels at day 28.

The cycle then repeats and continues into the next 28 day cycle. Body temperature

‘For female athletes, they have an extra balance to take into consideration: the menstrual cycle’

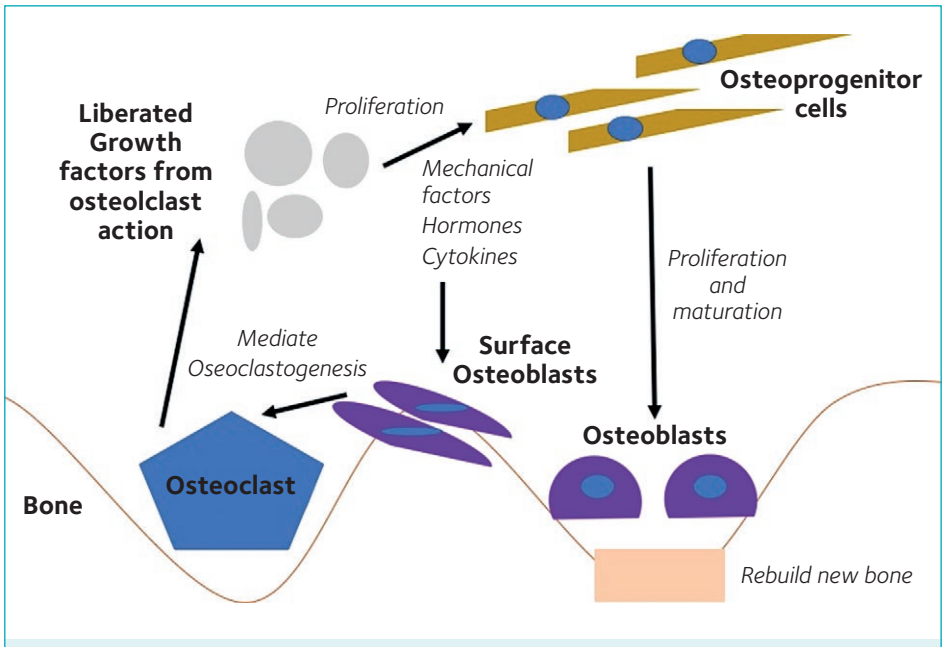

Figure 1. The balance of osteoblasts and osteoclasts in maintaining bone health.

also fluctuates during the cycle and rises by around 1-1.5 degrees Celsius during the luteal phase. LH is also linked with appetite and so the rise and fall can cause the female to feel hungrier during this time period. Oestrogen is a key regulator of bone resorption; without oestrogen there would be an excess of bone being broken down over new bone being formed, making the menstrual cycle an essential tool in maintaining bone structure.

Bone stability and structure

Bone remains in a state of constant turnover by two types of bone cells: osteoblasts and osteoclasts. (Fig. 1). Osteoblasts are involved in bone formation, whereas osteoclasts are involved in bone resorption. The balance between these two types of cells is vital to maintain a steady state of bone health. Bone resorption occurs at a much higher rate than formation; bone resorption takes just 30 days whereas the bone remodelling cycle takes 4 months. Therefore, a slight imbalance can lead to a bone fracture very quickly (Agerbaek *et al.,* 1991).

Bone also responds to physical activity and impact. The mechanostat theory (Frost, 1987) describes how the mechanical strain on the bone, caused by muscle forces during contraction, activates the surface osteoblasts, which begin the process of forming new bone. Continued activity causes an increase in bone mass, size and strength, while reduced mechanical deformation causes a decrease. During puberty, bone is most responsive to physical activity so this period of life is ‘the window of opportunity’ to increase bone cross-sectional area and density. There is evidence to show that the bone mineral content of people who were active during childhood is around 8-10% greater than those that were not, even if they are both active later on in life (Baxter-Jones *et al.,* 2008).

More is not always better

Elite female athletes, particularly those involved in sports that usually adopt a leaner physique with low body fat, are at a greater risk of disordered eating; they are more likely to disturb the balance between optimal health and recovery by reducing energy intake. Some population studies of high-level female athletes have shown up to 50% of the athletes demonstrate one or more disordered eating behaviours (Mountjoy *et al.,* 2014). The reasons for this disordered eating could be external pressures from teams, coaches and sponsors, or the athletes themselves having the belief that the leaner and lighter they are, the quicker they will be. These pressures may also cause the athlete to push their body to further extremes. By making it difficult to match energy expenditure with energy intake, they unintentionally end up with an energy deficit. Once the athlete reaches a level of negative energy balance, detrimental effects begin to take place.

The reduced intake will not only cause weight loss but, with a lack of energy, the liver will begin to release more ketone bodies. Ketone bodies are water-soluble molecules that are released from the break-down of fatty acids, which are used as the main energy source when there is a low energy availability. A build-up of these ketones can cause the blood pH to reduce to dangerously acidic levels, a process known as ketoacidosis. Muscles will become weaker as the body starts to preserve the small amount of energy it has been given, heightening risk of injury. Without the necessary energy intake, the menstrual cycle will most likely become irregular and eventually cease, which is known as amenorrhea. Amenorrhea is as prevalent as 65% in distance runners and 69% in professional ballet dancers (Mountjoy *et al.,* 2014). Without a regular menstrual cycle the levels of oestrogen are significantly reduced, which causes a disproportionate level of osteoblasts and osteoclasts, leaving a higher rate of bone resorption than formation. This may ultimately lead to bone injuries, osteopenia or even osteoporosis at a very young age, making any further career achievements even more difficult.

These three symptoms (disordered eating, amenorrhea and osteoporosis) became more prevalent in the 1990s and were termed ‘The Female Athlete Triad’ in 1997 by the American College of Sports Medicine (Fig. 2). Athletes may only present with one or two of the components but this does not mean they cannot be diagnosed with the triad. It has been estimated that only 50% of trained physicians are knowledgeable about the female athlete triad and are comfortable diagnosing and treating the condition (Curry *et al.,* 2014). More recently, the triad has been renamed as RED-S (Relative energy deficient syndrome). This re-naming is due to an increased number of patients presenting with various other symptoms (chronic fatigue, irritability, depression, long-term fertility issues, reduced immunity and reduced metabolic rate). RED-S is deemed to result from continual disordered eating. Being in a state of energy deficit for a long duration can disrupt numerous physiological systems, such as, but not limited to, cardiovascular,

gastrointestinal, endocrine and renal systems. Redefining the RED-S also allows male athletes who present with similar issues to be included (Tenforde *et al.,* 2014).

Current research has looked at the differing effects of the components of the triad on injuries, bone health, muscle health and the different nutritional patterns. At Manchester Metropolitan University, we have carried out our own research on some of the UK's most renowned female endurance runners, investigating the effects of altered menstrual cycle on bone health. Athletes with amenorrhea presented with a greater endocortical circumference (the outer circumference of the cortical bone) in the tibia and radius than controls. Only the eumenorrheic athletes (those with regular menstrual cycles) had a greater cortical area, in the tibia and radius, compared with controls. The athletes with amenorrhea had an expansion in bone size but not density, meaning they had wider but thinner bones.

More research is being conducted to better understand the issues, and accurate diagnosis will hopefully become more frequent. But what we really need is education at a young age, as most athletes become familiar with the triad only once they have been diagnosed with a bone injury. Prior to this, they may have never known why their menstrual cycle stopped, as it can be seen as a 'normal' thing to some when training at such a high level. If athletes are made aware of the symptoms and issues around the triad before they occur, then nutrition and menstrual cycles can be more closely monitored as they progress through their athletic careers. The increasing number of elite female athletes having children during their competitive careers offers hope to all younger athletes, and may even encourage them to take care of their bodies in a more informed way.

Summary

In general, female athletes do lead a healthy lifestyle and are able to balance their training needs whilst keeping their body healthy and menstrual cycle regular. When training becomes too much or a form of disordered eating is introduced, the risk for loss of menses and resulting reduced bone health becomes apparent. More research needs to be conducted to better understand the condition and allow physicians to be more confident in treating and diagnosing the condition. Ultimately, to eradicate the problem, education needs to be introduced at the very start of a female athlete's career.

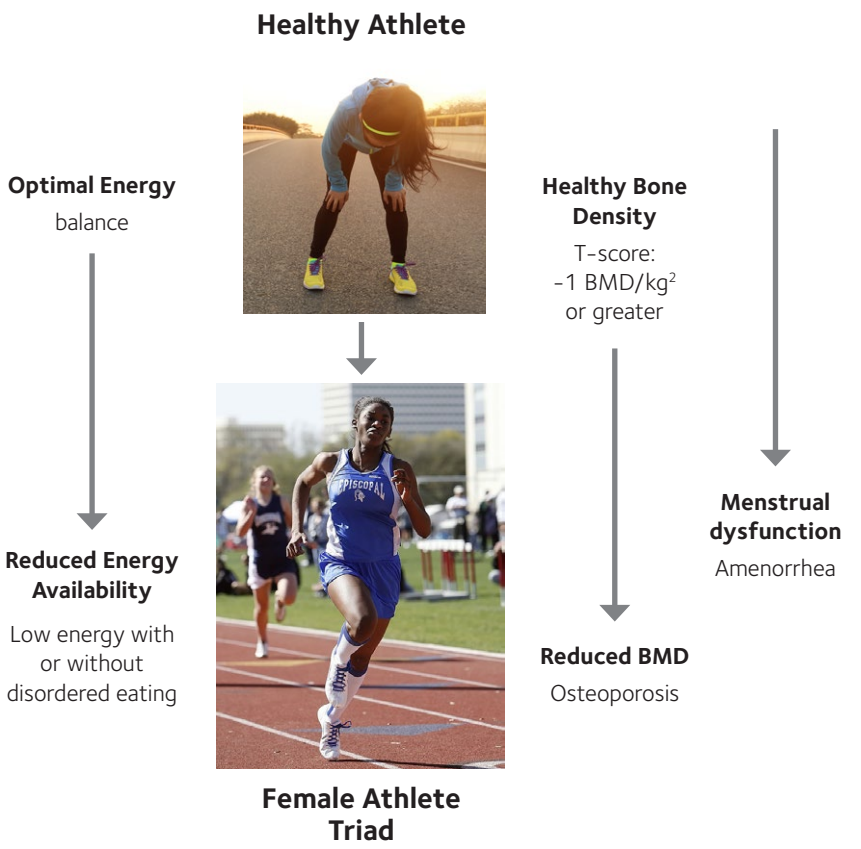

Figure 2. Components of the female athlete triad.

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L'Oréal-UNESCO early career fellowship success

Hannah Marie Kirton interviews Annie Curtis, awardee of the L'Oréal UK & Ireland Fellowship for Women in Science

Annie Curtis

Taking the next step as an early career researcher means recognising your potential to fund independent thinking and research. However, in light of funding limitations and the 'postdoc boom', it may seem that fellowship success is a battlefield, and not one for the faint-hearted. Some postdocs also claim that without a defined career pathway and record-breaking publications, the chances of fellowship success are nothing but pipe dreams. There are too many postdoc stigmatisms!

The prestigious L'Oreal-UNESCO Fellowship for Women in Science awards recognise outstanding female postdoctoral researchers, providing them the opportunity to independently further their early career research. This year, Annie Curtis, from the Royal College of Surgeons in Ireland (RCSI), Dublin, was one of five fellowship awardees, and here she shares her recent fellowship success, including some useful tips.

'I hope this shows early career researchers there are many paths into a science career'

Q: Annie, talk us through your career pathway, and how this led to your current research status.

A: After my genetics undergraduate degree at Trinity College Dublin I was between minds on whether I would do an MBA or PhD. I took some time off and worked as a research assistant at Duke University in North Carolina. Still undecided, I took another position as a research assistant at University College Cork. It was there that a postdoc told me I should really consider a PhD, and knew the exact head of a lab I should approach. This was Professor FitzGerald, leading Irish cardiovascular researcher, at the University of Pennsylvania, Philadelphia. In 2001, I started my PhD with Professor Fitzgerald, who introduced me to the world of circadian rhythms and how our body clock controls cardiovascular function. For instance, blood pressure is highly circadian; it increases in the early morning hours, hence the morning prevalence of heart attacks and strokes. It was an amazing experience working at UPenn, and Professor Garret still remains a fantastic mentor and support to my career.

Thereafter, I took a position as a Principal Scientist at GlaxoSmithKline in Pennsylvania for 2 years. However, the homing gene was strong, so in 2008 myhusband and I moved back to Ireland. I knew I wanted to stay in research, but the academic landscape in 2008 was pretty grim in Ireland, given the financial crash. I took a position at a main funding agency called Science Foundation Ireland until I figured out who was who in the academic field, and where the best opportunities were.

My return to academia came when I recognised that Professor Luke O'Neill, a world-leading immunologist at Trinity College Dublin, was awarded an ERC advanced grant. I knew I had to do another postdoc, but I also knew that I needed 5 years of security (and I was hoping I would start a family). I met Professor O'Neill over coffee, and once he started talking about his

research in innate immunity, I could see there was an opening to investigate the role of the body clock in immune cells. I spent 5 years in his lab, had two beautiful baby girls, and had the best time. In 2016, it was time to start my own laboratory, and I was fortunate to be awarded one of the StAR Awards from the RCSI. The position is tenure track and has allowed me to start my Immune Clock laboratory.

Q: What is your research background, and how did this inspire your fellowship application?

A: My research background is focused on the body clock in macrophages, and inflammation. I am also very interested in how immune cell metabolism, such as macrophages, shapes immune response. My fellowship application was to understand how the mitochondria in macrophages are changing over the course of a day and how this impacts on the inflammatory response.

I felt that the research project I was proposing was timely (pardon the pun!) due to immense progress in understanding how metabolism is affecting the immune system, but no one was looking at this in terms of the body clock. In essence, my research takes in three areas – body clocks, metabolism and inflammation – all within this one very important immune cell called the macrophage.

Q: Talk us through the steps of the L'Oreal UNESCO application and interviews.

A: The application for the fellowship is pretty straightforward. If you haven't written a grant before, it's a nice one to start with. The interview, held at the Royal Society London, included a five-minute presentation followed by questions from the panel. On the interview day, L'Oreal UNESCO invited school children to meet with women in a multitude of careers to challenge gender stereotypes. Young children form opinions about gender-specific roles from as young as five, so it's really important to ensure young children, especially young girls, see all the careers available to them.

Q: What aspects of the L'Oreal-UNESCO Fellowship process did you enjoy the most?

A: Without question, the interviews. It was fantastic to visit the Royal Society and meet the other women selected for interview, including the staff from L'Oreal. The whole experience was superb; it included posters from PhD students from around the UK, so we had the opportunity to see some really interesting science.

Q: What does being a L'Oreal-UNESCO winner mean for you?

A: Firstly, I really was deeply honoured to receive the fellowship. I am very passionate about women in STEM and therefore delighted my story would hopefully bring more girls (and boys) into a career in science. Also, as my career trajectory has been a bit atypical in that I worked outside of research for a number of years, I hope this shows early career researchers there are many paths into a science career. Plus, this fellowship really has made a huge difference in terms of the types of experiments I can do, including the flexibility the award offers in terms of childcare support.

Q: What other key aspects do you feel were a great help and support to your success?

A: A key aspect that helped was the mentorship I received from both Luke and Garret. They have been inspirational to me and are both current collaborators of mine. I also found the flexibility that Luke afforded me, when I started in his lab, was key. He allowed me to work on body clocks in macrophages, although he could have easily insisted I work on something he was interested in. It was this flexibility and support that allowed me to publish in this area and gain my own research niche that I could develop and grow into a career. For that I am truly grateful. I also found that RCSI is a superb place to work in terms of flexibility and support. In my first year at RCSI, I was completely protected from teaching. This was an immense help in allowing me to set up my research group.

Q: What makes a good candidate for a fellowship?

A: First and foremost, your research idea has to be unique and interesting. For most of us it's not that we don't have interesting research ideas, but rather that we are not very good at selling the research idea. Being able to write a compelling proposal is key, but it takes practice and more practice. I also think that you have to be really passionate about what you do, as that comes across in the proposal and especially at interview stage. So to summarise, have a stellar idea, strong writing skills, and passion.

Q: Since competition for funding is very high and restricted, how many applications did you submit before being given this prestigious award?

A: My first fellowship success was with Science Foundation Ireland in 2013. That enabled me to publish papers in the field of clocks and inflammation, which helped strengthen my credibility for this application. I then applied for the L'Oreal fellowship in 2011, but was unsuccessful. It stuck in my mind that, if possible, I should try again. This year was the last year in terms of my eligibility. I had completed 8 years as a postdoc, which is the cut-off point for this award. Since then I have applied for four other grants. I have heard back on two and didn't get either. The other two I am awaiting a decision on shortly, so fingers crossed. The one thing I have learned is that in this profession you have to build resilience. It is just a simple fact of life that most grants do not get funded, and that everyone's grants are often rejected. Nobody should take a rejection personally, just get back on the horse and apply for the next one.

Q: In your experience, what positive advice would you offer for unsuccessful fellowship applications?

A: A positive aspect of an unsuccessful application is the feedback that you receive from the reviewers. I always take on board the reviewers' comments and strengthen the next application by implementing the feedback that I feel is correct.

Q: How do you balance professional and personal life, particularly under the pressure and demand to strengthen and continue your success?

A: I really try and bring in my expertise of the body clock into my professional and personal life. I get up early and start my day so I am home by 4.30pm. I have the rest of the evening with my two little ladies and husband. I am not someone who can work long hours, and that helps maintain a good work life balance. Also, it's really important to have fun in work, so surround yourself with people that you really enjoy working with, to maintain a really healthy work–life balance.

Q: Finally, what's the ONE key piece of advice you'd give to an early career researcher applying for a fellowship?

A: Be yourself. Let your personality shine through in the application, it's often the applications that are a little different that catch people's attention. I know you said only one! But if I was to sneak in one other piece of advice I would say you have to work on something you are truly passionate about. Everything else falls into place after that!

Careers – no 'one size fits all' for scientists

'What matters most is how well you walk through the fire' *Charles Bukowski*

The career path of scientists is oft the result of happenstance; a chance meeting at a conference, a quirk in a dataset, a change in personal circumstance. There's no one size fits all for scientists' careers. We sought to highlight this with several case studies to encourage you on your way.

The winding road through research to medical school

Chloé Monnier
Medical Student, University of Nottingham, UK

I started studying biology and physiology fortuitously, in my hometown of Paris, at Université Paris VII Denis Diderot. It was rather uneventful except for the final years, which were punctuated by two summer internships at Northwestern University in Chicago. Before I knew it, I had completed a Master's degree.

I wanted to go to medical school and was initially planning on applying to schools in the US. Someone mentioned the UK offhandedly and I ended up focusing my application on UK universities, as I was doing this in a bit of a rush to meet the October deadline. Knowing I had a whole year ahead and not wishing to remain in Paris, I contacted the Chicago research team I had worked with previously. I was lucky to get a post-baccalaureate research fellow position there that kept me busy up until the beginning of my medical degree in Nottingham the next year.

Coming from France, where the education is - in my opinion - great, but not really conducive to developing self-confidence and self-reliance, spending some time abroad and working in research was the best thing that could have ever happened to me. I learnt that it is okay to make mistakes as long as you learn from them; it is okay to not know as long as you look it up, and it is okay to ask people for help. I also learnt to rely on whatever knowledge and abilities I have to solve a situation, and trust that I can make it work.

I am grateful for the school of thought that is science. Spending a couple of years studying cell metabolism and working in research has taught me to think critically and analyse every angle of a problem thoroughly, work as part of a team and value every member of that team. It has allowed me to travel and make friends and colleagues for life from all over the world. Having studied and worked in France and in the US, and enjoyed aspects of life in both countries, I felt uniquely equipped to make the best of studying and living in the UK. I now enjoy the multi-cultural campus of Nottingham University and the opportunities I've been given here to learn and stay involved in research whilst pursuing medical studies.

Although mine has been a bit of a scenic route to reaching medicine, I would not trade it for the world; the scenery sure was worth it.

Collaborations are the lifeblood of science

Carlo Lisci
PhD student, Cagliari University, IT

I'm in the third year of my second PhD in Molecular Medicine. I came from Cagliari University, Italy. Thanks to collaboration between research groups, I have been at the School of Life Sciences, University of Nottingham for a year now, with Dr Preeti Jethwa and Professor Fran Ebling. Throughout my career, I've always been busy and interested in nutrition. My first PhD, which I received in 2014, concerned feeding and human nutrition. Attracted by experimental science, I now do most of my work *in vivo* using animal models, because I believe that observation of *in vivo* phenomena is critical to our understanding of physiology.

At Nottingham, we use a beautiful experimental model, the Siberian hamster. It's a seasonal model of body fat, which demonstrates a long-day obese state (summer) and a short-day lean state (winter), associated with changes in food intake and energy expenditure. We are interested in a group of proteins called VGF-derived peptides which have been implicated in the regulation of energy balance. The collaboration began with Cristina Cocco, also from Cagliari University, and I now also work with Jo Edward Lewis.

We also collaborate with other groups and researchers at different universities. This is very important to me. The links between all the members of the research team are very fulfilling and stimulating. The various meetings in a serene environment allow true union between the members and the

formation of new ideas, both short- and long-term.

My wish is to continue to create a link between these universities, to encourage high-quality science, as it should be in every nation on this planet. I wish you all, good science.

The beauty of science is it takes you across borders

Rebecca Dumbell,
Postdoctoral Training Fellow,
MRC Harwell Institute, UK

I completed my PhD from the Rowett Institute of Nutrition and Health, University of Aberdeen in 2014. The Rowett had merged with the University a few years before I joined, and combined with the rural location at the time, this meant that it still had the feel of a research institute. Towards the end of my PhD I heard about a postdoc position coming up at the University of Lübeck in Germany through word of mouth. In a bit of a whirlwind I flew out to Germany for my interview the day after submitting my thesis, and I started the job a few months later.

Getting set up in my new job and new country was a challenge. I quickly learned that I needed a lot of documents, all from different offices located very far from each other, and they all had to be collected in a particular order. My EU passport smoothed the process and made my experience much easier than what I witnessed my non-EU colleagues go through. Within 1 week I had everything I needed, including a place to live, a bank account, health insurance and a pension plan.

I spent almost 2 years as a postdoc in Lübeck and I really loved living in Germany. Half of my colleagues were German and the rest came from all over the world, all speaking English in the lab. This was a lot of fun and we set up things like 'international cooking club' and, my personal favourite, whisky club. I found that as the only native English speaker I was the go-to proofreader; this certainly improved my grammar if not the work I was checking!

I now work at the MRC Harwell Institute in Oxfordshire as a Postdoctoral Training Fellow, and again find myself in a research institute in a rural setting. This comes with its own advantages and challenges. I have to go out of my way to build on my undergraduate teaching experience. But, once identified, these issues are overcome by connecting with people at the nearby University of Oxford, and with my wider professional network.

For me the chance to work abroad is a big draw for a scientific career; it built my confidence and expanded my professional network as well as providing a great experience. Coming back to the UK was right for me at the time but I'd not rule out going abroad again.

American academia, and achieving a work–life balance

Chris Shannon,
Postdoctoral Research Fellow,
University of Texas Health Science Centre, USA

Upon finishing my PhD in human metabolism, I was confident that moving on to a different research environment would be the smart move. When undertaking the increasingly competitive task of finding a postdoc, it certainly helps if you're not restricted to one geographical region. My initial criteria when postdoc hunting was simply that it should be 1) in a relevant field and 2) in a location that aligned with my active, outdoorsy lifestyle. I ended up in San Antonio, Texas – a large sprawling city where it's too hot to go outside most of the year and too spread-out to walk anywhere when it does cool down! Needless to say, my initial feelings towards the city itself were somewhat negative, but my project was interesting and I tried to focus on making the best of the resources available.

This lab I joined represents the basic science arm of the broader Diabetes Division and, demographically, San Antonio is probably one of the best places in the country to study Diabetes. Here, I've been fortunate enough to learn about the disease from one of the world-leading clinical researchers in the field. Most of the work done in my lab involves cell culture or mice models, and I've consequently become accustomed to many new experimental approaches and techniques. The strength of the division in running clinical trials also means I'm able to continue working with human tissues, which can be invaluable in putting together impactful manuscripts. The lab is very well-funded, and my conditioned frugality towards consumables and experimental setups was (and still is) strongly discouraged! This level of funding also meant that I wasn't initially expected to support my own salary with grant applications – a huge bonus when trying to be productive with experiments.

Despite the prevailing opinion about US academia, the work ethic at my institution seems fairly relaxed and people are granted substantial flexibility in their schedules. This probably isn't representative of other labs in the US and certainly depends on the PI, who in our lab happens to be from the UK too (which explains the ritualistic group tea breaks). Most of the neighbouring research groups are similarly multinational, and it would be easy to work here without ever really experiencing Texan culture. Fortunately, I've had plenty of down time away from the lab and have gradually learned to appreciate San Antonio for the lifestyle it offers and rich culture it carries. For me, this has meant joining a local sports team through which I've developed an incredible network of friends. The transient nature of postdoc positions can encourage a tentative approach to organising one's life when moving abroad, allowing you to engross yourself entirely in the job at hand. Establishing a life outside of work has been vital in putting my work here into perspective, and makes those inevitable scientific frustrations far easier to deal with.

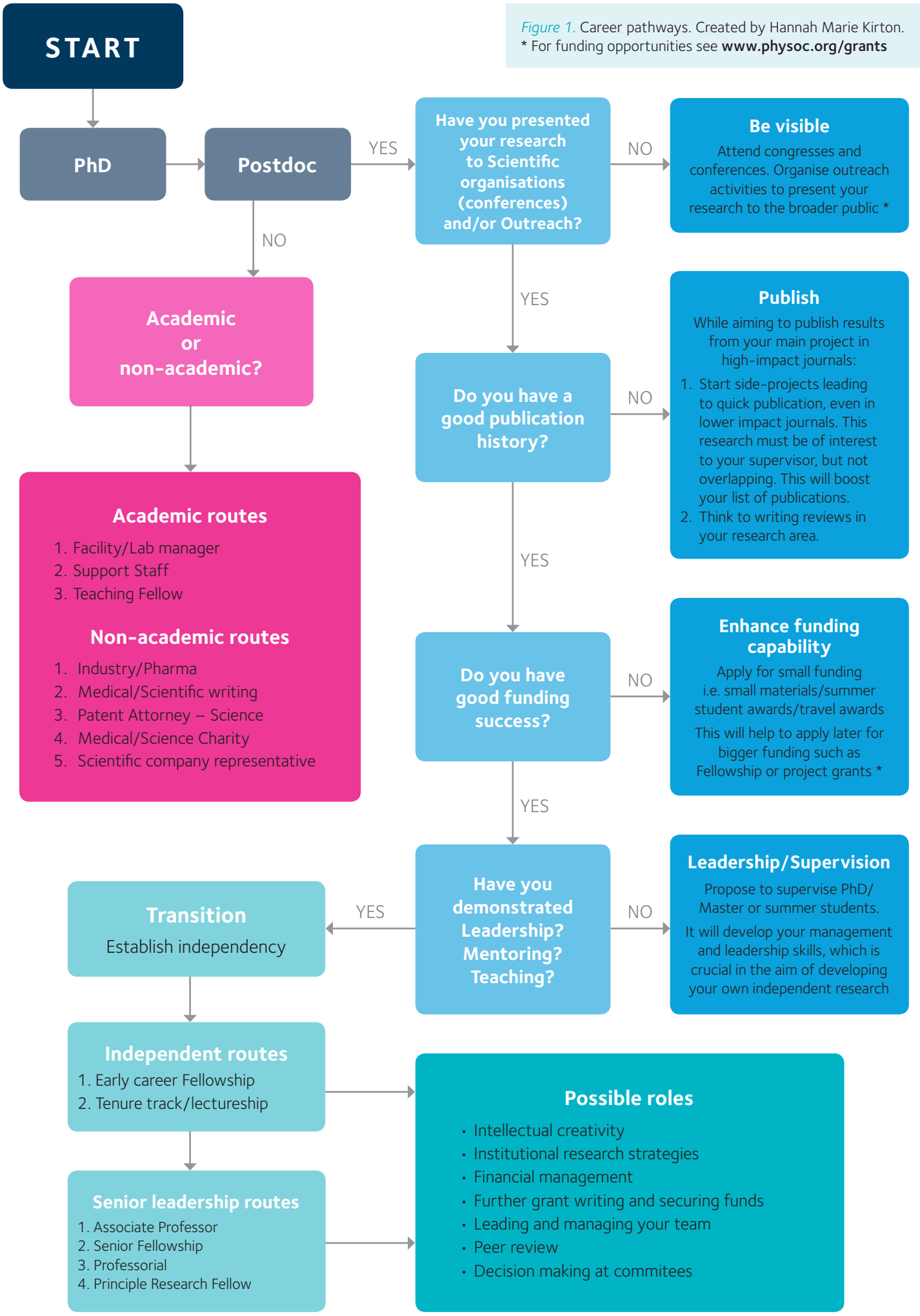


Figure 1. Career pathways. Created by Hannah Marie Kirton.
* For funding opportunities see **www.physoc.org/grants**

Two careers-related reflections from a poacher turned gamekeeper

Richard Malham,
Senior Research Policy and Integrity Manager
orcid.org/0000-0002-9477-6488

There are two things I can't stop banging on about whenever I have the chance to talk to researchers about careers. I like to think I've got a pretty robust perspective given that I have had the privilege of many perspectives on the issue: as a PhD student, working at the national level on careers policy (for biomedical researchers), and working at the University level on research policy that applies to a whole range of disciplines. The following are my personal opinions, and in no way reflect the position of any organisation I work, or have ever worked, for.

1. **Be smart in the system as it is**
   Make time to develop your career, don't kid yourself that you will *find* time when we all know that there is always more you could do at the bench. If you stay in academia, having some demonstrable skills and experience beyond the bench, such as event organisation, public engagement, working with commercial partners, etc., will be a concrete advantage. If you move out of academia, they become a crucial advantage. Developing them requires proactively dedicating time, and may require you being assertive and unapologetic in the face of attitudes like (to paraphrase) 'actively choosing to spend time away from the bench is heresy and a pointless distraction from the real work'. The return-on-investment is well worth sacrificing a fraction of your bench time: the stats on attrition are stark (American Society for Cell Biology, the Royal Society [Fig. 1.6 on p. 14] and Wellcome Trust [Fig. on p. 15]), so much so that the Royal Society released guidelines in 2014 for intervention at the PhD stage.

2. **Simultaneously push for change**
   When you spot issues with career structures/opportunities, get organised at the grassroots level and engage employers and funders (what a great way to get that skills and experience as per point 1!). They care and are open to ideas, but bear in mind that i) not all change is possible because funding/jobs must be rationed because demand outstrips supply, ii) employers/funders are far more likely to push change 'top down' after new ideas have already started to be pushed from the 'bottom up' and iii) it's not always their fault, so push in the right direction and don't make unnecessary 'enemies'. On the latter, do your research to find out where issues really come from: for example, issues you may have with funding and promotion decisions may actually be due to the behaviour of your fellow researchers (possibly even acting against institutional guidance) in their roles as peer reviewers and panel members, not by 'the University' as an organisation.

For those who feel that number 2 is too feeble, I'll leave you with a suggestion: how about challenging the widespread assumption (underlying the design of various careers-related processes) that competition-based rationing is *always* best (e.g. **www.timeshighereducation.com/news/universal-basic-income-better-option-research-grants**). Or seek a completely different type of society...

The quest for the Holy Grail of lectureship

Gisela Helfer,
Lecturer, University of Bradford, UK

After I graduated in Zoology at the University of Salzburg, Austria, I worked at the Max Planck Institute for Ornithology in Andechs, Germany. Here I found my love for science in general and chronobiology in particular. From Andechs, I started my northwards journey, first to do a PhD at the University of Birmingham and then to postdoc at the Rowett Institute in Aberdeen. Throughout my journey, I was very fortunate to meet some amazing scientists, mentors as well as peers, and it was always my ambition to succeed in academia. Six years of postdocing, three moves and two children later, I finally found the Holy Grail in beautiful Yorkshire. In March 2016, I started my permanent lectureship at the University of Bradford.

Academia has one of the longest apprenticeships that I am aware of. Undergraduate studies, plus/minus masters studies, PhD studies and then several years of postdocing. For me, this totalled to 14 years of apprenticeship. Despite this long training, I was little prepared for the job of a lecturer. Yes, I had some teaching experience. I supervised students in the lab, I occasionally lectured to undergrads and I even worked a few months as a teaching fellow. In my CV I called this 'extensive teaching experience' – little did I know. Because in reality I spent all my days and often nights (the joys of circadian rhythms research) in the lab or in the animal house. And I loved every minute of it!

Now, I am rarely in the #Helferlab. The brand-new set of pipettes that I proudly bought from my first grant is now exclusively used by my students, while I spend my time rushing from place to place. I run to see undergrads or I run to one of my countless meetings.

I admit that I miss being a postdoc. I miss being in the lab from morning to evening, I miss having a supervisor who keeps me right (although my mentor at the Rowett is only a phone call away) and I miss the untroubled life of only being responsible for the next set of experiments. Of course, I do not miss the dreadful months before the contract comes to an end.

Despite all of this, I enjoy being a lecturer. While the holy grail is not as shiny and golden as I thought it would be, the journey was certainly worth it, and I would do it all over again. Next goal: professorship.

This article was compiled by Jo Edward Lewis.

The postdoc problem

To be in academia, or not to be in academia?

Hannah Marie Kirton

Cardiovascular Research Fellow, University of Leeds, UK

Postdoctoral scholar: an individual with a doctoral degree engaged in mentored research or scholarly training; both instrumental in acquiring the professional skills needed for independence and leadership.

'Although we are increasing our profiles with glamourous funding and leadership skills or substituting our desired goal for a permadoc position, three-quarters of us still end up outside academia'

Worldwide, the number of PhD's and postdocs is outpacing the number of permanent senior academic positions. From 1999 to 2003 alone, there was a 31% increase in the number of PhDs. Several decades ago, most PhD's 'walked' into permanent academic positions upon completion of their PhD. But as the doctorate numbers rise, most find themselves funnelled into the world of the postdoc, with only a small percentage making it to permanent academic positions. Statistics in the U.K alone show that 19% of doctorates are employed in any academic job, but only 3.5% enter into permanent academic positions. And if you think escaping to America will improve your odds, Andrew Hacker and Claudia Dreifus reported that between 2005-2009 more than 100,000 doctoral degrees were awarded in the USA. In the same period, there were only 16,000 new professorships.

We face the challenge to cure major diseases – Alzheimer's, heart failure, cancer – and yet, academic institutions are faced with a crisis of declining funds. This is driving PI's to fire lab technicians, increasing the burden on the postdocs. Furthermore, fellowship success rates have reduced (from around 50% to 3-5% quoted for today's prestigious fellowships). Further still, the postdoc lifestyle brings pressures: to maximise publications, impact factor and citation rates, achieve independent funding success, and to mentor and teach. We face a burdensome work environment often working at multiple institutions with heavy workloads, playing havoc with any chance of a work-life balance. We are a cheap, highly motivated, disposable source of labour that boosts an institution's research capacity. Yet there is clearly a struggle to achieve higher academic status, which forces an ever-increasing number of talented early career researchers to question their next career move. It is therefore not so surprising we see PhDs and postdocs, the driving force of cutting-edge research, taking a swift exit from academia in the pursuit for other professions.

Permadocs, Superdocs ...Independence!

How do we correct the 'Postdoc Problem'? And how do we break through the barrier to climb the academic ladder?

In some countries, including the UK, governments are encouraging permanent postdoc positions, and limiting the number of years postdocs remain on short-term contracts. Some institutions, particularly in the US, are introducing senior postdoc positions – the superdocs. Such positions, created for talented postdocs who may have no desire to start their own labs, are classified as permanent senior staff scientists on higher paid wages. Superdocs can take on the role of a lab manager. They can conduct the science they love, while assisting in publication writing, mentoring trainees and advancing current technology, without the pressure of being the PI.

But many postdocs want to continue in academic research and are willing to endure the pressures of Brexit and the postdoc burden for a chance of becoming PI. And in doing so they are willing to fight and break through to independence for a tenured or full time academic staff position. And many are achieving this, with the help of external societies and university institutes lifting limitations and broadening the boundary for success, respectively. This is helping us diversify our approach to success and ease the burden of being an early career researcher.

If you, like many postdocs, are stuck as a so-called 'permadoc' – one who has fulfilled more than six years of postdoc experience – there are still ways to climb the academic ladder. For example, most societies and funding agencies have lifted the age restriction for fellowships. This not only secures research excellence in our society, but also enables senior postdocs to push for independence in a time of funding limitations. Funding bodies now also fully support applicants returning to research following a career break.

In addition to this, most learned societies and organisations, including The Physiological Society, support the pursuit of independence in the early stages of academia. This includes outreach funds, travel grants and vacation studentships to support summer students on a project piloted by an early career researcher. Collectively each of these awards allow Society members to promote their independent funding success and leadership. The Physiological Society also support early career conferences and other networking opportunities, physiologists in their first permanent academic position, and those returning to a permanent position after a career break.

What do we want and when do we want it?

Career Action Plan
Although we are increasing our profiles with glamourous funding and leadership skills or substituting our desired goal for a permadoc position, three-quarters of us still end up outside academia.

To retain talented early career researchers, we need to nurture new PhD's and postdocs through 'career action plans'. Firstly, we need to be honest and advise PhD's and postdocs about the 'ugly truth' of academia, and if needed, to take a realistic view early in their career path. This could come in the form of an institutional induction to highlight their rights, entitlements, and responsibilities in academia. In this manner, they have an understanding of what they can hope to achieve, and most importantly what actions to take to get there. This in turn warrants regular reviews on their progress, and an expectation for our institutions to demonstrate talent retention in the form of fellowships.

Mentoring and Postdoc Champions
Mentorship is also key, and can be sought through internal or external opportunities (including The Physiological Society). Mentor circles within institutes can also be particularly useful, enabling postdocs to interact and share their journeys. Institutional support is fragmented at best and often relies on word of mouth from one postdoc to another. Therefore a 'postdoc champion' – a permanent staff member aware of the needs of postdocs and how best to address them – within our Faculties and Schools could transmit a wealth of key and current knowledge to early career researchers.

A step down fellowship lane
Even with better action plans and mentoring, lack of funding remains an impediment at all levels of academia. Improvements are necessary at the institutional and research council level. We suggest institutions in receipt of funding for PhD and postdoctoral researchers should be expected to sign the Concordat on Early Career researchers. In addition, they should be required to demonstrate how they meet, or are working towards these recommendations.

To help with funding success, postdocs should be allowed full co-applicant status on grants; this would enable postdocs to develop their own research themes and move towards independence. Furthermore, postdocs are currently allowed time for teaching and clinical work. Why not build in time for research development and career progression? As Janet Metcalfe, Chair and Head of Research Career Development Organisation states, *'while funding from research councils to support postdocs are often attached with guidelines emphasising the importance of career development for the researchers, these expectations seldom translate into practice.'*

In essence, never give up! There are diverse ways to pursue independence and encourage new interventions that help recognise and retain early career talent in academia.

This article was edited by Jo Edward Lewis.

Annual General Meeting oral and poster competiton winners

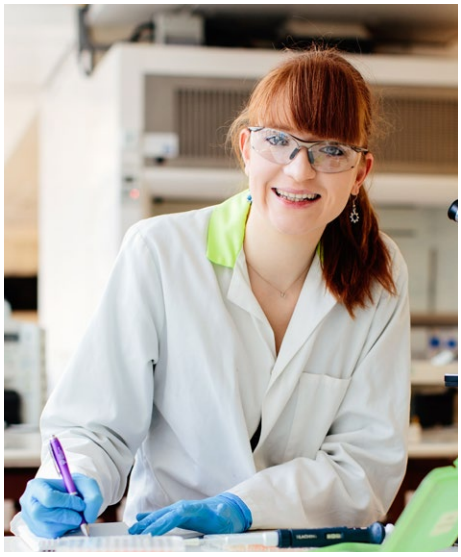
Victoria Meah

Cardiff Metropolitan University

Winner, oral presentations
Mum's heart: how does the heart change during pregnancy?

The mother's body systems change significantly during pregnancy to accommodate for the developing baby. Compared with the non-pregnant state, a healthy pregnant woman's heart changes in structure and function. The heart pumps harder and faster as a result of increased metabolic demand, increased blood volume, dilation of blood vessels around the body, elevated sympathetic activity and altered hormone levels.

Despite these apparently favourable changes, studies have shown reduced contractile function of the maternal heart in the second half of pregnancy. This suggests that the ability to pump blood around the body is reduced in healthy pregnant females, particularly during physical challenges, like aerobic exercise, that cause an increase in cardiac work. My PhD research has therefore investigated how the altered maternal cardiovascular system responds to light to moderate exercise. My findings have shown that healthy pregnant females in the late second trimester in fact have enhanced contraction of the heart, and are able to increase their pumping capacity during the additional challenge of exercise. It may be the case that women who develop cardiovascular complications are less able to adapt their cardiac function during physical challenge, whether that is pregnancy or exercise. Therefore, exercise could be used as a screening tool to identify these women at risk of pregnancy complications prior to the development of the disease.

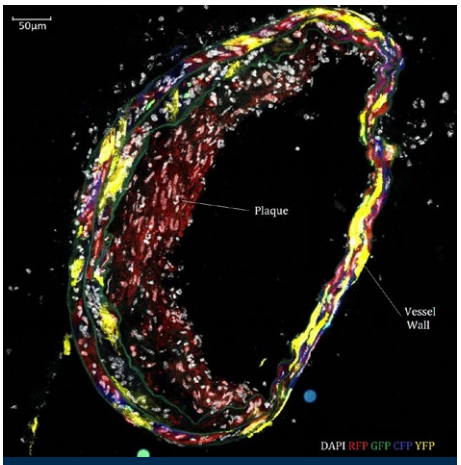


Annabel Taylor

University of Cambridge

Runner-up, oral presentations
Understanding the cause of clogged arteries

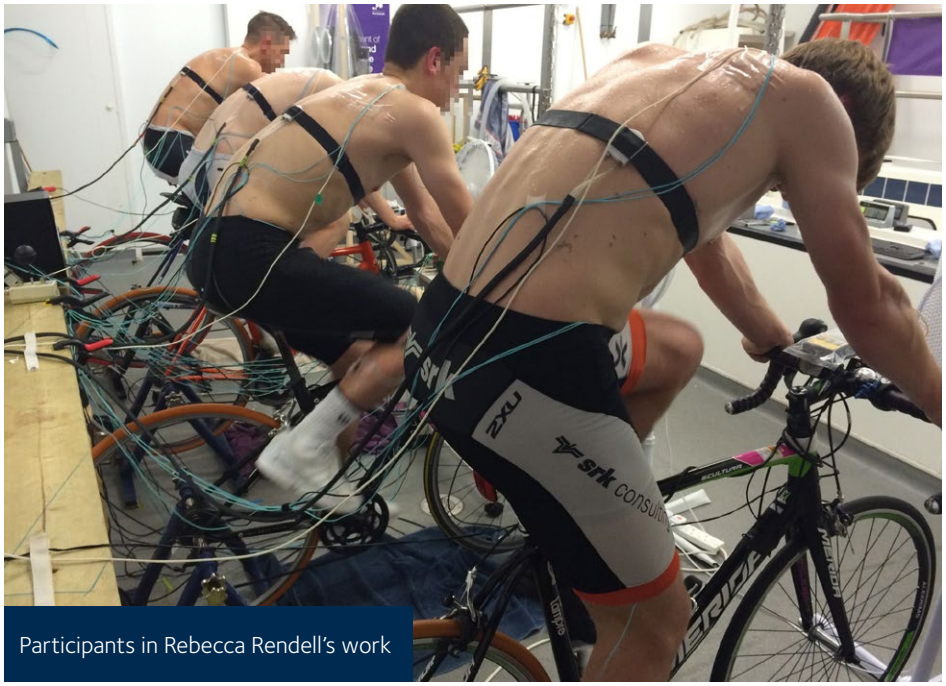
Vascular smooth muscle cells (VSMCs) are found in your blood vessels, where they regulate blood flow and blood pressure. However, during injury and inflammation, these cells lose the ability to contract and some instead begin to grow. This process allows for vessel repair, but when it malfunctions, it contributes to the formation of plaques on the wall of blood vessels, which can cause heart disease and stroke. In my research, I look at how individual VSMCs behave during plaque generation. To study this, we use a genetic model system called 'Confetti', which marks individual VSMCs randomly with one of four colours. Within the healthy vessel, VSMCs of all four Confetti colours are intermixed. In contrast, plaques have large regions of only one colour, demonstrating that the plaque is generated by expansion of a single VSMC. Currently, we are investigating how the cells which contribute to a plaque differ from those which do not. To explore this, we are using a new technique to compare gene expression of individual cells. In this way, we have identified many genes that are differentially expressed between plaque-susceptible and -resistant regions of the aorta, as well as between individual cells. We hypothesise that these genes mark or regulate the VSMCs which produce atherosclerotic plaques. We are now modelling this switch in gene expression *in vitro*, using Confetti VSMCs in a petri dish, to test the influence of these genes on individual cells. This research allows us to investigate the mechanisms behind selection of the cells that become plaques, and subsequent plaque development or treatment.



Transverse section of an aorta containing a plaque. The VSMCs in the blood vessel wall show random distribution of Confetti labels, whereas the plaque contains only red cells.

Rebecca Rendell

Bournemouth University



Participants in Rebecca Rendell's work

Winner, poster presentations
Double trouble: hypoxia and heat in athletic performance

In training, athletes use repeated exposure to hot and/or high-altitude environments, either outside or replicated in chambers or tents. Our understanding of the physiological adaptations to these environmental stressors, however, is limited to what happens when each occurs in isolation, not in combination. Therefore, this study examined i) the influence of overnight moderate hypoxia on the physiological adaptations to daily heat exposure (known as heat acclimation [HA]), and ii) whether HA (with and without combined hypoxic stress) affects endurance performance in a temperate, sea-level environment.

Eight trained males undertook two 11-day HA programmes with daily 90-minute exercise-heat exposures (40°C, 50% relative humidity [RH], core temperature = 38.5°C), once with overnight hypoxia (O_2 equivalent to ~2400 m) and once without. In both conditions, HA was evident after 5 days, demonstrated by reduced core and mean skin temperature, heart rate and sweat sodium concentration; core temperature was further reduced after 10 days of exposure. Additionally, the fluid component of blood (plasma volume) and the concentration of red blood cell (RBC) stimulating hormone (plasma erythropoietin) increased following HA with no change in the total mass of haemoglobin in the RBCs. While endurance performance may be improved in temperate (22°C, 50% RH), normal-oxygen environments following HA (demonstrated by improved peak power output, lactate threshold and work done in a cycle time-trial), this was unaffected by an additional hypoxic stressor. Although these findings are mechanistically important, this observation is also practically relevant; athletes preparing for competition in a hot environment should not be concerned about concurrent exposure to a moderate-hypoxic stressor.

Sam Scott

Liverpool John Moores University

Runner-up, poster presentations
Improving fitness by bringing the workout home

Many people fail to meet the physical activity guidelines, putting them at increased risk of metabolic diseases. This is largely due to barriers such as a lack of time, limited access to facilities and equipment, difficulty with transportation and inadequate financial resources. I investigated a novel home-based high-intensity interval training (HIT) programme designed to remove these barriers and improve the health of previously sedentary obese individuals. Thirty-two sedentary obese adults were allocated to one of three 12-week exercise training groups: home-based HIT (Home-HIT), laboratory-based HIT (Lab-HIT) or home-based moderate intensity continuous training (Home-MICT). Home-HIT consisted of simple bodyweight exercises (e.g. star-jumps, burpys, mountain-climbs) in an unsupervised place of the participant's choosing. The Lab-HIT group attended the laboratory for supervised cycle training. Home-MICT performed 30-50 min continuous moderate intensity exercise (swimming, cycling or running). We monitored compliance and exercise intensity in the home groups using a heart rate monitor and mobile phone application that could be remotely monitored by the research team. We found high session completion rates in all three groups at the required exercise intensity (Home-HIT = 96%; Home-MICT = 88%; Lab-HIT = 97%). Home-HIT was comparably effective at increasing a range of physiological measures with Lab-HIT, including aerobic capacity, body fat percentage and blood vessel health, which are indicative of a lower cardiovascular disease risk. To conclude, this is the first study to successfully implement a Home-HIT training programme in previously sedentary obese individuals. Despite being unsupervised and having no encouragement, the Home-HIT group had high adherence rates at the prescribed exercise intensity, comparable with the fully supervised Lab-HIT group. Home-HIT appears effective at minimising many of the barriers to exercise, and may therefore represent an effective strategy to improve public health by increasing physical activity participation.

Meet the Affiliate Working Group

The Affiliate Working Group ensures Affiliate Members receive the required support from The Society, and are aware of and engage with our activities. It also helps Affiliate Members be aware of the resources available to them in the early stages of their career.

Jo Edward Lewis

University of Nottingham

The neuroendocrine role of FGF21

'It is seldom at the frontier that discoveries are made but more often in the dustbin'
– Alan Bennett, The Library Book

Or in our case, the -80°C freezer. This quote by Yorkshire's finest (sorry Fran, current boss and proud Blade) accurately describes our latest publication, *FGF21 is an insulin-dependent postprandial hormone in adult humans*, my proudest scientific moment to date. Dr Ricardo Samms, Prof Fran Ebling, Dr Kostas Tsintzas and I uncovered that fibroblast growth factor 21 (FGF21) levels in the blood respond acutely to changes in insulin, rather than glycaemia, in the post-prandial period.

Having gained my PhD in 2015, and spent the subsequent year's postdoc-ing and parenting, my research aims to understand the control of energy metabolism by the brain. We are currently focusing on the role of a type of brain cell called tanycytes whose cell soma are embedded in the ependymal lining of the third ventricle (in addition to our work on FGF21).

Recently elected deputy early career researcher at the British Society for Neuroendocrinology, I also aim to improve the post-doc experience.

Hannah Marie Kirton

University of Leeds

The importance of securing independent funding

I have a love for both cardiology and neuroscience, which I vow to maintain in my academic pursuit. This journey began as a neuroscience PhD student in the laboratory of an inspiring supervisor, at the University of Leeds. He instilled my passion for ion channel physiology, and hunger to follow in his footsteps, which led to my postdoctoral role in cardiovascular research at Leeds, researching the arrhythmic heart in diabetes. During this time, I have continued to collaborate with my PhD supervisor, leading to my recent Boehringer Ingelheim funding success. This enabled me to work at the University of Texas Health Science Center, San Antonio, developing cutting edge research techniques, and also demonstrating an established technique to the host team. This experience increased my research expertise, expanded my scientific skillset, allowed me to bring back novel skills to my home institute, expanded my ability to financially support independent research, reinforced networking skills and future collaborations, and boosted my status due to working in an international laboratory. While publications are key to academic success, do not underestimate the power of independent funding success!

Peter Aldiss

University of Nottingham

Understanding brown fat

Since my undergraduate degree (Exercise, Nutrition and Health BSc) I have worked for a cardiovascular disease prevention service in Nottingham and then for the Paediatric Diabetes team at Nottingham University Hospitals. I then co-authored my PhD fellowship and my BHF funded work at UoN is focussed on how brown fat (fat that burns energy and produces heat) between the shoulder blades and around the blood vessels, responds to a high-fat diet, the environment and exercise training. I was very fortunate to chair my suggested symposium at the European Congress on Obesity midway through my second year which has led to collaborations with a number of the eminent speakers involved. I recently presented one of my projects at the EU Young Endocrine Scientists (EYES) meeting in Porto. Now, in my final year I am working on completing my lab work, publishing the third review from my intro chapter and writing up my first study for publication.

Kimberley Whitehead

University College London

Cracking sleep: physiology and beyond

I worked in the NHS as a clinical scientist between 2006 and 2015 before transferring to academia. I currently work at UCL and specialise in the development of the somatosensory system (the sensation of touch, pain, etc.) and the structure of sleep in pre-term infants. However, my clinical experience has taught me that understanding physiology alone cannot fully explain our experiences of health and disease. Especially in the field of sleep and sleep disorders, societal pressures have a massive impact. For this reason I'm really excited to have set up a collaboration with Professor Matthew Beaumont, also at UCL, who researches disturbed sleep via a humanities-based approach. I hope that this inter-disciplinary collaboration will open up new avenues to understand the ways that physiology intersects with our social circumstances. It also offers opportunities for broad-based public engagement activities and I'm pleased to be organising an evening event at the Grant Museum in London about how sleep varies across the animal kingdom (28 February 2018), and a daytime event which will include talks from sleep experts across a wide range of disciplines (10 January 2018).

Mathew Piasecki

Manchester Metropoltan University

Wondering why we all lose our nerve

I'm a Research Associate in Musculoskeletal Sciences at Manchester Metropolitan University, where my research focus is physical frailty and its association with the age-related loss of motor nerves (called skeletal muscle motor units). It's actually somewhat of an extension of my PhD which I finished in December 2015, but it pays a little more. I'm also interested in the effects of lifelong exercise on skeletal muscle, along with many others who are trying to answer the question 'does exercise keep us young?' The answer is it probably doesn't, but it certainly helps a bit. I've been a member of The Physiological Society since 2010 when I joined as an undergraduate, and I've been the Affiliate representative for just over 2 years. The formation of the Affiliate Working Group is a great example of how the Society recognises that our early career researchers are the future of Physiology, and they should be supported in any way possible. I look forward to meeting as many Affiliate Members as possible at the Future Physiology meeting in Leeds!

Jessica Piasecki

Manchester Metropolitan University

The interaction of muscle and bone health in aging

I have been involved in research for around 5 years. I first started my career with a MSc at Manchester Metropolitan University researching young female athletes and the effect of menstrual cycle disturbances on bone health. I gained an insight into managing a research project from start to finish, as well as developing scientific laboratory methods. From there I went on to manage the largest cohort of master athletes in the UK, working as a research assistant on the 'VIBE' (Vertical Impacts on bone health in the elderly). This was a collaborative project between MMU and the University of Bristol. I am now enrolled as a PhD student and the research focus has remained on bone health, as we are investigating the relationship between sarcopenia, muscle loss associated with aging, and osteoporosis, bone weakening associated with aging. I have been a member of The Physiological Society for a few years and I took the opportunity to join the Affiliate Working Group after reading about it in the newsletter. It has presented several opportunities and challenges, and I would encourage anyone to get involved with something outside of their day to day job.

Calum Wilson

University of Strathclyde

Engineer turned physiologist inventing new ways to study the inside of arteries

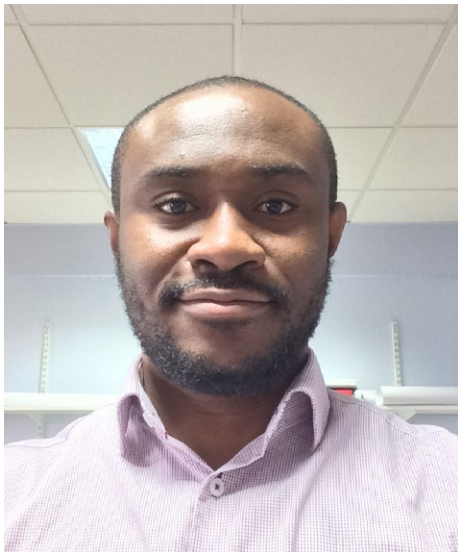
I am a Sir Henry Wellcome Postdoctoral Research Fellow at the University of Strathclyde, where I work to understand how arteries and veins control the flow of blood around our bodies. I have always been fascinated by how things work, but I was a little slow to appreciate biological research and initially set out to train as an engineer. Somehow, I found myself in a physiology lab for my EngD studies and I have been there ever since. My work involved the design and application of a novel microscope which I was fortunate enough to first describe in *The Journal of Physiology*. As a research fellow, I now use advanced microscopy to study calcium signalling in the innermost layer of arteries. Last year, I again submitted a study (performed with a friend and PhD student) to *The Journal of Physiology*, which was ultimately awarded *The Journal of Physiology's* Early Investigator Award 2016. It truly was an honour for us to receive this award, not least because it was the second time that the Editors of *The Journal* chose to recognise our work, but also because it demonstrated the openness of physiologists to the opinions of those from outside the discipline.

Rachel McCormick

University of Liverpool

Sharing physiology and promoting future physiologists

My name is Rachel McCormick and I am a postdoc at the University of Liverpool. Our research focuses on why our muscle gets weak as we age and what we can do to prevent this. My work specifically looks at changes that occur in microRNAs, molecules that regulate which genes are on or off, in the ageing muscle. I have been a member of The Physiological Society for over 3 years and an affiliate representative for two years. Within The Society I also have a role in the Education and Outreach Committee and the Affiliate Working Group. I think it is so important that what we discover in the lab is fed back to the public, and that new researchers, as the future of The Society, can voice their opinions.



Emmanuel Amabebe

University of Sheffield

The why and how of pre-term birth

I completed my PhD in Reproductive and Developmental Medicine at the University of Sheffield in 2016, where I investigated the cervicovaginal fluid metabolite and microbiomial profile patterns that predict preterm birth and explored key patho-physiological mechanisms of inflammation-associated preterm birth. This is because vaginal microbial community and their metabolic by-products can influence pregnancy outcomes and are useful tools for the detection of woman at high risk of premature delivery. I am currently a Postdoctoral Research Assistant at the same University where, as part of the ECCLIPPx™ team (**www. ecclippx.group.shef.ac.uk**), I work to validate novel techniques/devices for accurate prediction of premature birth and applications for their regulatory approvals for use in clinical practice to assess the integrity/competence of the cervix and vaginal microenvironment in pregnancy. As an Affiliate member of The Physiological Society, I have enjoyed several travel grants to both local and international conferences and workshops to present my work and learn new research skills and techniques that have immensely impacted my career path from postgraduate to my current postdoctorate position. I am delighted to be a member of the Affiliate Working Group and representative of the group on the Membership and Grant Committee.

Jade Bearham

St Georges University, London

Linking industry and research – studying glucose sensors

I am currently a PhD student at St Georges University of London, with my research focused on the development of molecular sensors for measuring glucose in airway secretions. Before this I completed a Bachelor's degree in Biochemistry at the University of Sussex. Both my undergraduate degree and my PhD have enabled me to spend time working within the industrial sector, firstly spending time at Novo Nordisk in Copenhagen and more recently at Astra Zeneca in Gothenburg. I am fortunate that this has enabled me to experience the similarities and the differences between the academic and industrial approach to projects. I have had the opportunity to form a valuable network that spans across both sectors, which I feel is invaluable for connecting research discoveries from different fields and beneficial for possible future collaborations, especially as I near the end of my PhD.

Dan Brayson

King's College London

Sharing a love of cycling science

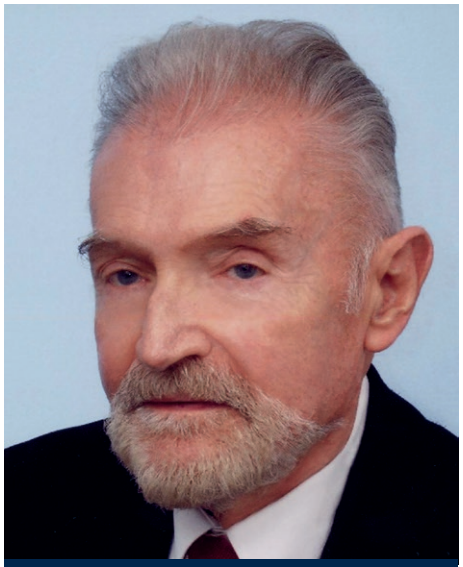
I'm currently 'post-docing' at King's College London investigating the ways in which hearts malfunction as part of heart disease. Mainly though, I like riding bikes and have hosted a 'cycling science' themed public engagement event with support from The Physiological Society and I recently completed an ultra-endurance bike race across Europe. Here's me with a rubbish view 2500 metres up in the mountains of Austria during the race.

More questions about the Affiliate Working Group?

For more information, email Membership Engagement Manager Jen Brammer at **jbrammer@physoc.org**

Obituary:

Professor Andrzej Trzebski 1928 – 2017



Professor Andrzej Trzebski

'Despite the modest financial support … Trzebski transformed his department into a highly respected centre of experimental and clinical physiology'

Andrzej Trzebski was an internationally recognised physiologist and an outstanding medical teacher. He was born in 1928 in Warsaw, Poland. His education was seriously affected by the Second World War and Poland's occupation by Nazi Germany. After the war, he completed his higher education and he started to study at the Medical Academy of Warsaw in 1950. While studying medicine, he became fascinated with physiology and he took up a post as a research and teaching assistant in the Department of Human Physiology. In 1956, he presented his MD thesis and accepted a Fellowship at the CNRS in France. He then spent a further two years at the Laboratoire de Neurophysiologie in Paris, where he began his studies on the role of the CNS in chemoreception. There he demonstrated that acute lack of oxygen induces an arousal response via the reticular activating system (the parts of the brain and spinal cord controlling awareness and consciousness). In 1960, he returned briefly to Poland before going to the USA with a grant from the Rockefeller Foundation for 2 years to research in the Department of Physiology and Bockus Research Institute of the University of Pennsylvania in Philadelphia. He continued his investigations into the interactions of pressure and chemical signals from the arteries and the messages they send to the brain and spinal cord to balance our heart and lung function. This was to be his principle scientific interest through his long, active research life.

From 1964 to 1967, he was Visiting Professor in the University of Yogyakarta in Indonesia, funded by the World Health Organization. His role was to organise medical education and scientific research at the University. After that he was appointed to the Chair of the Department of Human Physiology at the Medical Academy of Warsaw and returned to Poland. He established an active research group in Warsaw and attracted over the years several students who have since developed their own distinctive careers in Poland and abroad. His area of interest overlapped with that of Sidney Hilton in Birmingham. As a result, a significant interaction between the laboratories followed. Several students and fellows moved between the two laboratories, and joint publications appeared. Notably, Janusz Lipski, now a Professor in Auckland, NZ, spent time in the early 1970's working with Robin McAllen and Mike Spyer and subsequently published papers with them and John Coote.

Despite the very modest financial support for science and teaching in Poland in the 1970s –1980s, Trzebski transformed his department into a highly respected centre of experimental and clinical physiology. He was a generous host to visiting scientists and was exceedingly proud of Poland's history and culture. He played a very full part in international meetings and workshops on the control of heart and lung function. He was quick to his feet with challenging questions but was always polite and encouraging. He always considered the clinical significance of observations and very early in his career suggested that the increased arterial chemoreceptor discharge could have a major role in the development of high blood pressure (hypertension). Interestingly, it has taken until the last decade for this to be seriously considered. Clinical studies are now evaluating whether cutting the sinus nerve, a nerve in the heart, may be useful when conventional drug treatment is ineffective.

Andrzej Trzebski was a member of the American, German and UK Physiological Societies and of the Council of the International Union of Physiological Sciences (1977–1986). He served as the President of the International Society of Arterial Chemoreception (1988–1989). He was a member of the Polish Academy of Sciences and also a member of the Polish Academy of Arts and Science. Notably, after 1989, with the re-establishment of democracy in Poland, he was actively engaged in the restoration of university status for the Medical Academy of Warsaw and for a renewal of the independent status of universities in Poland.

Written by Ewa Szczepanska-Sadowska & Mike Spyer

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Experimental Physiology

Regular aerobic exercise reduces endothelin-1 mediated vasoconstrictor tone in overweight and obese adults

Caitlin Dow, Brian Stauffer, Danielle Brunjes, Jared Greiner & Christopher DeSouza.
102(9), 1133-1142 (16 July 2017)

Overweight and obese individuals have an increased risk of cardiovascular disease. This may arise from problems with the control of blood vessel diameter. This control involves the release of the transmitter endothelin from the lining of the blood vessels. The role of endothelin was investigated in 37 sedentary human subjects; 25 overweight and 12 normal. Only the overweight subjects were made to exercise for 3 months, and a wide variety of fitness measurements were made on both groups. Most exercising subjects walked, but some incorporated jogging as their fitness improved in order to maintain their heart rate within the prescribed range. Compliance with the exercise programme was checked every 2 weeks. The results of a wide variety of measurements showed that regular aerobic exercise had beneficial effects on blood vessel size in previously sedentary overweight and obese adults.

DOI: 10.1113/EP086454

Pretreatment with fish oil attenuates heart ischemia consequences in rats

Alcione Lescano de Souza Junior, Jorge Mancini Filho, Rosângela Pavan Torres, Maria Cláudia Irigoyen & Rui Curi.
102(11), 1459-1473 (4 October 2017)

Fish oil has yet more benefits. We investigated whether the recovery of heart function in male rats after a cardiac event benefitted from previous diet supplementation with fish oil rich in ω-3 polyunsaturated fatty acids. Changes in heart inflammation and metabolism were evaluated to address the possible mechanisms involved. We compared fish oil with soybean oil which is rich in α-linoleic acid (ω-3 polyunsaturated fatty acid which is widely recognized to induce inflammation) to assess the involvement of inflammation in the heart ischaemia-induced injury and dysfunction. Fish oil had a wide range of beneficial effects. Fish oil pretreatment, not soybean oil, protected against heart ischaemia, as indicated by a small damaged area and preservation of contractile function. These findings were associated with increased left ventricle ATP content and maintenance of the coronary blood flow with no change in pro-inflammatory cytokine levels.

DOI: 10.1113/EP086332

The Journal of Physiology

Differential effects of late gestation maternal overnutrition on the regulation of surfactant maturation in fetal and postnatal life

Mitchell C. Lock, Erin V. McGillick, Sandra Orgeig, I. Caroline McMillen, Beverly S. Mühlhäusler, Song Zhang, Janna L. Morrison.
595(21), 6635–6652 (24 August 2017)

Overfeeding sheep mothers risks fetal complications. There is increasing evidence linking maternal obesity and neonatal pulmonary complications. This study shows that offspring of overfed sheep suffer from slower maturation of surfactant production and a reduction in the number of surfactant-producing cells lining their lungs. The reduced capacity for surfactant production in new-born lambs as a result of maternal overfeeding may affect the transition to air breathing at birth. While these deficits are repaired by 30 days after birth, the affected lungs showed altered glucose transport and fatty acid metabolism. By further refining our knowledge of the mechanisms linking in utero insults to impaired development, lung development may be better understood. Therapeutic targets may be identified to preserve lung function in at-risk newborns during birth.

DOI: 10.1113/JP274528

Median preoptic glutamatergic neurons promote thermoregulatory heat loss and water consumption in mice

Stephen B. G. Abbott & Clifford B. Saper.
595(20), 6569-6583 (13 September 2017)

Cold and thirsty transgenic mice! Optically-activating genetically targeted glutamate neurons in the median preoptic nucleus caused hypothermia and intense drinking in conscious, freely behaving mice. The two responses were not always seen in the same animal, and different regions seemed to be involved. The hypothermia was caused by increased skin blood flow, and was so great that animals often used shivering thermogenesis to warm up once the stimulation stopped. There were large diurnal variations in the responses to stimulation. Water drinking during neuronal stimulation was much greater in the dark cycle when mice are usually awake, and the stimulation woke mice up during the light cycle when they are asleep. The intensity of drinking diminished with repeated bouts of drinking and appeared to be gated by non-osmotic signalling related to the consumption of water.

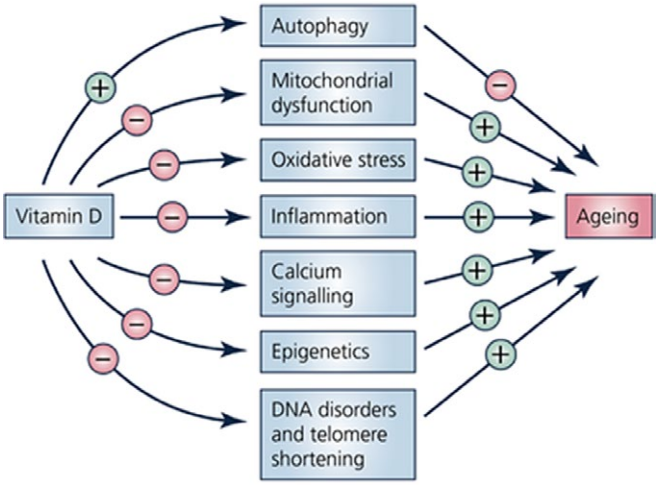
DOI: 10.1113/JP274667

Vitamin D deficiency accelerates ageing and age-related diseases: a novel hypothesis

Michael J. Berridge.
595(22), 6825–6836 (31 October 2017)

In this topical review, with 6 pages of references, a distinguished expert on intracellular signalling proposes a central role for Vitamin D in slowing human ageing. He proposes that vitamin D controls the activity of a number of important ageing processes. It promotes autophagy, which acts to slow down the ageing processes by

Ageing process



removing faulty mitochondria. Vitamin D also acts to reduce oxidative stress, inflammation, calcium signalling, epigenetic effects and DNA disorders including telomere shortening, which act to drive the processes of ageing. With vitamin D deficiency, the activity of these ageing processes increases so that the rate of ageing speeds up, and conditions that lead to diseases such as Alzheimer's disease are initiated.

DOI: 10.1113/JP274887

Physiological Reports

Exercise training dose differentially alters muscle and heart capillary density and metabolic functions in an obese rat with metabolic syndrome

Marcus Vinicius Machado, Aline Bomfim Vieira, Fabiana Gomes da Conceição, Alessandro Rodrigues Nascimento, Antonio Claudio Lucas da Nóbrega & Eduardo Tibirica.
102 (12) 1716–1728 (26 October 2017)

Exercise is good for rats as well as humans. The effects of different levels of exercise were studied on rats fed a high fat diet. This was designed to have the same effects as exhibited in humans suffering from the metabolic syndrome triggered by lack of exercise and a poor diet. The exercise was on motorised treadmills on which rats were encouraged to run by electric stimuli. Animals that received the high fat diet were randomly separated into either a sedentary group or eight different exercise groups that varied according to the frequency, duration and intensity of training. After 12 weeks of aerobic exercise training, the body composition, aerobic capacity, blood circulation, and capillary density in the heart and skeletal muscle were evaluated. The results showed that exercise frequency and duration were the main factors affecting the density of capillaries in the skeletal muscle. Capillary density in the heart was related only to exercise intensity.

DOI: 10.1113/EP086416

Consequences of advanced aging on renal function in chronic hyperandrogenemic female rat model: implications for aging women with polycystic ovary syndrome

Chetan N. Patil, Lorraine C. Racusen & Jane F. Reckelhoff.
5(20) 19 October 2017

To investigate whether women who secrete male hormones at unusually high levels suffer from an elevated risk of kidney disease a female rat model has been studied. This model involved implantation of dihydrotestosterone (DHT) pellets. By 16 weeks of age, the implanted female rats exhibit elevated blood pressure and modest proteinuria with elevated glomerular filtration rate (GFR), likely due to high glucose levels associated with insulin resistance. The rise in blood pressure and metabolic dysfunction is similar to observations made in women with polycystic ovary syndrome. By 22–25 months of age the rats suffered from 60% reductions in GFR, 40% reductions in renal plasma flow, significant increases in proteinuria and kidney injury molecule-1 excretion, and reductions in urinary nitrate/nitrite excretion, compared to age-matched control females. These data suggest that with aging, high levels of male hormones produces chronic kidney disease in these female rats.

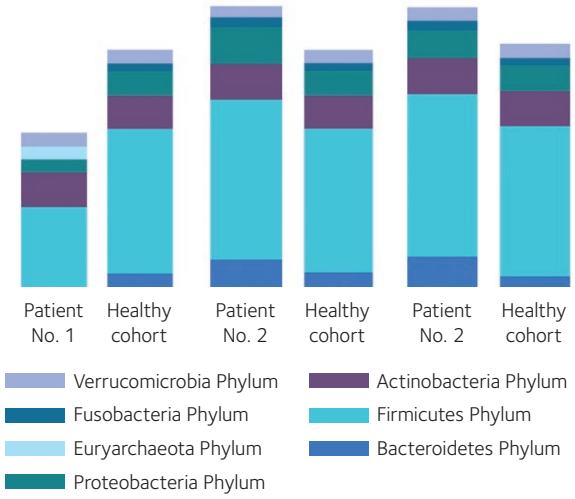
DOI: 10.14814/phy2.13461

Gut inflammation and dysbiosis in human motor neuron disease

Julie Rowin, Yinglin Xia, Barbara Jung & Jun Sun.
5 (18) 26 September 2017

The bacterial and fungal population (the microbiome) of the human gut has been referred to as an organ in its own right, containing an enormous population of individual cells. New evidence suggests changes in the gut microbiome may contribute to the development of neurodegenerative diseases, such as Parkinson's and Alzheimer's disease. This study examined the gut microbiome, and evaluated markers of intestinal inflammation in five patients with motor neuron disease. Fecal samples were analyzed for bacterial content, inflammatory biomarkers and short chain fatty acids.

Relative bacterial abundance at the phylum level



All patients showed intestinal malfunction indicated by a decreased diversity of the microbiome and other indicators compared to healthy cohorts. The authors suggest that the human microbiome might provide an early mediator of neurological diseases.

DOI: 10.14814/phy2.13443

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