Society for Endocrinology

ISSUE 152 SUMMER 2024
ISSN 2045-6808

THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

Spotlight on EARLY CAREERS

Special features
PAGES 6–19

A word from THE EDITOR...

Welcome to our Early Career Takeover issue!

Early career member involvement and support at the Society have changed recently – including moving from a single committee to the inclusion of elected early career members on each Society committee. So, at *The Endocrinologist* HQ, we felt it was particularly important to showcase the work, achievements and career perspectives of our talented early career colleagues. This issue therefore brings you exactly that, with diary pieces and feature articles from early career prize winners and members, alongside career perspectives and hints and tips from those who are more experienced.

When reviewing the submitted articles, I was particularly struck by **'A week in the life of a junior doctor'**, written by our very own Editorial Board member, Vincent Simpson. The diary entry is a very frank and honest description of an on-call week for a junior doctor, balancing patient needs with clinical demands and the volume of patients yet to be seen. All that is in addition to the pulls of home life that having a young family brings.

With public engagement an increasingly important aspect of academic life, some excellent **hints, tips and advice are provided by Caroline Gillet**. Meanwhile, our **'words to our younger selves'** feature some sage advice on finding mentors, pursuing your passions and saying yes to opportunities!

Reflecting on my career to date and what I would say to my younger self, I would certainly echo all the words from this feature and say don't be afraid to ask for advice. My successful grant applications have almost all been the ones that have been read by and had extensive feedback from people both directly in my field and to the left of my field. So do put yourself out there, be brave and ask for help!

Wishing you a restful summer.

KIM JONAS

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Registered in England No. 349408
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CONTENTS

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ON THE COVER...

P6–19
EARLY CAREERS
In the spotlight

P21
SOCIETY GRANTS
Jeremy Tomlinson
Grants Panel Chair

Become a contributor... Contact the Editorial office at **endocrinologist@endocrinology.org**

The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the AUTUMN 2024 issue: **10 July 2024**.

Front cover image ©Shutterstock

Martin Fassnacht

COULD YOU HOST A VISITING PROFESSOR?

Martin Fassnacht, the Clinical Endocrinology Journal Foundation Trust Visiting Professor, is one of the plenary lecturers for **SfE BES 2025**. He will be touring endocrine centres in the UK during the week commencing 3 March 2025.

Martin is Professor of Endocrinology at the University of Munich, Germany. He leads a large translational research group, has been principal investigator of several phase II and III trials in adrenal tumours, and has authored more than 300 publications.

For a chance to host him at your institution, **find out more** and email us at **awards@endocrinology.org** by **21 June 2024**.

HELP TO IMPROVE ENDOCRINOLOGY NEWS COVERAGE

Do you want to help journalists report on hormone-related science more accurately?

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- ✓ **build new professional relationships** by connecting with fellow members through the member directory
- ✓ **keep track of upcoming member events** via your event profile.

Don't forget, you login using your email address instead of your membership number. For any queries about the new system, email **members@endocrinology.org**.

Clinical Resource HUB

SHARE YOUR EXPERTISE ON THE CLINICAL RESOURCE HUB

Has your clinic introduced measures that have improved your practice or service delivery? If so, you could help to improve and unify patient care by sharing your resources with our member community on the **Clinical Resource Hub**. Visit the hub to find out more.

SOCIETY CALENDAR

26 September 2024
ENDOCRINE GENETIC TESTING
Birmingham, UK

1 October 2024
NATIONAL TRAINING SCHEME FOR THE USE OF RADIOIODINE IN BENIGN THYROID DISEASE
Birmingham, UK

14–15 October 2024
UK JOINT IRISH–UK ENDOCRINE MEETING
Belfast, UK

3 December 2024
REPRODUCTIVE ENDOCRINOLOGY
London, UK

10–12 March 2025
SfE BES 2025
Harrogate, UK

www.endocrinology.org/events for full details

GRANT AND PRIZE DEADLINES

2 October 2024

MEETING GRANT

OUTREACH GRANT

RESEARCH GRANT

TEACHING GRANT

TRAVEL GRANT (including travel to SfE BES 2025)

www.endocrinology.org/grants for full details of all Society grants and prizes

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ENCOURAGE YOUR STUDENTS TO CHOOSE ENDOCRINOLOGY

Save 22–23 October in your diaries for our Endocrinology and Diabetes Taster Sessions, held in collaboration with the Young Diabetologists and Endocrinologists' Forum.

Taking place virtually, the sessions provide the perfect opportunity for your trainees to learn what inspired experts to specialise in endocrinology and why it remains a lifelong passion. **Register here for the Taster Sessions**.

HOT TOPICS

Hot Topics is written by Victoria Chatzimavridou-Grigoriadou, Sophie Clarke, Craig Doig, Edouard Mills, Gareth Nye, Bhavna Sharma and Vincent Simpson

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the **Members' Area of the Society website**. *Endocrine Connections*, *Endocrinology, Diabetes & Metabolism Case Reports* and *Endocrine Oncology* are open access and free to all. Publishing in *Endocrine Oncology* is currently free.

JOURNAL OF ENDOCRINOLOGY

Insulin induces bioenergetic changes and alters mitochondrial dynamics in podocytes

Diabetic nephropathy is a common complication of diabetes. It is often characterised by early stage hyperinsulinaemia and insulin resistance in insulin-sensitive cells, including podocytes (epithelial cells within the kidneys). The diabetic milieu induces shifts in podocyte bioenergetics, closely associated with mitochondrial dynamics. The precise impact of insulin on podocyte mitochondrial morphology remains unclear. This study aimed to explore insulin's effects on mitochondrial dynamics and bioenergetics in human podocytes.

Audzeyenka *et al.* showed that short term insulin exposure inhibited oxidative respiration parameters while increasing glycolysis flux. Extended insulin treatment led to enlarged mitochondria, reduced expression of mitochondrial fission markers DRP1 and FIS1, and heightened mitophagy. These findings reveal insulin's previously unrecognised role in modulating oxidative respiration, glycolysis and mitochondrial dynamics in human podocytes. Importantly, the duration of insulin stimulation emerges as a crucial factor influencing its metabolic and molecular effects, indicating significance for clinical and experimental studies of diabetic nephropathy.

Read the full article in *Journal of Endocrinology* **261** e230357
https://doi.org/10.1530/JOE-23-0357

JOURNAL OF MOLECULAR ENDOCRINOLOGY

No extra-adrenal aldosterone production in various human cell lines

Aldosterone, a mineralocorticoid hormone, directly and indirectly regulates the activity of the kidneys and other organs/tissues (e.g. vascular tissue and heart), with stimulatory effects on Na^+ and water reabsorption, as well as on K^+ and H^+ excretion, thus playing an important role in blood pressure regulation. There remain conflicting reports on the existence of local aldosterone in extra-adrenal tissues, including the brain and cardiovascular system, which are mainly based on evidence from semi-quantitative methods.

Durrer *et al.* have explored this potential phenomenon in a number of well characterised cell lines, in an attempt to shine light on this physiological issue. They supplemented this extensive study with samples taken from patients with primary hyperaldosteronism, with further study of their peripheral blood cells.

The authors conclude that there was no significant aldosterone production in various well characterised, purchased, immortalised and primary human cell lines, including mononuclear cells of healthy subjects and of patients suffering from primary hyperaldosteronism. This has a wide-ranging impact on our research, treatment and understanding of this condition.

Read the full article in *Journal of Molecular Endocrinology* **72** e230100
https://doi.org/10.1530/JME-23-0100

ENDOCRINE-RELATED CANCER

Genetic syndromes linked to insulinoma and glucagonoma

Insulinomas and glucagonomas are rare tumours originating from the neuroendocrine cells of the pancreas. Though predominantly sporadic, up to 10% of insulinomas and non-functioning glucagon-secreting tumours are linked to inherited syndromes. These primarily include multiple endocrine neoplasia type 1, with some insulinomas also associated with tuberous sclerosis complex and neurofibromatosis type 1.

In this comprehensive review, Marini *et al.* provide a detailed exploration of the clinical implications and genetic foundations of these tumours, as well as the critical role of targeted genetic testing and surveillance for their early detection and management. They delve into the genetic mutations, their influence on tumour behaviour, and the range of treatment options, from surgical interventions to potential pharmacological treatments such as mTOR inhibitors. Interestingly, they highlight how the study of these genetic tumour syndromes has expanded clinical, therapeutic and molecular knowledge, benefiting both hereditary and sporadic cases. As advocated by the authors, given the rarity of these conditions, international collaboration is necessary to enhance our understanding and improve outcomes for affected patients.

Read the full article in *Endocrine-Related Cancer* **31** e230245
https://doi.org/10.1530/ERC-23-0245

CLINICAL ENDOCRINOLOGY

Hypoparathyroidism and mortality after total thyroidectomy

One of the commonest complications of total thyroidectomy (TT) is hypoparathyroidism due to unintentional removal or damage to the parathyroid glands and/or their vascularisation. While transient hypoparathyroidism is common, the condition is only chronic (present for more than 12 months postoperatively) in a minority of patients. Importantly, previous studies suggest that chronic hypoparathyroidism might affect mortality.

This study by Reinke *et al.* used population-based registries to evaluate the frequency of hypoparathyroidism and mortality in patients undergoing TT in Denmark between 1998 and 2017. Based on 7,912 patients who underwent TT within the study period, the prevalence of hypoparathyroidism was 16.6% at 12 months postoperatively. After adjusting for confounders, they showed the risk of death due to any cause following TT was significantly higher in those who developed hypoparathyroidism (hazard ratio (HR) 1.34). However, subgroup analysis revealed that mortality was only higher in cases with malignancy (HR 2.48), and not when surgery was performed for benign indications, such as goitre (HR 0.88) or thyrotoxicosis (HR 0.86).

Therefore, they conclude that patients with hypoparathyroidism do not have an increased risk of mortality following TT, unless the surgery was for malignancy.

Read the full article in *Clinical Endocrinology* **100** 408–415
https://doi.org/10.1111/cen.15037

CONTINUED ON **PAGE 5**

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ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

12 years of missed follow-up for a pituitary mass

Functioning gonadotrophin-secreting pituitary adenomas are rare. These benign tumours are difficult to diagnose, due to their insidious onset and slow growth, and are often misdiagnosed as polycystic ovary syndrome in women and as sexual dysfunction in men.

Noor *et al.* report a case of a 42-year-old father who presented with COVID-19 and a historical brain mass which had been found on a trauma computed tomography scan 12 years earlier. He had long-standing dizziness and vision impairment (right eye) that were never investigated. On examination, he had bilaterally enlarged testicles (>25cm^3) and a left monocular temporal defect. Blood tests showed raised luteinising hormone (6.4IU/l), follicle-stimulating hormone (FSH; 31.4IU/l) and testosterone (50.31nmol/l) as well as hypothyroidism (thyrotrophin 3.54mIU/l, free thyroxine 6.6pmol/l). A 09.00am cortisol measurement was normal (274nmol/l). Pituitary magnetic resonance imaging confirmed a 30×23×22mm expanding mass in the pituitary fossa extending to the suprasellar cistern.

He started levothyroxine and hydrocortisone preoperatively. Transsphenoidal surgery was successful (histology confirmed an FSH-positive gonadotrophin-secreting adenoma). Testicular size (17.9–21.1cm^3) and hormonal abnormalities normalised postoperatively.

This case highlights the difficulty of diagnosing functioning gonadotrophin-secreting pituitary adenomas and the importance of reviewing historic brain imaging.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* EDM-22-0322 **https://doi.org/10.1530/EDM-22-0322**

ENDOCRINE CONNECTIONS

The changing landscape of diabetes technology

This article by Lakshman and colleagues reviews continuous subcutaneous insulin infusion pumps, glucose monitoring devices and closed loop systems. Elaborating an intriguing history of the development of automated insulin delivery systems, it starts off with their invention back in 1963, when the equipment was the same size as an army backpack!

The development of control algorithms, including fuzzy logic controllers, might sound complicated, but interestingly they were invented in plain logic (based on the 'fuzzy logic' of insulin titration utilised by experienced diabetes practitioners). In more Gen Z terms, the DIY closed-loop movement, with the online collaboration of communities of diabetes patients (and their families) in the development of their own artificial pancreas system (#wearenotwaiting), would excite all of us on Twitter.

Overall, this article would attract present prescribers with a review of available technologies, scientists working in diabetes tech, and the nerd in all diabetologists looking inward to everyday practice.

Read the full article in *Endocrine Connections* **12** e230132 **https://doi.org/10.1530/ec-23-0132**

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

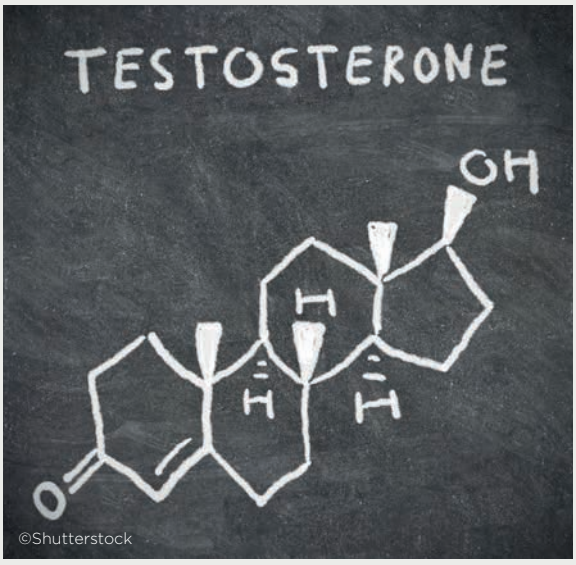
Testosterone and progression to diabetes in men with hypogonadism

Male hypogonadism is associated with an increased risk of prediabetes and type 2 diabetes. Testosterone replacement increases muscle mass and is associated with improved insulin sensitivity, and there are data to suggest that progression from prediabetes to diabetes is slower in men with hypogonadism who are treated with testosterone compared with those who are untreated.

As part of a prespecified nested study, investigators in the randomised TRAVERSE (Testosterone Replacement Therapy for Assessment of Long-Term Vascular Events and Efficacy Response in Hypogonadal Men) Trial compared markers of glycaemic control in hypogonadal men receiving testosterone gel (1.62%) and placebo. There was no significant difference between testosterone and placebo groups with respect to relative risk of progression from prediabetes to diabetes. For those known to have diabetes at baseline, there was no significant difference in risk of glycaemic remission between the two groups. Changes in glycated haemoglobin (HbA1c) and fasting glucose were not significantly different between the testosterone and placebo groups.

In this study, there was no evidence that, in men with prediabetes or diabetes, testosterone treatment was associated with any improvement in markers of glycaemic control, or in rate of progression from prediabetes to diabetes. Men in this study had mild hypogonadism, which could explain this finding; additionally, whilst fasting glucose and HbA1c were reviewed, other more sensitive markers, such as oral glucose tolerance test, might have shown different findings.

Read the full article in *JAMA Internal Medicine* **184** 353–362 **https://doi.org/10.1001/jamainternmed.2023.7862**



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Functional constraints on the number and shape of flight feathers

Movement is a key ecological function that greatly influences an organism's body structure. New ways of moving can lead to significant changes in body form, which can drive species diversification. Despite new fossil discoveries, it is unclear if flying evolved once or multiple times among dinosaurs. The flight abilities of these dinosaurs are also disputed. For modern birds, flight evolved through modifications of feathered limbs and tails.

By examining number and shape of flight feathers in modern birds, Kiat *et al.* found that these features are closely linked to flight ability, showing important functional constraints. Traits evolve at different rates, with some reflecting ancient conditions and others current flight capabilities. Mesozoic birds and *Microraptor* have feather structures similar to modern flying birds, while anchiornithines have different feather structures, suggesting they could not fly.

These findings support the idea that flight in dinosaurs originated once and that early feathered wings are not well-represented in the current fossil record.

Read the full article in *Proceedings of the National Academy of Sciences of the USA* **121** e2306639121 **https://doi.org/10.1073/pnas.2306639121**

FINDING COMMON SOLUTIONS TO RARE DISEASES

WRITTEN BY KREEPA G KOOBLALL

Kreepa G Kooblall gave the 2023 Early Career Prize Lecture (Science) at SfE BES 2023 in Glasgow. We are delighted to include this summary of her award-winning work here.

Skeletal dysplasia syndromes are rare genetic disorders caused by the abnormal development of bone and cartilage. Currently, more than 461 heterogeneous skeletal dysplasia syndromes have been reported. While individually they are rare, together they account for an estimated overall prevalence of ~2.3 cases per 10,000 live births.[1,2]

Skeletal dysplasia syndromes normally first present at a young age. Their prenatal diagnosis is often difficult, due to heterogeneity both within and among disorders. Moreover, because of their rarity, clinical investigations into these disorders remain challenging, as do finding possible treatments and cures.[1,2]

MARSHALL–SMITH SYNDROME, MALAN SYNDROME AND *NFIX* VARIANTS

Marshall–Smith syndrome (MSS) and Malan syndrome (MAL) are two examples of congenital skeletal dysplasia syndromes. The skeletal and neural abnormalities in patients with MSS or MAL are caused by heterozygous mutations affecting the nuclear factor I/X (*NFIX*) gene.[3,4]

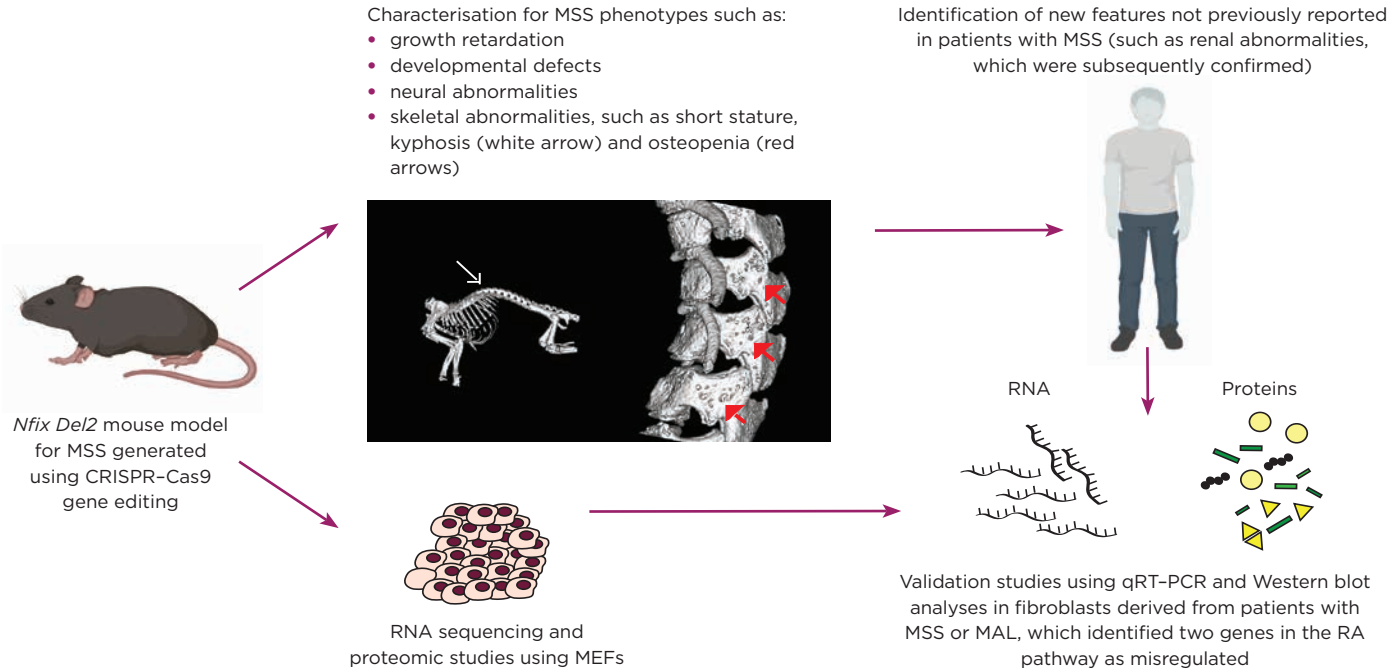
MSS is caused by frameshift mutations that affect the C-terminal part of the *NFIX* gene, leading to aberrant transcripts escaping the nonsense decay mechanism (NMD) and resulting in the production of dysfunctional mutant NFIX proteins that are believed to behave in a dominant negative manner.[3,4] In contrast, MAL is due to mutations that predominantly affect the N-terminal part of the *NFIX* gene, leading to NFIX haploinsufficiency.[3,4] NFIX is a transcription factor which plays an important role in the regulation of gene expression during the development of many organs and tissues (including the skeleton and nervous system).[5]

THE IMPORTANCE OF MOUSE MODELS FOR RARE GENETIC DISORDERS

Since NFIX is a ubiquitously expressed protein, and because MSS and MAL are rare multisystem disorders, it is difficult to obtain tissue samples from the patients, who are mainly children with mental and physical impairments living in different countries. Therefore, to circumvent this problem and to find a common solution for MSS and MAL, we have generated a mouse model for MSS (since it is the more severe of the two disorders). This enables us to study the effects of mutant *NFIX* and understand the mechanisms underlying the aetiology of MSS, as well as providing a useful tool for investigating possible treatments for MSS, and potentially MAL.

In order to generate a mouse model for MSS, we used the CRISPR–Cas9 gene editing system to target a two-nucleotide deletion in *Nfix* exon 7, which is the most commonly mutated exon in patients with MSS. We used *in vitro* expression assays to demonstrate that this frameshift mutation was not cleared by the NMD and led to the production of a dysfunctional mutant NFIX protein with aberrant function.[6] We therefore characterised this *Nfix Del2* mouse model for features of MSS and showed that, in contrast to patients with MSS who are heterozygous for *NFIX* mutations, the heterozygous $Nfix^{+/Del2}$ mouse was viable, normal and fertile. In contrast, the homozygous $Nfix^{Del2/Del2}$ mouse had short stature and developmental delays, as well as skeletal (including kyphosis, osteopenia, reduced bone mineral content), cranial, neural (due to abnormal brain morphologies), hepatic and renal abnormalities.[6] However, phenotypic differences between organisms are not uncommon, and can be attributed to allelic variation, modifier genes, genetic variations, genetic background and environmental conditions in animal models versus in patients.[7]

Figure. A mouse model for MSS has helped identify new features in patients which should be monitored as part of their care, as well as new genes and pathways which are altered, that could potentially be therapeutic targets for MSS and MAL. qRT–PCR, quantitative reverse transcription–polymerase chain reaction.



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Thus, *Nfix*$^{Del2/Del2}$ mice may represent a mouse model for MSS, in which patients commonly have short stature, developmental delays, skeletal abnormalities (including craniofacial defects, osteopenia with increased fracture rate, kyphoscoliosis, decreased bone density[8]) and intellectual disability due to non-specific brain abnormalities.[3,9,10] Moreover, following our identification of likely renal dysfunction in the *Nfix*$^{Del2/Del2}$ mice, investigations were undertaken by ultrasound in two patients with MSS, and this revealed the occurrence of renal cysts and nephrocalcinosis in these cases.[6]

IDENTIFYING POTENTIAL THERAPEUTIC TARGETS FOR MSS AND MAL

In addition to helping identify new features in patients with MSS that should be monitored as part of their routine care, the *Nfix*$^{Del2/Del2}$ mice have also been useful in identifying potential therapeutic targets for MSS.

We used mouse embryonic fibroblast cells (MEFs) derived from the *Nfix Del2* mice for RNA sequencing and proteomic analyses, in order to identify genes and pathways that are misregulated in patients with MSS. We chose to initially undertake RNA sequencing and proteomics studies in MEFs, because mice generated from the same genetic background show reduced genotypic variability compared with fibroblasts derived from unrelated patients with MSS. This approach therefore maximised our chances of identifying statistically significantly altered genes and pathways.

Validation studies using fibroblast cells derived from patients with MSS or MAL have confirmed that two genes involved in the retinoic acid (RA) pathway were misregulated at the RNA and protein levels both in MEFs obtained from the *Nfix*$^{Del2/Del2}$ mice and in fibroblasts from patients with MSS or MAL. This may indicate a possible misregulation of the RA pathway in these patients, and the possibility that drugs targeting the RA pathway might be of therapeutic benefit to these patients with skeletal dysplasia.

KREEPA G KOOBLALL
Academic Endocrine Unit, OCDEM, University of Oxford

This work was undertaken in my role as a post-doctoral research scientist in the laboratory of Professor Rajesh Thakker (Academic Endocrine Unit, OCDEM, University of Oxford).

Find out more about the Early Career Prize Lectures

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CAN A KISS TREAT LOW SEXUAL DESIRE IN MEN AND WOMEN?

WRITTEN BY EDOUARD G MILLS, WALJIT S DHILLO AND ALEXANDER N COMNINOS

We are delighted to publish this summary of Edouard G Mills' award-winning 2023 Early Career Prize Lecture (Clinical) from SfE BES 2023 in Glasgow.

LOW SEXUAL DESIRE: A COMMON CAUSE OF PERSONAL DISTRESS

The human sexual response is essential for reward, satisfaction and, most significantly, reproduction and species survival. Under normal physiological conditions, sexual response depends on an appropriate balance between sexual excitatory and sexual inhibitory brain pathways, which together regulate human sexual behaviour.

However, dysregulation in this system can result in persistent low sexual desire, with resultant marked distress to the individual, termed hypoactive sexual desire disorder (HSDD). Epidemiological studies indicate that HSDD affects around 8% of men and 10% of women,[1] making it one of the most prevalent sexual health conditions. Recent insights indicate that, in response to sexual stimuli, those suffering with HSDD display excessive activation of higher level cognitive brain regions (involved in self-monitoring and self-judgement), which suppresses lower level sexual brain centres, thereby impeding normal sexual function.[2] Consequently, HSDD has marked detrimental effects on quality of life, interpersonal relationships and fertility. Remarkably, despite the considerable clinical burden, there are no licensed therapies for men, and in women the available treatments are limited by their effectiveness and side-effect profiles.

Taken together, there is a significant unmet need to identify novel, safe and effective therapeutic strategies for HSDD and for psychosexual disorders more broadly. Indeed, a potential therapeutic target could be the reproductive neuropeptide kisspeptin, which has been the focus of our recent research, as summarised here.

KISSPEPTIN AS THE MASTER REGULATOR OF THE REPRODUCTIVE AXIS

Over the last two decades, kisspeptin (encoded by the non-human *Kiss1* gene and human *KISS1* gene) has emerged as the master regulator of reproduction, due to its position at the apex of the reproductive axis.[3] The principal site of kisspeptin action is in the hypothalamus. Here, kisspeptin acts as a crucial upstream regulator of gonadotrophin-

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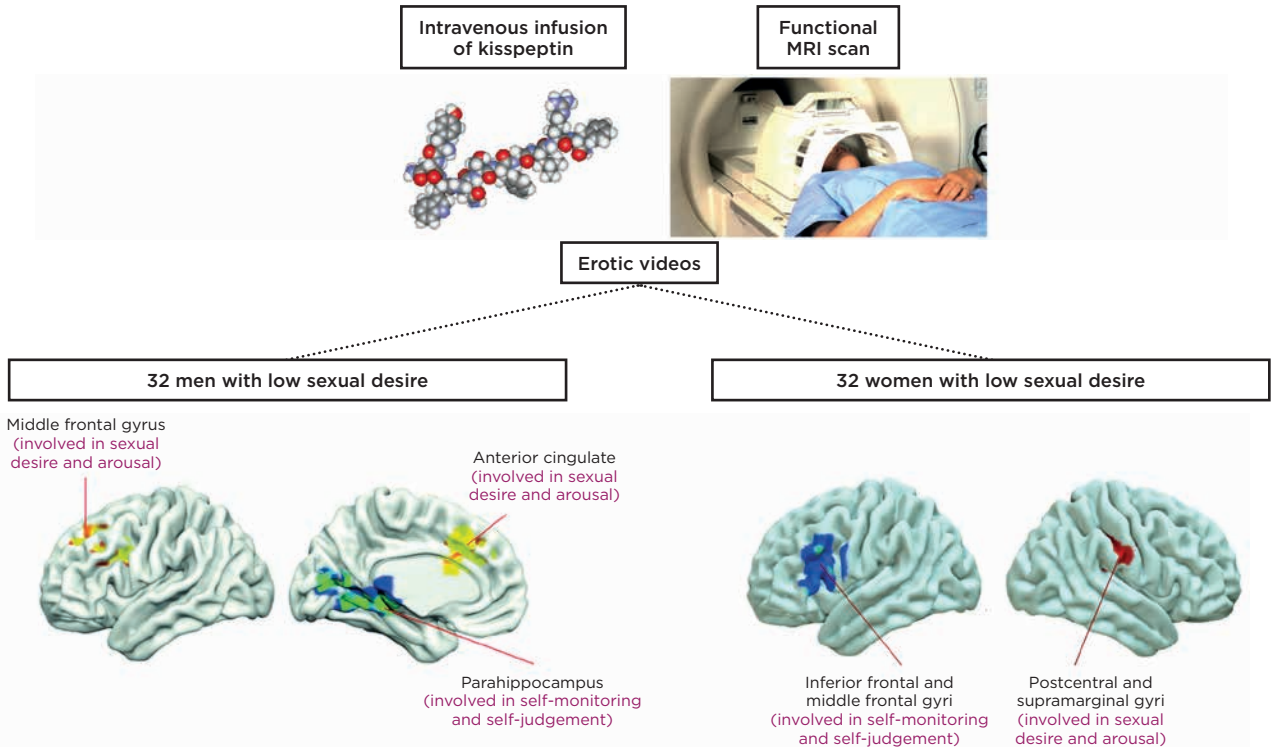

Figure. Effects of kisspeptin administration on functional MRI sexual brain activity whilst watching erotic videos: 32 men and 32 women with low sexual desire attended for two study visits (once for a 75-minute intravenous infusion of kisspeptin and again for a rate-matched placebo), as part of a randomised and blinded-protocol. Red and yellow areas show relative activation to erotic videos during kisspeptin administration compared with placebo. Blue and green areas show relative deactivation to erotic videos during kisspeptin administration compared with placebo.

releasing hormone secretion, which, in turn, controls downstream gonadal function via luteinising hormone and follicle-stimulating hormone. Due to this key role in regulating physiological reproductive hormone secretion, research interest in targeting kisspeptin pathways to treat common reproductive disorders in humans has accelerated, including for hypothalamic amenorrhoea, hyperprolactinaemia and male hypogonadism, and as a safe ovulation trigger in an *in vitro* fertilisation setting.

KISSPEPTIN AND SEXUAL BEHAVIOUR

Beyond the hypothalamus, both kisspeptin and its receptor are extensively distributed throughout important cortico-limbic brain regions (i.e. the behavioural and emotional control centres of the brain) in rodents and humans.[4] Accordingly, this sets the scene and provides a neuroanatomical framework for an expanding pool of preclinical animal data demonstrating that kisspeptin signalling modulates key aspects of reproductive behaviour, including sexual motivation[5] and erections.[6]

Turning to humans, we were the first to show that kisspeptin administration enhances limbic brain activity in response to sexual stimuli in healthy men with normal sexual function, with associated reductions in sexual aversion.[7] In subsequent work, we demonstrated that kisspeptin administration also potently enhances brain responses to olfactory and visual cues of attraction in healthy men.[8]

Collectively, these preclinical animal findings and our earlier data in healthy men led us to postulate that kisspeptin could have translational potential in people who are distressed by low sexual desire.

CAN KISSPEPTIN IMPROVE SEXUAL FUNCTION IN MEN WITH LOW SEXUAL DESIRE?

The introduction of functional magnetic resonance imaging (fMRI) affords an exciting tool to non-invasively investigate the clinical and mechanistic effects of kisspeptin administration on human sexual behaviour. This specialised neuroimaging technique measures brain activity by detecting changes in blood flow during a specific task, and so produces a brain activation map showing which regions are involved in a particular process (such as sexual desire and arousal).

To test our hypothesis that kisspeptin administration may enhance sexual brain activity in people with low sexual desire, we first recruited 32 eugonadal men with HSDD.[9] Each participant attended for two study visits, for intravenous infusion of kisspeptin for 75 minutes and for administration of a rate-matched placebo, as part of a randomised and double-blind protocol. At each study visit, we examined changes in fMRI brain activity in response to the participants watching erotic videos in the MRI scanner, as well as physiological (using continuous penile rigidity monitoring) and behavioural measures of sexual desire and arousal.

Here, we demonstrated that kisspeptin administration robustly deactivated brain regions involved in self-monitoring and self-judgement (such as the parahippocampus), whilst simultaneously increasing brain activity in sexual arousal centres (such as the anterior cingulate and middle frontal gyrus). Indeed, in response to kisspeptin's acute restoration of sexual brain activity, we observed significant increases in penile tumescence (by 56% more than placebo) and behavioural measures of sexual desire (including increased 'happiness about sex'), providing functional and behavioural relevance.

CONTINUED ON **PAGE 9**

CONTINUED FROM **PAGE 8**

CAN KISSPEPTIN IMPROVE SEXUAL FUNCTION IN WOMEN WITH LOW SEXUAL DESIRE?

Having demonstrated robust clinical effects in men, our next important and logical step was to investigate whether kisspeptin could offer promise for women. In a subsequent study of 32 premenopausal women with HSDD, participants undertook a similar fMRI protocol to that described above.[10] Indeed, highly congruent with our earlier findings in men with HSDD, in response to erotic videos, kisspeptin again deactivated brain regions involved in self-monitoring and self-judgement (such as the inferior frontal and middle frontal gyri), whilst increasing brain activity in sexual arousal centres (such as the postcentral and supramarginal gyri). Of behavioural relevance, this acute restoration of sexual brain activity was associated with significant increases in self-reported ratings of 'feeling sexy', which is important as a positive body image is a key determinant of sexual desire and arousal.

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SUMMARY AND FUTURE DIRECTIONS

Across a series of clinical studies, we provide the first human evidence showing that kisspeptin administration in people with low sexual desire acutely and safely modulates sexual brain activity, which ultimately enhances sexual desire and arousal. Given this, further studies are now warranted, investigating more prolonged chronic kisspeptin protocols and in broader patient cohorts (such as different sexual identities and orientations).

Our exciting data raise additional directions for future clinical investigation. Kisspeptin can easily and safely be administered via subcutaneous and intranasal delivery. These simpler administration routes therefore warrant evaluation in this patient cohort, as they are advantageous compared with the intravenous route utilised in our work to date.

To this end, our data identify kisspeptin-based therapeutics as an exciting, much-needed and well-tolerated potential addition to the treatment armamentarium for managing low sexual desire and psychosexual disorders more broadly.

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Clinical Lecturer in Endocrinology, Imperial College London

WALJIT S DHILLO
Professor in Endocrinology and Metabolism and Consultant Endocrinologist, Imperial College London

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Find out more about the Early Career Prize Lectures

CENTRAL ADIPOSITY, SERUM CALCIUM AND KIDNEY STONE DISEASE

WRITTEN BY CATHERINE LOVEGROVE

We are delighted to include this summary of the 2022 Early Career Prize Lecture (Clinical) given by Catherine Lovegrove at SfE BES 2022.

Through my research into kidney stone disease, I aim to improve our understanding of the genetic causes of this condition within the general population, and the care we offer patients, by providing better treatment and prevention strategies.

Kidney stone disease is a common condition, affecting approximately 1 in 5 men and 1 in 10 women by the age of 70 years. It accounts for over 85,000 hospital attendances per year in England.[1,2] Half of people experiencing a kidney stone will have a second within approximately 10 years, and recurrent kidney stone disease is linked to an increased risk of chronic kidney disease.[3,4] Despite the high prevalence of kidney stones, our understanding of the underlying environmental and genetic causes is incomplete, hindering our ability to effectively treat and prevent them.

RISK FACTORS FOR KIDNEY STONES

Observational epidemiological studies suggest that obesity is a risk factor for kidney stones. Obesity is linked to metabolic syndrome, a cluster of diseases including central adiposity, hypertension, dyslipidaemia and impaired glucose tolerance, which have also been linked to kidney stone disease in observational studies.[5,6] How adiposity and metabolic syndrome are associated with an increased risk of kidney stones is uncertain. However, postulated mechanisms include altered urine composition, altered serum biochemistry and systemic inflammation. I wanted to investigate how obesity and metabolic syndrome are linked to kidney stone disease, and used a technique called Mendelian randomisation, which aims to overcome some of the limitations that affect observational studies, including reverse causality and residual confounding.

CONTINUED ON **PAGE 10**

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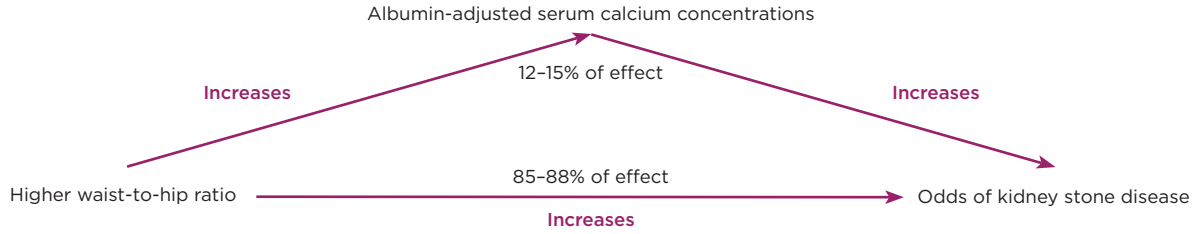

Figure. Higher waist-to-hip ratio has a causal effect to increase the odds of kidney stone disease, which is partially mediated via increasing serum calcium concentrations.

Mendelian randomisation uses genetic variants, randomly inherited at conception, to assess the causal relationship between a risk factor and an outcome.[7] An analogy is frequently made with a 'genetic randomised control trial'. This comparison does not adequately capture the complexity involved in identifying causal relationships; however, it can be a useful illustration. Briefly, Mendelian randomisation uses genetic associations with a risk factor (often identified from genome-wide association studies) to generate exposure and control groups. The risk of an outcome in these genetically predefined groups is subsequently evaluated. The technique can also be employed with continuous variables.

MY WORK FOR THE EARLY CAREER PRIZE

Using data from the UK Biobank and FinnGen studies, I was able to look for causal relationships between obesity and kidney stone disease.

First, with collaborators from the Nuffield Department of Population Health (University of Oxford), I confirmed that higher general adiposity (body mass index, BMI) and central adiposity (waist circumference, WC; waist-to-hip ratio, WHR) are independently associated with an increased risk of kidney stones in sex-stratified and combined-sex observational analyses in the UK Biobank.

Next, to facilitate Mendelian randomisation analyses, I performed a genome-wide association study of kidney stone disease in 8,504 cases and 388,819 controls in the UK Biobank, and meta-analysed these findings with data from the FinnGen study.[8,9] I undertook Mendelian randomisation analyses and showed that an increase in BMI, WC and WHR of one standard deviation is associated with increased odds of kidney stone disease (odds ratio (OR) 1.36, 95% confidence interval (CI) 1.25–1.48; OR 1.35, 95% CI=1.07–1.71; OR 1.33, 95% CI=1.18–1.50 respectively). This supported the findings from observational analyses. Multivariable analyses indicated that general and central adiposity are independent risk factors for kidney stone disease and bi-directional analyses showed no effect of kidney stone disease on BMI, WC or WHR.

Having confirmed that increased adiposity causally increases risk of kidney stones, I wanted to identify the mechanisms underlying this finding. Therefore, I systematically evaluated the effects of serum and urinary biochemical phenotypes, components of metabolic syndrome and markers of systemic inflammation on the odds of kidney stone disease. I found that increasing albumin-adjusted serum calcium concentrations by 0.08mmol/l increases the odds of kidney stones by 48%, and that a higher WHR causally increases serum calcium concentrations independently of BMI (an increase in WHR of one standard deviation elevates serum calcium concentration by 0.12mmol/l, SE 0.02). Interestingly, higher BMI had no effect on serum calcium after adjusting for WHR. These findings suggest that central adiposity, but not general adiposity, increases risk of kidney stones via effects on serum calcium concentrations. Using mediation Mendelian randomisation analyses, I estimated that ~12–15% of the effect of higher WHR on increasing the odds of kidney stone disease arises from effects on serum calcium concentrations (see Figure).

I found no evidence that hypertension, dyslipidaemia, markers of glycaemic control, or systemic inflammation increases liability to kidney stones in Mendelian randomisation analyses. I did identify that type 2 diabetes may increase the odds of kidney stone disease. However, multivariable analyses with BMI and WHR indicated that this effect is probably confounded by co-existing adiposity.

IMPLICATIONS AND FUTURE WORK

My work highlights the importance of general and central adiposity as causal risk factors for kidney stone disease, and reports the novel finding that higher WHR increases serum calcium concentrations. This has implications for counselling patients to reduce their risk of kidney stones through lifestyle modifications, such as diet and exercise, and provides impetus to investigate the role of weight loss therapies to prevent kidney stones. Finally, these findings motivate research into how higher WHR increases serum calcium concentrations to identify novel therapeutic opportunities and translate results for patient benefit.

CATHERINE LOVEGROVE
MRC Clinical Research Training Fellow and Clarendon Scholar, Nuffield Department of Surgical Sciences, University of Oxford

The author is a urology trainee in the Thames Valley region, undertaking an MRC Clinical Research Training Fellowship and studying for a DPhil in Surgical Sciences at the University of Oxford, supervised by Dr Sarah Howles and Professors Dominic Furniss and Michael Holmes. This research has been published as Lovegrove CE et al. *2023* Journal of the American Society of Nephrology *https://doi.org/10.1681/ASN.0000000000000238.*

Find out more about the Early Career Prize Lectures

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IF YOU COULD TALK TO YOUR EARLY CAREER SELF WHAT WOULD YOUR ADVICE BE?

I would tell myself that finding the right people to support your research is just as important as picking what research (topic) you do.

CHANNA JAYASENA
Imperial College London

Nobody's career looks the same as everyone else's, and everyone feels imposter syndrome at some point – but you deserve to be here. Everything takes time, so pace yourself and keep good records – both of your work and of conversations you might want to follow up on later!

REBECCA DUMBELL
Nottingham Trent University

Put yourself out there and develop a network of academic friends early on. Build your academic 'tribe' who understand and support you, as they are going through the same work/life imbalance as you are. Each mentor has a different role in a different part of your career, but seeking mentorship independent of where you work and your field is very helpful. Finally, it's a marathon and not a sprint – think strategically about the race – how to prepare, practise, etc.

LI CHAN
William Harvey Research Institute, London

Step outside your comfort zone and don't be afraid to embrace new career opportunities.

JACOPO SCOTUCCI
University of Cambridge

I would go back to the first year of my PhD, which was pretty tough because I had gone from being a really competent endocrinology registrar to a molecular biology novice. I would tell my younger self to practise, be patient and ask for help, and I would reassure myself that – with the support of my brilliant supervisors – I would get there in the end. I would also say that, although there are challenges and setbacks, this is all building an inner mettle and tenacity to keep on going, which will be hugely helpful throughout your career.

SAIRA HAMEED
Imperial College London

Enjoy the time you have for science during the early years of your research career. The long hours, pressures to get data for your thesis, publications, grants, fellowships and concerns about future career prospects are difficult. But, afterwards, you will miss being able to spend your days reading the literature, designing and carrying out experiments, and making new discoveries. You will have increasingly less time to do this as you progress, so enjoy it while you can!

VICKY SMITH
University of Birmingham

Pursue your passion – if you enjoy what you do, your work will not feel like work. Ideally your passion should align with a clinical need! Find a supportive environment with a healthy culture and kind mentors, who will nurture and support your development.

ALI ABBARA
Imperial College London

My advice would be to not be afraid to show that you don't know something. You're not an imposter - no one knows everything or expects you to, and being open and curious is how you learn and start meaningful collaborations. That, and if you find an aspect of your research that sparks passion, follow it!

MELISSA E WRIGHT
Cardiff University

CONTINUED ON PAGE 19

POLYCYSTIC OVARY SYNDROME
THE MALE COUNTERPART

WRITTEN BY KATARZYNA SIEMIENOWICZ

The impact of prenatal influences on lifelong health is well-established. Unfortunately, many children are born with compromised lifetime health trajectories. Fetal development can be affected by disruptions in hormonal interactions, which can have consequences for the entire lifespan. Polycystic ovary syndrome (PCOS) is an example.

WHAT IS POLYCYSTIC OVARY SYNDROME?

PCOS is a common endocrine disorder that affects over 10% of women. It is characterised by reproductive and metabolic abnormalities. Women with PCOS have irregular periods and difficulty getting pregnant. They may also have an array of metabolic problems, including insulin resistance, type 2 diabetes, obesity, dyslipidaemia and non-alcoholic fatty liver disease (NAFLD). A common hallmark of PCOS is that women have increased androgen concentrations, including during pregnancy.

There is ongoing debate about the causes of PCOS. Although it runs in families, a robust genotype has not been identified. However, there is evidence that androgens may play a role in the programming of PCOS. Pregnant women with PCOS have higher androgen concentrations and decreased placental aromatase activity when compared with pregnant controls.[1] Daughters of women with PCOS are more likely to develop PCOS.[2] They have increased cord blood testosterone concentrations, longer anogenital distance (a marker of gestational androgen excess exposure) and increased sebum production, collectively indicative of increased *in utero* androgen exposure.[3] There is also strong evidence from animal studies that prenatal androgen overexposure in rodents, monkeys and sheep results in adult reproductive and metabolic disorders that parallel those seen in women with PCOS.[4]

'MALE PCOS' – HUMAN EVIDENCE

Women with PCOS also have sons. Is there any evidence from human studies that males from the pregnancies of women with PCOS are also affected? And, if so, to what extent?

To date, there have been relatively few studies on the sons and brothers of women with PCOS. Emerging evidence indicates that they develop hyperinsulinaemia and dyslipidaemia, characterised by elevated triglycerides and cholesterol, which, alongside an increased risk of obesity, predict a potentially increased risk of cardiovascular disease.[5]

The increased cholesterol levels in pubertal sons of patients with PCOS seem to be an early indication of metabolic dysfunction.[6] The metabolic changes in these sons are likely to be independent of gonadotrophin and sex steroid levels, although they have elevated anti-Müllerian hormone (AMH) concentrations during childhood.[7] Besides hormonal and metabolic abnormalities, 'PCOS' males experience early-onset alopecia, excessive hair growth or acne. Early-onset androgenetic alopecia is suggested to be a prominent marker of 'male PCOS'.

'MALE PCOS' – ANIMAL STUDIES

A recent study using a clinically realistic ovine model of fetal androgen overexposure demonstrated that adolescent male sheep that were prenatally androgenised are accurate phenocopies of males from pregnancies in human PCOS, with elevated AMH, hyperinsulinaemia and evidence of dyslipidaemia, such as increased triglycerides and cholesterol.[8] Further hepatic omics analysis revealed that 1,084 genes and 408 proteins were altered in the livers of these 'PCOS' males. Perhaps counterintuitively, cholesterol synthesis was decreased in these ovine males, but their hepatic cholesterol uptake and secretion were dysregulated. These males had decreased expression of hepatic *CYP7A1*, which is the rate-limiting enzyme responsible for converting cholesterol to bile acids. As a result of this perturbed cholesterol metabolism, 'PCOS males' had increased concentrations of hepatic total and free cholesterol, as well as increased expression of markers of lipid droplet accumulation.

Hepatic cholesterol accumulation is an important factor underlying the development and progression of NAFLD. There is strong evidence showing that increased cholesterol accumulation can impact mitochondrial membrane fluidity and overall mitochondrial function. Consequently, mitochondrial function was altered in 'PCOS' males.[9] Nearly 50% of hepatic genes and proteins associated with oxidative phosphorylation were downregulated, indicating decreased oxidative phosphorylation, functionally realised in decreased hepatic ATP generation in these adolescent ovine males.

The study also demonstrated that 'PCOS' males had a significantly increased hepatic bilirubin content coupled with decreased hepatic detoxification and antioxidant potential, mirrored in the circulation. They also had an increased hepatic reactive oxygen species, with an indication of increased DNA damage. As a result of hepatic metabolic dysfunction, prenatally androgenised males had increased expression of profibrotic genes and proteins, coupled with increased hepatic collagen deposition, indicating early fibrosis, again reflected in the circulation by increased concentrations of fibrotic proteins, which positively correlated with plasma cholesterol levels.

IN CONCLUSION: NAMES ARE IMPORTANT!

Sons born to mothers with PCOS are at risk of developing hyperinsulinaemia, dyslipidaemia and obesity. Elevated cholesterol concentration is an early marker of metabolic dysfunction in pubertal sons of patients with PCOS.

In a preclinical ovine model, male offspring exposed to high levels of androgens during fetal life develop markers of metabolic dysfunction found in sons from PCOS pregnancies. These adolescent ovine males also develop a hepatic gene and protein signature reminiscent of an intrahepatic cholestasis-like condition, with altered cholesterol trafficking, increased hepatic cholesterol accumulation, altered mitochondrial metabolism of lipids, mitochondrial dysfunction, and early-life liver damage, which may result in lifelong health issues.

Therefore, it is important to recognise that fetal androgen excess associated with PCOS pregnancies is a risk factor for poor metabolic health for both sexes. This awareness has prompted the suggestion that PCOS be acknowledged as 'metabolic reproductive syndrome', thus encompassing the potential for poorer lifelong health in both males and females.[10]

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An interview with… VASILIS CHORTIS

Vasileios (Vasilis) Chortis is a clinician scientist in endocrinology, who has just returned to Birmingham after completing a research fellowship at Harvard Medical School in Boston, MA, USA. Here, he talks to *The Endocrinologist's* Associate Editor Craig Doig about his stint in the States.

Tell us about yourself and your career so far

I spent most of my clinical and academic training at the University of Birmingham and University Hospitals Birmingham. I trained both in clinical and in more basic and translational research. My clinical studies, in Professor Wiebke Arlt's lab, included applying mass spectrometry-based steroidomics and metabolomics to dissect adrenal tumour biology and develop new diagnostic tools. The basic and translational research focused on studying adrenal cancer biology in cell line models. I completed my PhD in 2017 and my clinical training as an endocrinologist in 2020.

In 2021, I moved to the USA to work as a post-doctoral research fellow in Dr David Breault's lab at Boston Children's Hospital and Harvard Medical School, where I trained in preclinical *in vivo* models of adrenal development and tumourigenesis. I have just returned to Birmingham and started work as an Associate Professor of Endocrinology at the University of Birmingham and as a Consultant Endocrinologist at University Hospitals Birmingham.

'I focused on choosing the right lab for my next step in research rather than the country.'

How did move to Boston come about?

When I finished my PhD, I decided I would like to continue working in translational adrenal research. I started looking for a lab in which I could train in preclinical *in vivo* models of adrenal disease, with a focus on adrenal tumours. I contacted Dr Breault, who leads one of the world's leading centres in mouse models of adrenal development and tumourigenesis.

As it happened, his lab had just developed a new genetically engineered model of adrenocortical carcinoma, driven by the two most common mutations in human patients. This provided an excellent opportunity to probe translationally important adrenocortical carcinoma biology questions in a unique *in vivo* model. I interviewed successfully for a position as a post-doctoral researcher, and made plans to move to Boston at the end of my clinical training. COVID made things more complicated, and I had to defer my move by more than a year, but I was finally able to move there with my wife in 2021.

What were you hoping to gain from a move to the USA?

My main aim was to acquire a new skill set that would allow me to expand the scope of my work as a translational adrenal researcher, acquiring experience in disease-relevant preclinical *in vivo* models. David Breault's lab matched my training needs perfectly. So I focused on choosing the right lab for my next step in research rather than the country. Having said that, I always wanted to spend some time living in the USA, both as a personal life experience and to see how a different research system works in practice.

Do USA and UK research environments differ?

The systems are similar, in that most research funding is allocated centrally through competitive applications at a national level. Success rates for major grant applications are similarly low, so funding certainly does not come easily in the USA either. My feeling was that the system in the USA is better at supporting early career researchers and setting them up for success, especially when it comes to clinician scientists. On the other hand, eligibility for many funding schemes in the USA is dependent on citizenship or visa status, so the UK is more open to foreign-born researchers taking their first steps in the country.

The experience of working in a lab in the USA was not too different from a UK one. I think this is much more dependent on the principal investigator than on the country, and I was fortunate to work in very supportive and productive environments in both countries. The time to secure ethical or safety approval to proceed with your planned scientific work is certainly substantially shorter in the USA, especially in animal research.

Finally, an interesting trend I observed in Boston is that industry is fast-replacing academia as the career destination of preference for most post-docs, to a greater degree than is currently seen in the UK.

How has it benefited you ?

My experience was overwhelmingly positive. I worked in a very supportive environment that provided high quality training, excellent mentorship, and freedom to explore my research interests and ideas. I certainly feel I have grown a lot in experience and confidence as a clinician scientist as a result of my time in Boston. I have built strong collaborative links that I hope to maintain throughout my career, both at Harvard and with other centres in the USA.

On a personal level, I got a good taste of life in another country, met new friends, and even got to watch a few NBA games! My wife also tells me that New England winters have made me more tolerant of the UK weather, although this effect does seem to wear off gradually.

'I have grown a lot in experience and confidence as a clinician scientist as a result of my time in Boston.'

What are your plans now ?

I am currently trying to wrap up the projects I worked on in the USA and complete the publication outputs. Going forward, I will try to secure funding to start my career as an independent investigator, with a focus on the study of adrenal cancer and other adrenal tumours, combining translational and clinical research to improve treatment and diagnostic options for patients with these conditions. I have also been delighted to be able to return to clinical work, a part that I missed during my fellowship in Boston.

A WEEK IN THE LIFE OF A JUNIOR DOCTOR

WRITTEN BY VINCENT SIMPSON

The reality of life as a junior doctor is brought to us by Editorial Board member Vincent Simpson, during a challenging on-call week. Vincent is a diabetes and endocrinology doctor and researcher into the diagnosis of diabetes, based in Exeter.

FRIDAY

07.00: I wake feeling slightly nauseous at the thought of starting my night shift in 13 hours. Night shifts are the most difficult part of the job, mixing physical exhaustion, unwell patients, and reduced support from the wider multidisciplinary team (MDT). Despite that, you will never bond with colleagues more than when working overnight. Bonded through stress and snacks.

I'm in an irritable mood for the rest of the day, but I arrive at work ready to start at 20.20. I place my stethoscope in my pocket with a faded, unreadable quote from Dr Who on the ID tag: 'Do what I do. Hold tight and pretend it's a plan.' The tag was a gift from my wife after passing PACES (Practical Assessment of Clinical Examination Skills) and becoming a registrar. A motto to help me get through another set of night shifts.

I'm surprised to find only nine people waiting to be seen; maybe tonight will be okay.

Patient A is in his 80s and has been in bed for a week. I get interrupted eight times in an hour trying to help him. Each small question takes me away from concentrating on his problems. I start from scratch each time to avoid making a mistake that could cost him his life and me my license. It takes me an hour to finally see him and treat his pneumonia with antibiotics and intravenous fluids. I hope he survives the night.

SATURDAY

It's 03.30, and I have been working for seven hours. The only thing I want to do is collapse in bed and sleep, instead I get more coffee.

I wake up a woman in her 90s. She looks frail and is curled up in bed. I feel terrible for waking her up so early in the morning, but I know if I don't and I miss something, the system won't be very forgiving of my empathy.

On my way out of the door, I check on patient A. He survived the night and looks a bit brighter in the morning light. I hope he can get back to his family.

10.30: I arrive home and fall into bed, only to be woken five hours later by my daughter's smiling face saying 'Pappa!' I feel hungover from the lack of sleep.

I often joke that marrying a doctor is a terrible idea. We are barely at home, and when we are at home, we are too tired to be present. Currently, those words carry more weight than usual. My wife looks almost as exhausted as I am, single-handedly looking after our daughter all weekend, except she will not get any days off and will be back at work on Monday.

I have been working a few hours when one of the other doctors comes to me for advice about a patient who has had four CT scans in the last year. A quick back-of-the-envelope calculation tells me this is the equivalent of 800 transatlantic flights. She would enjoy the flights more than being stuck in a hospital again.

SUNDAY

01.20: I'm halfway through eating my lunch when my bleep goes off. 'MET call in Creedy ward.' I leave my coffee and food to go cold and hope to return to it soon.

07.41: I'm taking a quick toilet break before the handover. My bleep goes off, and it's another MET call. Why do they always happen when I'm taking a break?

The rest of the day is a blur; before I know it, I'm back at work.

I arrive at the hospital, only to be told to head directly to resus. The day registrar is there with a sick patient, and stays an hour late to ensure treatment is not delayed. I doubt they will be reimbursed in any way or the sacrifice recognised by anyone other than me.

> *'Do what I do. Hold tight and pretend it's a plan.'*

MONDAY

It's 03.55, and, despite my team's best efforts, there are still 16 people waiting to be seen. Each person waiting is someone's loved one, but I have to make sure I listen carefully to the person in front of me so they feel cared for at their most vulnerable. The people waiting will have to wait, I am only human.

I walk home, having handed over nine people who are left to see. I wake at 15.30, glad I don't have to go in again for another night. I spend the evening watching TV with my wife, trying to concentrate but struggling. I'm glad not all weeks are as tough as this one.

TUESDAY

I wake at 07.20 to find 56 WhatsApp messages about how difficult it is to attend clinics as a trainee doctor. Being constantly rotated every four to six months for eight to ten years does very little for building the relationships with consultants. You need to be able to attend clinic and continue to develop as a doctor. Unsurprisingly, younger doctors' morale is at an all-time low.

WEDNESDAY

It's my academic day. The morning starts with PhD students and post-docs presenting some of their work. It is a great opportunity to learn new things that I can apply in the clinic when I see patients. In the afternoon, I work on my PhD proposal. I hope it is successful. A PhD would give me time to focus on developing my academic skills without having to worry about keeping up with clinical work.

THURSDAY

I analyse data in the morning for the Diabetes UK conference, but struggle because of sleep deprivation.

At 13.15, I chair the diabetes MDT before attending the diabetes virtual clinic.

I finish the day with an emergency appointment with a young man with a new diagnosis of diabetes. I have to tell him the bad news that he has type 1 diabetes. Understandably, he struggles to accept it, as it will affect every part of his life. There will be no decision he will make that won't be affected by his new diagnosis. I hope that the latest technology might offer him some hope…

MY JOURNEY INTO ENDOCRINOLOGY NURSING

EMBRACING COMPLEXITY AND COMPASSION

WRITTEN BY COSMINA SCHITEANU

As I reflect on my journey into the world of endocrinology nursing, I am filled with a sense of awe and gratitude for the experiences that have shaped my career.

It all began in 2016 when, after gaining my nursing qualification in my home country Romania, I made the bold decision to embark on a new chapter in the UK, seeking both professional growth and personal fulfilment. Little did I know that this decision would lead me down a path of discovery and passion unlike any I had experienced before.

Assigned to the diabetes and endocrinology ward at Royal Stoke University Hospital in Stoke-on-Trent, I was initially apprehensive about the challenges that lay ahead. With a family history of type 1 diabetes, I couldn't help but feel a personal connection to the patients under my care. However, as I immersed myself in the complexities of endocrine disorders, I soon realised that this was where I was meant to be.

'Each encounter has taught me invaluable lessons about empathy, compassion and the importance of holistic care.'

©Shutterstock

One of the biggest hurdles I faced in my journey was grappling with the intricate roles of hormones and metabolic pathways that govern the body's functions. However, with each passing day, I found myself drawn deeper into the mysteries of endocrinology, fuelled by a burning desire to understand and help my cohort of patients.

My turning point came when I stumbled upon a book entitled *Advanced Practice in Endocrinology Nursing*.[1] This comprehensive resource served as a guide, providing me with invaluable insights and equipping me with the knowledge and confidence to navigate the complexities of the field, alongside the unwavering support of my colleagues and consultants.

I found myself drawn by this field and I became determined to deepen my understanding and expertise in this area. In pursuit of this goal, I embarked on a journey of continuous learning, completing modules in health assessment and non-medical prescribing. These experiences not only expanded my skill set but also reinforced my commitment to provide the highest standard of care to my patients.

Furthermore, my involvement with the Society for Endocrinology provided me with opportunities for collaboration and professional growth. Inspired by the organisation's mission to advance the field of endocrinology, I seized the chance to enrol in a work-based module offered by Oxford Brookes University, further solidifying my knowledge and expertise.

As I continue my journey in endocrinology nursing, I am filled with a profound sense of purpose and gratitude for the privilege of serving those in need, from the challenges I have faced to the triumphs I have celebrated.

I have had the privilege of witnessing the resilience and strength of countless patients facing the daily struggles of managing their conditions. Each encounter has taught me invaluable lessons about empathy, compassion and the importance of holistic care.

I am reminded time and time again of the profound impact that small acts of kindness and compassion can have on patients and their families. Whether it's lending a listening ear during moments of uncertainty, providing reassurance and encouragement during treatment, or simply offering a comforting presence, these gestures of empathy and compassion can make a world of difference in the healing process. This is reinforced by Hildegard Peplau's Interpersonal Relations Theory[2] which emphasised the nurse–patient relationship as the foundation of nursing practice.

> '*Nursing has made great progress from being an occupation to becoming a profession in the 20th century. As the 21st century approaches, further progress will be reported and recorded in cyberspace – the internet being one conduit for that. Linking nurses and their information and knowledge across borders – around the world – will surely advance the profession of nursing much more rapidly in the next century.*' Hildegard Peplau

I would like to thank the consultants in my department who have supported, encouraged and guided me to pursue endocrinology.

COSMINA SCHITEANU
Royal Stoke University Hospital

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WHY YOU SHOULD APPLY FOR THE LEADERSHIP AND DEVELOPMENT AWARDS PROGRAMME

WRITTEN BY LISA OWENS

I was honoured to receive one of the Society for Endocrinology's Leadership and Development Awards in 2022. Since then, this programme has benefited me in many ways, including supporting my attendance at the annual SfE BES conference and the Leadership Retreat. I was also selected to participate in the SfE BES Programme Committee, which I have now been a part of for two years.

My involvement with the Society goes back many years. When I reflected on my career in endocrinology, in preparation for this article, the Society's enduring positive impact on my development became crystal clear to me. I first attended and presented at SfE BES 2016 in Brighton, and have attended and presented at the majority of the annual conferences since. When I was a student, I received Travel Grants from the Society to support my attendance. I was awarded the Early Career Research Grant in 2019, which allowed me to continue my research at Imperial College London after I completed my PhD. Students and trainees with whom I have completed research projects have also received Travel Grants, which has allowed them to attend and present at meetings too.

'When I reflected on my career in endocrinology … the Society's enduring positive impact on my development became crystal clear to me.'

Membership of the Programme Committee has been very rewarding. We get to review and discuss many of the latest advances in the specialty, to see what should be included in the programme. It has also helped me to keep in touch with my UK colleagues, now that I am back working in Dublin, and has facilitated meeting lots of new people. I have also found it invaluable to have access to expert colleagues, to discuss challenging cases and get advice when needed. I have since been asked to be a committee member for the Joint Irish–UK Endocrine Meeting in Belfast in October, and the Society's inaugural Reproductive Endocrinology meeting, which will take place in Birmingham in December.

I participated in the Leadership Retreat, which is part of the Leadership and Development Award Programme, in October last year. Not only were the location and the company great (Hogarth's Hotel in Solihull is so nice!), I have definitely utilised some of the skills and insights that we garnered over the two-day retreat in my consultant role. Attending a course like that, and reflecting on your own leadership style and practices, is something I would highly recommend, especially to junior consultants or academics.

'Involvement with the Society has undoubtedly benefited my career over the years, and I am sure it will continue to do so in the years ahead.'

I am passionate about reproductive endocrinology, and I have been delighted to see growth in interest in this field in recent years. It is crucial that we inspire and train many more reproductive endocrinologists, so it is great to see more of this content included in the Society's activities. I am really looking forward to the Society's dedicated Reproductive Endocrinology event this year.

I strongly encourage you to apply for the Leadership and Development Award Programme if you are considering it, or to apply for membership of one of the Society's committees. Involvement with the Society has undoubtedly benefited my career over the years, and I am sure it will continue to do so in the years ahead.

LISA OWENS
Consultant Endocrinologist, St James's Hospital, Dublin, Ireland
Senior Lecturer in Medicine, Trinity College Dublin, Ireland

PIONEERING CHANGE THROUGH PUBLIC ENGAGEMENT

WRITTEN BY CAROLINE GILLETT

Caroline Gillett is an Assistant Professor in Patient and Public Involvement and Engagement in the College of Medicine and Health at the University of Birmingham. She collaborates closely with many early career researchers and clinician scientists working in endocrinology.

WHAT IS PUBLIC ENGAGEMENT WITH RESEARCH?

When we say 'public engagement with research', we are normally referring to interacting with members of the public to share our knowledge, current ideas or future plans. Listening is a critical part of this, as public engagement is 'by definition a two-way process ... with the goal of generating mutual benefit'.[1] If we simply talk *at* people, we may never know if we are being understood or, perhaps even more critically, if we are missing out on alternative explanations or approaches of value.

For example, it often becomes very clear to us how we might improve a presentation that we have delivered, following the questions or suggestions raised by those in attendance. This feedback process highlights to us where we may have been unclear – or even potentially biased in our approach or thinking. We might tweak our presentation for clarity or change how some of the research is conducted in future (e.g. by trialling a new analytical technique that is brought to our attention).

The idea that our audience might have something useful to add only really becomes 'controversial' for some people when the attendees that we are talking about are non-academic members of the public. For the most part, the public make helpful comments or ask questions driven by genuine interest and curiosity. This experience can itself be re-invigorating for researchers, who are 'reminded' of how what they do stimulates excitement and hope for others. Occasionally, of course, really 'left-field' interrogation can leave us all stumped; but this is often thought-provoking in itself!

Certainly, I am not here to advise any researchers to pander to public opinions based on misinformation. In fact, it's important that scientists do disagree in such instances, and signpost to high quality evidence where possible (The Society for Endocrinology's strategy highlights the role of endocrinologists in combatting misinformation.) However, in engaging with challenging characters during public debate, we at least learn to come better prepared to tackle similar opinions and situations in future.

'Lore + (Dis)order' public engagement sciart exhibition, organised and curated by Caroline Gillett in 2022. Artist Agi Haines; photo Hayley Salter

CONTINUED ON PAGE 18

CONTINUED FROM **PAGE 17**

We may also better familiarise ourselves with the different origins of misinformation too. It strikes me that this is especially relevant within endocrinology, as so many non-experts purport to be experts. Look no further than the countless social media profiles happily monetising supplements or other 'solutions' to vulnerable people, who may have really complex health conditions and needs. Understanding these sources and the supposed 'evidence' they draw on may help us counter spurious claims more effectively.

WHAT IS PUBLIC INVOLVEMENT IN RESEARCH?

Public involvement in research takes engagement several steps further. Here, we do not only listen, but we also make a *commitment* to share decision-making, through evaluating and acting on the feedback and ideas we receive. Of course, sometimes we cannot take suggestions forward. However, we position ourselves to clearly explain why and where this might not be possible, because of specific limitations (mandatory regulations, funding restrictions, lack of evidence, skills etc.), making research more transparent and accountable.

Effectively, we are talking about partnering with the public to do research *with them*. We include patients and/or carers in this definition, and the involvement of these groups is particularly important in the context of biomedical or clinical research. The National Institute for Health and Care Research (NIHR) defines involvement as 'an active partnership between patients and the public and researchers in the research process, rather than the use of people as "subjects" of research'.[2]

Involvement of the 'DAISy–PCOS Leaders' (diverse women with lived experience of polycystic ovary syndrome) in co-designing and co-delivering community engagement activities to raise awareness about PCOS and our research. Photo Hayley Salter

It should be possible to involve members of the public at every stage of the research cycle, from defining or prioritising the research question itself, to study co-design and data collection, right the way through to data interpretation, dissemination and beyond. Once again, this can seem a 'radical' approach, particularly to those on the discovery end of fundamental scientific research. In contrast, many on the clinical end of research tend to already be undertaking such activities to a lesser or greater degree, even if they may not recognise it as 'patient and public involvement' (PPI).

In reality, what we are talking about is the public working with researchers to define and challenge what is deemed an acceptable and feasible research approach. That is, they understand the advantages and limitations of the approach and why that approach (as opposed to the others available) is the right one for the given circumstances. It's therefore not necessarily about training the public up on how to 'conduct research' using a highly technical piece of lab equipment – which would obviously take many years of experience and practice to master!

However, in other research fields, some capacity building might not be unreasonable or time-prohibitive, especially as it could add unique insights and value, which outweigh the costs. Take for instance a qualitative research project on the experiences of patients with endocrine cancer. The researchers might involve people with relevant lived experience to support them in co-designing the interview questions and in analysing and interpreting the data collected. This might involve training them to use a software tool to code the data into emerging themes, which will later be cross-referenced across multiple reviewers for consistency. Differences of opinion can then be discussed to reach agreement on the final themes selected for interpretation. We might anticipate, for example, that those with lived experience of endocrine cancer might pick up on (i.e. code) subtle themes within the transcripts that other reviewers might be 'blind' to. Their involvement should thus hopefully make the research more representative and relevant, as perspectives have been appropriately widened, and/or consistency across more stakeholders has been further established.

WHY DO ENGAGEMENT AND INVOLVEMENT MATTER?

A lot of research is publicly funded, so it seems only right that we can evidence how this research is addressing societal needs and priorities. Publicly sharing what we do through engagement activities is one means of achieving this, and actively involving the public in the research process is another. As an absolute bare minimum, I believe we can always involve citizens in our research to improve our engagement efforts: for example, through designing public engagement linked to our research together. Nowadays, most research funders want to see engagement and involvement within projects. Indeed, NIHR and several other major charity funders actually require grant applicants to consider how they will meaningfully embed public involvement into their projects. It is not uncommon for members of the public to be involved in the grant review or interview process. You may also consider involving a public co-applicant to strengthen your proposal by showing how they will contribute to the governance and public accountability of your project over its duration.

Ultimately, though, this is about driving high quality research that is more societally relevant, accessible, representative and impactful. Involvement can help us avoid 'invisible' pitfalls which lose us time and resources in the long run. For instance, involvement might highlight barriers to trial compliance, cultural sensitivities that we should be mindful of, or poor recruitment procedures. Meaningful collaboration with the end users of our research is mutually beneficial, as it improves research quality and uptake – and surely we all want this?

CONTINUED ON **PAGE 19**

CONTINUED FROM **PAGE 18**

PRACTICAL HINTS AND TIPS

Engagement can be so broad, from public talks and workshops, to creative art installations and community festival activities. There are lots of great ideas and case studies for public engagement on the National Co-ordinating Centre for Public Engagement (NCCPE) website.[1] Check if your organisation has a public engagement and/or outreach team, as there may be local funding or existing opportunities with which you can get involved. Similarly, many organisations will also have great people supporting PPI and most would be happy to give you advice and tips on setting up a PPI group, costing for involvement and general good practice. You could ask to shadow a PPI meeting, for example. The NIHR[2] and UK Standards for Public Involvement[3] have excellent guidance as well.

My main advice is to always think about your aims and what will make your activity mutually beneficial to you and to those you seek to engage or involve. Evaluating your approach and reflecting on feedback are also really important, to continually build upon best practice.

Don't underestimate the costs, but please don't let this put you off either. I'd far rather that researchers gave it a go and learned through making a few honest mistakes than never started at all. This is also an evolving space, so there's still time to be one of the pioneers in endocrinology!

CAROLINE GILLETT
Assistant Professor in Patient and Public Involvement and Engagement, Institute of Metabolism and Systems Research, College of Medicine and Health, University of Birmingham

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IF YOU COULD TALK TO YOUR EARLY CAREER SELF WHAT WOULD YOUR ADVICE BE?

"Say yes to extra opportunities offered to you, and then continuously seek out new ones across the full breadth of your work. These extra opportunities will teach you new skills, provide variation and satisfaction, and you never know where they may lead.
ALEXANDER COMNINOS
Imperial College London

"Opportunities often arise in unexpected places and life has a habit of working things out, so avoid over-thinking things and focus on what you enjoy.
NICK THOMAS
Royal Devon University Healthcare NHS Foundation Trust

"If you want to be successful, find yourself a good mentor who understands how it works but will allow you to grow as an individual.
ZOI MICHAILIDOU
Nottingham Trent University and the Society's Science Committee Chair

"Appreciate your brilliant mentors, because you're lucky to have them. They will support you to grow your potential and realise your ambitions.
AMIR SAM
Imperial College London

Your Society
Helping your career flourish

We support early career scientists, clinicians, nurses and associated professionals working in all hormone-related fields, providing you with the funding, resources and professional development opportunities for a successful career in endocrinology and beyond.

Society for Endocrinology

SECURE FUNDS

Our early career members can apply for all of the **SOCIETY'S GRANTS**. Whether you need funding to travel to an event, organise a meeting, support your research, fund your outreach activities, or assist with your teaching initiatives, there are Society grants for you.

BECOME A LEADER

The Society's **LEADERSHIP AND DEVELOPMENT AWARDS PROGRAMME** recognises and nurtures emerging talent in endocrinology. This programme can accelerate your career through: dedicated leadership training, access to an advisory group of senior members who can provide advice and support, opportunities to get involved with the Society's governance, and more!

MAKE NEW CONNECTIONS

Whether it's by attending **OUR EVENTS**, joining one of our **ENDOCRINE NETWORKS**, browsing our **MEMBER DIRECTORY** or **JOINING A COMMITTEE**, Society membership offers you the opportunity to network with others who share your passion for endocrinology – this could open the door to your next research collaboration or job opportunity, as well as providing you with new perspectives on your work.

HAVE YOUR SAY

We need early career members on **OUR COMMITTEES** to give their individual perspectives on the issues that matter in our field, and to make sure our Society is supporting those starting out in their careers. In return, committee membership gives you the chance to use your skills in new ways and to work with colleagues from all career stages and subspecialties whom you wouldn't otherwise meet. Look out for our next committee vacancies in the autumn!

DEEPEN YOUR KNOWLEDGE

We're committed to your professional development. **SOCIETY EVENTS** keep you updated on the advancements in endocrine research and clinical practice, with CPD points available for attendance; our **CLINICAL RESOURCE HUB** gives you inspiration and tools from other members to improve your own clinical practice; and free access to the **SOCIETY'S JOURNALS** makes it easy to stay up to date with the latest research in endocrinology.

REACH NEW AUDIENCES

The Society can support your public engagement activities, providing opportunities to talk about your work to wider audiences.

- Apply for an **OUTREACH GRANT** to fund activities to engage patients or the public with endocrinology.
- Join our network of **MEDIA AMBASSADORS** to ensure accurate reporting of endocrinology in the media.
- Become a content editor for our public-facing website: **YOU AND YOUR HORMONES**.
- Take part in our **SCHOOLS' OUTREACH PROGRAMME**.

Jeremy Tomlinson
WHY YOU SHOULD APPLY FOR SOCIETY GRANTS

Jeremy Tomlinson is Professor of Metabolic Endocrinology and a consultant endocrinologist based in the Oxford Centre for Diabetes, Endocrinology and Metabolism at the University of Oxford. He has served on a number of local, national and international grant panels, including positions at the British Heart Foundation and Medical Research Council.

Jeremy became Chair of the Society's new Grants Panel in 2023. We caught up with him to find out about his new role, as well as to hear how the Society's grants have changed, and his advice for early career members on writing successful grant applications.

How did you become involved with the Society?
I have been a member of the Society for Endocrinology for almost 25 years – ever since I first decided that I wanted to pursue a career in endocrinology. I've had a number of roles, including serving on the Clinical Committee, being part of the SfE BES Programme Organising Committee, helping to establish the Leadership and Development Awards Programme (and sitting on the assessment panel), as well as being a convenor for Clinical Update. I was also one of the convenors of the Society's Adrenal and Cardiovascular Network, a member of our governance review team, and I sat on the Society's Council of Management for several years.

How has the Society helped your career?
The Society for Endocrinology has played a really important part. It has provided me with the opportunities to work with, collaborate with, and form friendships with like-minded clinicians and scientists across the UK and beyond. It has been a huge privilege to sit on Society committees that provide the highest quality training, facilitate high quality research and make a positive difference to patient care. It was a great honour to be awarded the Society for Endocrinology Medal in 2021. It is these experiences that have inspired me to encourage others to pursue a career in endocrinology.

Why were you keen to become Grants Panel Chair?
In all walks of life, it is always important to give something back. Recognising the huge benefits I have had from the Society for Endocrinology, I was keen to try and help by taking up the role of Grants Panel Chair. I have seen first-hand the benefits that grants from the Society can have for individuals – especially those at early career stages and for nurses, midwives and other allied health care professionals. Providing support for their work, education and research is so important, and I see this as a really important part of the Grants Panel remit.

How will the changes to our grants benefit early career members?
We have hopefully made the application process a little more straightforward and focused. Having three opportunities to apply for funding throughout the year will mean that there is less of a rush to meet a specific deadline, and that there is time to make sure that each application is as good as it possibly can be when it's submitted. Often taking a little extra time and getting feedback on applications – perhaps from more senior and experienced colleagues – can maximise the chances of success.

What opportunities will arise from all members being eligible for all grants?
It is important that we try and fund the best proposals and the best research, but the benefits to the field and the benefits to the applicant are also important criteria. From personal experience, I know the benefit that securing your first grant (however small) can have. Therefore, particularly for early career members, there is a real opportunity to stress and emphasise this as part of the application. Although we are opening up applications to all members, our assessment of what an application will mean to an individual (relevant to their career and their career stage) forms a really important part of the assessment criteria.

How will the Grants Panel judge early career applicants fairly against experienced colleagues, ensuring transparent allocation of funding?
Much of this is about 'impact'! Whilst people often think about the impact that their proposal might have on patients, participants or delegates (which is, of course, fundamentally important), it is also very important to consider the personal impact. How will this grant funding impact me? It may well be your first research grant, it may be the stepping stone to larger applications or a personal fellowship, and it may be something that takes you in a slightly different direction from your research supervisor, moving you towards research independence. As an early career researcher, you may have much more to gain from this than a potentially well-funded established investigator.

When we established the grants panel, we also wanted to provide early career members with opportunities to be part of the panel, to perhaps gain their first experience of how funding panels operate. There will certainly be opportunities for new panel members in the future, so if this is something that interests you, I would strongly encourage you to apply when there are vacancies.

Will this change have a big impact on early career endocrinologists?
Having worked and been involved with other specialties, the breadth of grant support that the Society for Endocrinology offers is really exceptional, and we mustn't take it for granted. The Society has always made huge efforts to support individuals at the earliest stages of their careers: it continues to support undergraduate studentships. It is really important that we continue to support and encourage people to become part of the endocrine community. I hope that, by restructuring our grants, the Society will continue to deliver on that aim, with even more junior members applying for support.

What is your advice to early career members writing grant applications?
First, make sure you do apply – do not think that these awards are for others – your application may be just what we're looking for. Definitely do read the guidance and the application form and make sure you answer all the questions that have been asked, rather than simply including what you think should be in the form!

I would always ask a more senior and experienced colleague to look over the application and provide some open, honest and robust feedback. Make sure you give them sufficient time (not just the day before the deadline). Writing grant applications is a skill that we all have to learn. The more we do it, the better we get.

Finally, don't be put off by rejection – that happens to us all. I don't know anyone who has not had a grant application rejected. Often, it's not that the application is bad, but resources and funding pots are always finite, and sometimes it's just that there isn't enough money to go around. Don't give up!

Find out more about the Society's new grants

Steven Millership on
NEW VIRTUAL COFFEE CHATS

Steven Millership is a Research Fellow at Imperial College London, whose postdoctoral work investigated the function of imprinted genes, particularly in the insulin-secreting β cells of the pancreas. Steven is also Early Career Editor of two Society for Endocrinology journals: *Journal of Endocrinology* and *Journal of Molecular Endocrinology*. We caught up with him to learn about his career to date, as well as his role in the new series of Virtual Coffee Chats from the Society.

Please tell us about your research and current projects

Predominantly, my work investigates β cell function and heterogeneity, with a focus on the epigenetic pathways that control them. I have always been fascinated by secretory/hormone systems and their effect on whole body metabolism. This work comes with important ramifications for human metabolic disease (obesity, type 2 diabetes). The potential to have a positive impact on these conditions is ultimately what drives us to do the research.

Who inspires you most in your field of research?

My PhD supervisor, Professor Vladimir Buchman, was a huge influence on me when I started working in the lab; our group was like a family. Professor Buchman taught me multiple cell biology and biochemical assays and was never too busy to discuss something. We celebrated successes, such as publications and grants, with champagne and a gathering, which made the whole process so much more rewarding. Recently, I have been inspired by scientists including Professor Claes Wollheim, who I met at the European Association for the Study of Diabetes 2023 Annual Meeting. At the age of 80, he took the time to warmly encourage the work of even the earliest career scientists, and asked important and interesting questions. He is truly inspiring to the next generation.

'Too often in academia there is a temptation to have "tunnel vision" and stick to your own groups' established interests and techniques.'

What is involved in your role as Early Career Editor for the journals?

I oversee the peer review of assigned papers and select and invite reviewers for peer review, as well as promoting the journals to the endocrine community and providing feedback on their strategic development. Shining a light on important new research is crucial and I feel it is critical in the early stage of your career to be exposed to multiple research topics, angles and methods to enhance and streamline your productivity and effectiveness in your own field.

Too often in academia there is a temptation to have 'tunnel vision' and stick to your own group's established interests and techniques which, in my opinion, does not lead to a successful career in scientific research. I wanted to support the publishing community by facilitating high quality peer review and publishing processes, while also casting the net wider on my own research understanding and exposure. I have done this by immersing myself in multiple aspects of the latest endocrine-related research outside of my own specialty.

'We hope this series will help increase the visibility of early career researchers, fostering their professional development and helping build a strong, supportive scientific community.'

What are the plans for Virtual Coffee Chats?

The Society is launching a new series of Virtual Coffee Chats, offering authors of recently published papers an opportunity to connect with its scientific community. These online sessions aim to bring together individuals with complementary skills, knowledge and research interests to discuss the latest research. We hope this series will help increase the visibility of early career researchers, fostering their professional development and helping build a strong, supportive scientific community.

We'll be announcing the date and details of the next Virtual Coffee Chat session soon, so keep an eye out on your member emails and Society social media.

DO YOU KNOW A RISING STAR?

The **Rising Stars 2024 Special Collection** will highlight the breadth and depth of research undertaken across basic endocrinology by early and mid-career researchers, published across *Journal of Endocrinology* and *Journal of Molecular Endocrinology*.

The collection is now open for submissions. Led by Senior Editor Professor Massimiliano Caprio, 'the collection will combine novel themes, challenging projects and the enthusiasm of young authors from around the world.'

For more information, or to submit an article, email **joe@bioscientifica.com**.

Miles Levy on ENDOCRINE GENETIC TESTING 2024

Professor Miles Levy is a consultant endocrinologist at the University Hospitals of Leicester, and Honorary Associate Professor at Leicester University. Miles is on the Founding Group for the Society's **Endocrine Genetic Testing** event, taking place this September. We spoke to him about the importance of endocrine genetic testing, why the new Genomic Laboratory Hubs (GLHs) are making testing easier, and how this event can prepare you for the future of clinical practice.

What sparked your interest in endocrine genetic testing?
A few years ago, the subject of genetics came up after a Clinical Committee meeting. I had a run of patients with endocrine tumours due to germline mutations, and we had decided to set up an endocrine genetic clinic. This also coincided with research in our department involving the use of circulating cell-free tumour DNA to monitor cancer. Endocrinology lends itself to molecular diagnoses, and we thought we would be ahead of the game to become the first major adult specialty to really develop endocrine genetics for the NHS. After a chat with Márta Korbonits, Ruth Casey and Paul Newey, we decided to go for it, and devised the first Endocrine Genetic Testing event, which ran in 2023.

'Within the next few years, endocrinologists will be using resources like PanelApp (a way of looking at what each gene panel consists of) as if they've always been doing it.'

Can you explain the significance of endocrine genetic testing in today's clinical practice, and what it will mean for the future?
Undertaking genetic tests is going to become part of routine clinical practice. The introduction of GLHs means that we can now test for genes in our endocrine patients without worrying about who is going to pay for it (the NHS will). As long as a patient is eligible for testing on the National Genomic Test Directory, we can do the test.

Of course, we need to know what to do with the result and what the gene panels consist of, which is where training events like Endocrine Genetic Testing come in. In the clinic, we have also developed a really **user-friendly website** that helps endocrinologists work out what gene tests to do in real time. Endocrinology is the first adult specialty to do this.

Within the next few years, endocrinologists will be using resources like **PanelApp** (a way of looking at what each gene panel consists of) as if they've always been doing it. In addition, we will be predicting which tumours and conditions our patients are likely to get, based on inherited conditions. We will also be able to predict a patient's response to treatment by genotyping the clinical problem that we are presented with, such as the likely response to treatment in patients with endocrine tumours based on somatic mutation.

What main objectives do you hope to achieve through this event?
The main aim is to give clinical endocrinologists the confidence to consider testing for genetic conditions in their own patch. The event will encourage people to understand which routine conditions we should be doing genetic tests on, and how to think about interacting with our clinical genetics colleagues. There is likely to be more mandated training in this area in the endocrinology curriculum for specialist registrars, so we are planning to engrain this formally in endocrinology training. It is still early days, having only run one event last year, so it is an iterative process in terms of the course.

What training need is this event fulfilling?
We have developed this event to ensure consultants and specialist registrars can go through the basics of genetics and work through the kinds of cases they will see in real life. In endocrinology, we are fortunate to have brilliant clinicians and scientists who are some of the best clinical geneticists around.

The day consists of two halves. The morning revolves around lectures on basic principles in genetics and how they relate to the endocrine clinic. This includes both ethical and scientific issues. In the afternoon, workshops will address common situations, such as multiple endocrine neoplasia, familial phaeochromocytomas and paragangliomas, hereditary calcium problems and reproductive genetic topics, such as congenital adrenal hyperplasia.

All the speakers are brilliant and at the top of their game, including Márta Korbonits, Paul Newey, Ruth Casey and Sasha Howard. We will also have help from speakers from Exeter, who are world leaders in the genetics of diabetes mellitus.

What are your top five reasons to attend?

1. To know who you should be doing genetic tests on in an endocrine clinic.
2. To understand how to do a genetic test in real life.
3. To find out how to interpret the result and what the funny letters and numbers mean on a genetics report!
4. To ask all the stupid questions everyone else always wanted to ask, in small, supportive groups.
5. To work through real-life endocrine cases to equip you for the clinic.

Endocrine Genetic Testing will be taking place on Thursday 26 September in Birmingham.

KAREN CHAPMAN
MY CAREER IN ENDOCRINOLOGY

Karen Chapman is Emeritus Professor of Molecular Endocrinology at the University of Edinburgh. She is also an Adjunct Professor at the University of Western Australia.

Before her retirement a little over two years ago, Karen led research into glucocorticoid action in the University of Edinburgh/British Heart Foundation Centre for Cardiovascular Science. She was also active in other areas, including lead roles in equality, diversity and inclusion for the University, as well as for the College of Medicine and Veterinary Medicine, and was involved in several Society for Endocrinology activities. She is married to Stephen Chapman and they have three children.

MY EARLY CAREER

My journey was perhaps a bit unusual for someone in the Society for Endocrinology. I did my PhD in the field of bacterial DNA recombination and repair at Newcastle University. Part of my research consisted of using Sanger sequencing, in its infancy in the early 1980s, to sequence just two genes in *E. coli*, something that would easily be accomplished in a few hours now!

After my PhD, I was lucky to obtain a fellowship from the Royal Society, and later one from the European Molecular Biology Organisation to pursue a post-doc in the USA with Mark Ptashne at Harvard University, Cambridge, MA, working on the *E. coli* cAMP receptor protein, a ligand-activated transcription factor. This was a hugely formative experience that taught me how to think as a scientist. It was also very insightful – I reflected on how, as a new post-doc in the UK, I would have feared the competition from the Ptashne lab, yet that competition was now me! It was an important lesson and one I've shared with trainees suffering from 'imposter syndrome'.

In the 1980s, ground-breaking molecular biology research was happening all around me in Cambridge/Boston and it was a tremendously exciting time to be there. It instilled in me the importance of sharing (and debating) new research findings, not necessarily just in my own particular area. Especially memorable were the afternoon (4pm) lab tea breaks, which were rigorously observed, when everyone in the group gathered to discuss anything from the latest research news from neighbouring labs or recently published papers, to the Celtics basketball results. It's easy to lose sight of how important these social occasions can be, when now it often feels like research is 'too busy' or pressured to take time out to chill with labmates. It was a lot of fun too. James (Jim) Watson visited the lab when I was there, and I was also introduced to the cellist Yo Yo Ma in the corridor one day!

A MOVE TO STEROID HORMONE RESEARCH

Whilst at Harvard, I heard a talk by Keith Yamamoto, whose lab had just cloned the glucocorticoid receptor. The story he presented of how the glucocorticoid receptor regulates gene networks sounded just like the *E. coli* system I was working on at the time. When an opportunity came up to work on steroid regulation of gene expression with George Fink and colleagues at the Brain Metabolism Unit in Edinburgh, I jumped at it, and began exploring what determined the specificity of steroid hormone action. It was during my time there that I was introduced by Chris Edwards to a young clinician scientist, Jonathan Seckl, fresh from his PhD research and newly recruited to Edinburgh. He was going to work on mineralocorticoid and glucocorticoid actions in the brain. We started working together almost immediately and, not long after that, I moved across to the University of Edinburgh to join Jonathan and Chris in the (then) Department of Medicine.

I was intrigued by the idea of an enzyme determining specificity of action of steroid hormones, and began working on the 11β-hydroxysteroid dehydrogenases at the start of the 1990s. All these years later, there is still so much to discover about the 11β-HSDs, especially their effects on cellular redox and metabolism, as well as what they might do in metabolism of other oxysterols, like bile acids. Stay curious! My collaboration and research partnership with Jonathan – funded by a series of joint grants and supported by the many fantastic research students and post-docs that we jointly supervised and worked with – lasted well over three decades and resulted in the publication of over 70 co-authored papers and reviews.

BECOMING AN ENDOCRINOLOGIST

Of course, an interest in glucocorticoids takes you down many paths. I often felt like a 'Jack of all trades' (and wishing I was able to master at least some of them!). The 11β-HSDs took me from placental biology and early-life programming of adult disease risk to inflammation and immunity, and even touched on cellular metabolism. I kept an interest in the glucocorticoid receptor itself as well, which ultimately brought me, in recent years, to the fetal cardiovascular system, and back to the early-life origins of adult cardiovascular disease risk.

Because my interest in steroid hormone action arose from the role of the receptors as transcription factors, it took me some time to realise that I was becoming an endocrinologist! I don't think I was even aware of endocrinology as a discipline when I moved to Edinburgh. It was when I joined the Hormone Group (a joint committee between the Biochemical Society and the Society for Endocrinology, which was responsible for organising conference symposia) that I first became aware of the Society for Endocrinology and realised how pervasive endocrinology is. Ten years later, as a member of the Society's Science Committee, I most definitely identified as an endocrinologist!

THE ROLE OF THE SOCIETY

The Society has been a companion to me on my career journey as an endocrinologist. It's provided a welcoming and supportive community and the opportunity to meet and engage with so many people, with hugely diverse backgrounds and career paths. On the Science Committee and Programme Organising Committee, I loved being able to suggest symposia on my favourite topics with speakers that I wanted to meet (my alternative career would have been in scientific publishing). As a member of Council and, later, as General Secretary, it was very rewarding (and insightful) to work closely with the executive team and other Society staff.

Council, in particular, exposed me to a diverse range of perspectives of endocrinologists from different fields and career paths, which broadened my views and deepened my appreciation of what the Society offers to its members – so much more than simply an annual conference. I was also tremendously privileged to contribute to shaping the future of the Society, as part of a Journals Review working group, which led to the merger of the editorial boards of the *Journal of Endocrinology* and *Journal of Molecular Endocrinology* and, more recently, through a governance review of the Society. All I can say to people who are new to the field (and especially those who may not yet consider themselves endocrinologists) is to get involved – nothing ventured, nothing gained!

AND THE BEST PART OF THE JOB?

Without a doubt it's the people. It's been incredibly stimulating and refreshing working with so many of the brightest and best young people, especially the trainees I've been involved with. I've had so many amazing colleagues and students in Edinburgh over the years. I've benefited from a fantastic network of peer mentors, who have supported me along the way and encouraged me to put myself forward when opportunities have arisen.

Two in particular deserve mention: Val Kelly, a research technician who came with me from the MRC Unit to the University, we worked closely together for almost 40 years, and Megan Holmes, with whom I shared an office for many years, and who has been a long-standing collaborator as well as a close friend. Indeed, it is the many friendships and collaborative relationships – from research students to senior colleagues and members/staff at the Society – that have made a career in endocrine research so rewarding and fulfilling.

HOW DO I... DECIPHER LIPIDS?

WRITTEN BY MATTHEW CONROY

The world of lipids is a complex one. Lipids range from membrane phospholipids, fatty acids and sterols, through to the steroid hormones, cannabinoids, pheromones and plant pigments. It's tricky to make sense of such a vast array of chemistry.

That's where LIPID MAPS comes in. The LIPID MAPS consortium (**www.lipidmaps.org**) was formed over 20 years ago in the USA and sought to explore the lipidome. To do this, lipids had to be first defined, and then classified. The LIPID MAPS classification system is now internationally recognised, and we also provide a host of resources, databases and tools to support the lipidomics community in their research.

CLASSIFYING LIPIDS

LIPID MAPS defines lipids as hydrophobic or amphipathic small molecules formed by condensations of thioesters and/or isoprene units. They are classified into eight categories (see Figure 1), each sub-divided into two or three more levels.[1] These cover fatty acids through to antibiotics, via sterols and steroid hormones.

HOW TO EXPLORE LIPIDS

This classification system organises the LIPID MAPS Structure Database (LMSD; **www.lipidmaps.org/databases/lmsd**), containing over 48,000 lipids from all domains of life. Now based in the UK, but with international partners, our new MRC funding will allow us not only to expand the database with more lipids, but also to add biochemical reactions and pathways by which they are made and degraded.

Lipids in the database come from the scientific literature, but many have also been brought in from other databases too. Each lipid has its own dedicated web page showing the two-dimensional structure of the molecule and, optionally, a three-dimensional model can be displayed. Names and synonyms are listed along with the mass and formula, and a facility to calculate m/z values for various adducts. Where available, links to mass spectra in the Massbank of North America are provided, as are cross references to other databases such as ChEBI and PubChem. Recently we've been adding the information about where a lipid has been curated from, including the taxonomic species, to aid users in finding more context for the molecule in question.

HAVE WE CATALOGUED ALL THE LIPIDOME?

From the whole of life, absolutely not (yet!), and almost certainly there are molecules to be added, even from humans. In terms of documenting the reactions which transform lipids, we've only just begun. Please do get in contact if you spot a hole!

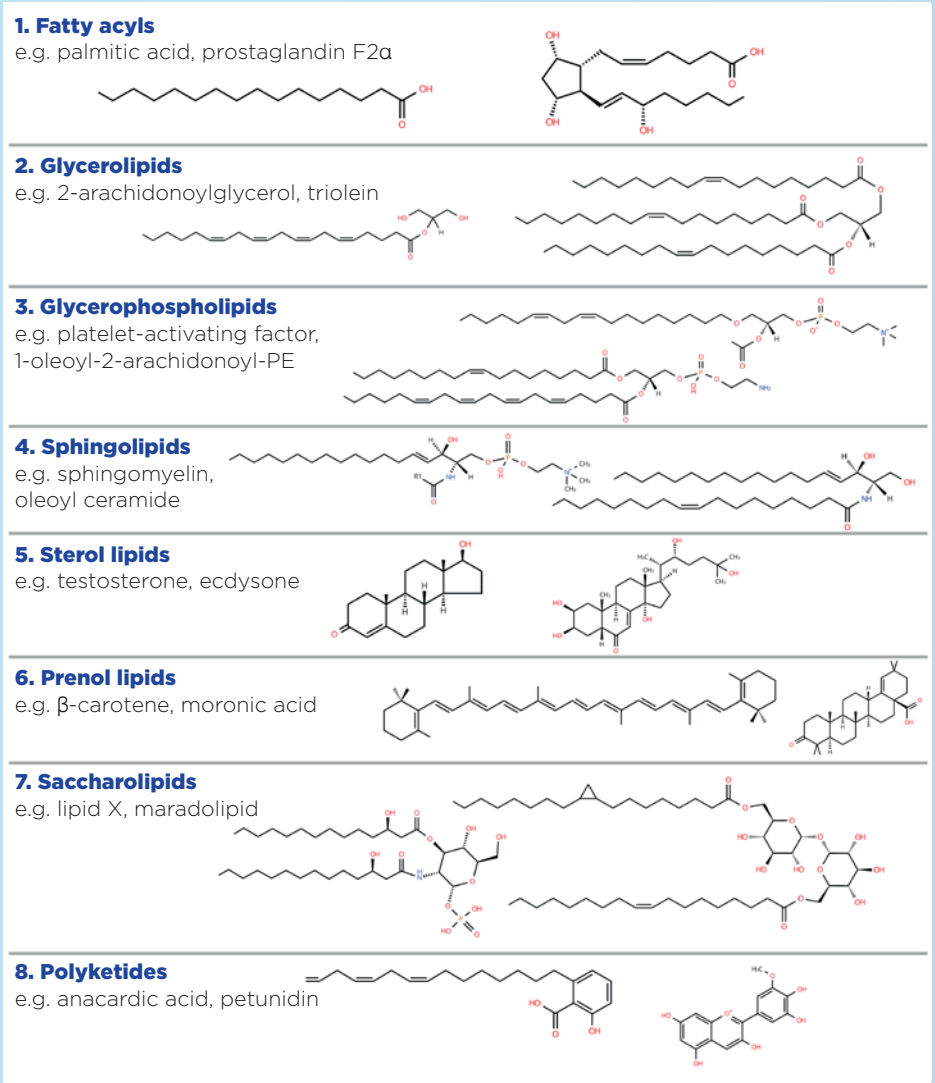
HOW DO RESEARCHERS MINE THE DATA?

The database can be browsed via the classification hierarchical tree, or searched directly from the top of the LIPID MAPS homepage using names, formulae, m/z values or computational identifiers. More advanced search functionality allows searching for chemical substructures as well as properties, such as the number of hydroxyls and/or double bonds. No specialist skills are needed to look through the LIPID MAPS databases, and the whole site is freely available to everyone.

A RANGE OF TOOLS

We're not just about cataloguing lipids, there is a range of tools available for mass spectrometry and lipidomics analysis too. There are also tools for structure drawing, to generate diagrams of chemical structures for a range of lipids in standardised orientations. We've just updated the sterol drawing tool to include the three classes of steroid hormones: pregnanes, androstanes

Figure 1. The eight LIPID MAPS categories to classify lipids, and examples of each.



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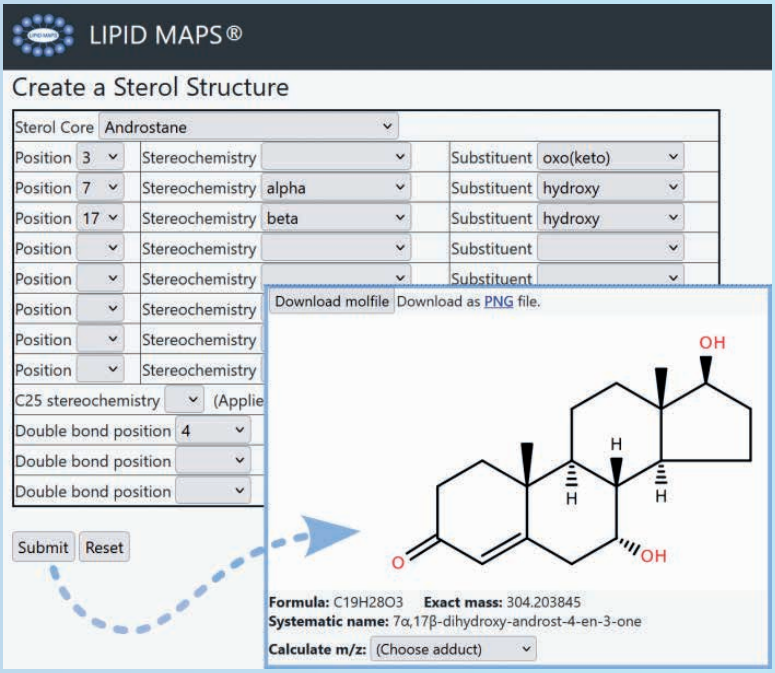


Figure 2. The sterol drawing tool at LIPID MAPS. Input the parameters and a diagram of the molecule is produced, in this case, 7α-hydroxytestosterone.

and estranes. Simply input information about the molecule as shown in the image, such as position of double bonds, and the **tool outputs a diagram for you** (Figure 2).

HOW TO INTERACT WITH LIPID MAPS

We've made lots of updates in the last few years; check out our recent paper that describes them.[2] There's a range of educational resources on the LIPID MAPS site, including podcasts and monthly webinars which are streamed live and also available on our YouTube channel (**@lipid_maps**).

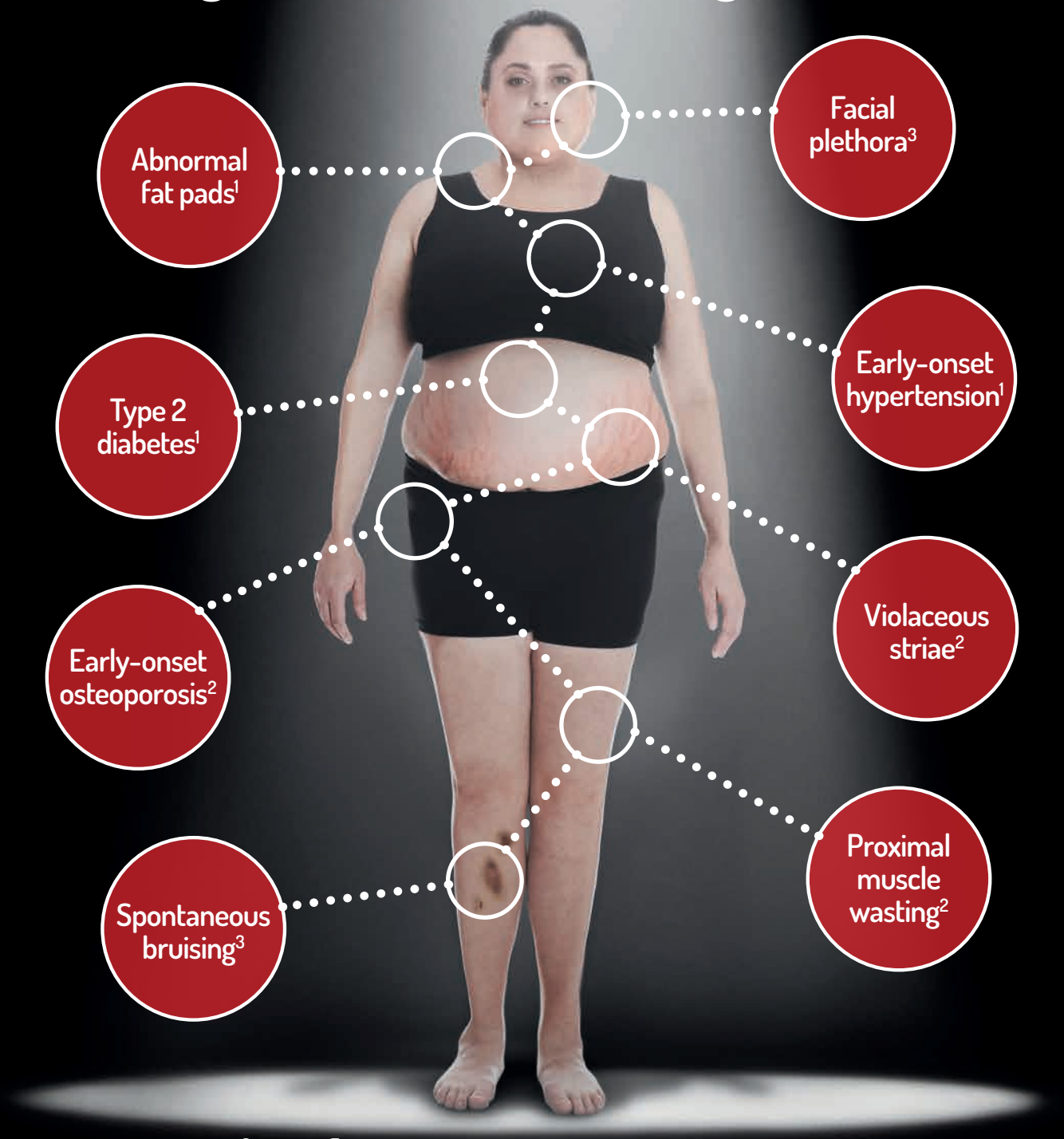
Our regular 'Lipid of the Month' feature highlights a particular molecule which might be involved in anything from modulating appetite to moulting in insects. Our 2021 training school presentations are there too, and we're planning our next training school (face-to-face) for next year. We're also on X (**@lipidmaps**) as well as Facebook and LinkedIn, and there's a community forum linked from our homepage. We look forward to seeing you!

MATTHEW CONROY
Biocurator, LIPID MAPS Databases, based at Cardiff University.

REFERENCES

1. Fahy E *et al.* 2005 *Journal of Lipid Research* https://doi.org/10.1194/jlr.e400004-jlr200.
2. Conroy MJ *et al.* 2024 *Nucleic Acids Research* https://doi.org/10.1093/nar/gkad896.

Although the condition might be rare...



...the features are common

Perhaps it's Cushing's syndrome, perhaps it's something else? If you connect any of these dots within a patient, consider referring them to a specialist endocrinologist.

For a clinician's guide to recognising Cushing's syndrome's signs and features, email **cushings@connectthedots.health** and help shine a light on this rare condition.

HRA Pharma
Rare Diseases
A Perrigo Company

Connect the dots

References: 1. Pappachan JM *et al. J Clin Pathol.* 2017;70:350–359. doi:10.1136/jclinpath-2016-203933
2. Nieman LK. *Endocrinol Metab.* 2018;33:139–146. 3. Yorke E *et al. Int J Endocrinol.* 2017; 1547358.

UK/NPR/0015 Date of preparation: April 2024