AI in endocrinology
Our brave new world

Also in this issue
The EYES community meet in person in Zagreb
How your EYES Committee works for you
Days go by so fast and another autumn is here. We should pause to appreciate our achievements. We often get so carried away by our daily activities that we do not have a chance to reflect upon the work and results we leave behind.

EYES News has come from a trial version of an online newsletter design tool, a laptop in a small coffee shop on the corner and pure optimism, to create something meaningful for the EYES community. Here we are now, with a huge Editorial Board, the professional publishing skills of a copywriter and a graphic designer, our own ISSN, and stories lined up for issues to come. Excitingly, starting with this issue's engaging interview with Pierre Val, we will conduct live interviews with our amazing scientists, and share these with a broader community on the ESE YouTube Channel, in a new playlist called EYES News: Amazing Scientists. In this issue's pages, you will also find the freshest stories on the use of artificial intelligence (AI) in adrenal endocrinology, diabetes, reproductive endocrinology, thyroid disease and osteoporosis. Could an article like this Editorial be written by an AI Editor bot in the future? Hopefully not.

You can also read here about the EYES Annual Meeting in Zagreb, Croatia, the COST Action Harmonisation project, and a reminder of the benefits to early career investigators of ESE membership. Then there is news of the amazing return of the ESE Summer School, the EnGiOl (Young Italian Endocrinologists) meeting and an invitation to ECE 2023 in Istanbul, Turkey.

This is my last issue of EYES News as Editor. All it took was everything! But I was blessed with the best mentor and the best team I could wish for. For me, personally, one of the most important missions is to inspire profound communication, knowledge and creative thinking. If we have achieved this with our work, at least for one early career investigator, my job has been done right.

See you soon, and good reading.

Antoan Stefan Šojat
Editor, EYES News

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EYES Co-Chair report

The EYES Committee is hard at work. We can feel this by the amount of interaction we are having, not only within our community, but also with other endocrine and scientific communities: undertaking projects, writing articles and planning joint ventures.

The new season for applications for the EYES Observership Programmes is approaching. We are expanding the number of centres, connections and research projects. Meanwhile, previous awardees are returning from their placements with a whole new level of inspiration and new-found skills and projects, eager to take on the world.

EYES News is developing, and now has a wonderful flow within its pages. We can’t wait to read the future issues. This is Antoan’s last issue as Editor, and we welcome the Editorial Board’s very own, very experienced Walter Vena, who is stepping up to the position of Editor.

We were pleased to be part of the relaunch of the ESE Summer School; it went terrifically well and the feedback has been amazing. The EYES Committee organised a fantastic session on breast and progesterone. We also invited the attendees to join in all of our activities while playing football on fresh Tyrolean grass! They were very keen to learn about our projects and what we do, and many new friendships were formed.

September brought us together for our most important event: the 9th EYES Annual Meeting in Zagreb, Croatia. It took place in person; we were back, together, doing what we love most. The Local Organising Committee’s incredible work made this meeting unique and unforgettable, in a great venue, worthy of what our meeting has become. We heard top notch science, saw ground-breaking results and posters, and sparked future collaborations and a whole new world of ideas to work with. EYES ‘legends’ Ljiljana Marina and Daniele Santi gave us memorable talks and reminded us of all our community has achieved together. Our EYES round table discussion demonstrated how much we are doing right by the number of questions and ideas we heard from our early career investigators. We could write reams about the social programme and all the little things that create our warm feeling of being a community and part of something larger. Our hearts are full and we are inspired to do even more after such a positive energy boost.

So, with all this happening, we should just say ‘Let’s get down to business’.

Lina Paschou
Antoan Stefan Šojat
EYES Co-Chairs

Key dates for your diary

See www.ese-hormones.org/events-deadlines and watch your inbox for emails with details, early bird rates, free places and grant information!

3 November 2022
ESE Spotlight on Science: Towards Novel Biomarkers in Endocrine Cancer
Online

3–5 November 2022
Clinical Challenges of Cushing’s Syndrome across the Lifespan: the Long-Lasting Problems
Munich, Germany

16–17 November 2022
European Cancer Summit
Brussels, Belgium

20–23 November 2022
EuroPit 2022
Annecy, France

28–29 November 2022
3rd Euro Diabetic and Endocrinology Congress
Paris, France

29 November 2022
ESE Talks... Rare Diseases II: a Joint Webinar from ESE, Endo-ERN and ESPE
Online

10–12 January 2023
ESE Clinical Update on Obesity and Female Reproduction 2023
Online

13–16 May 2023
ECE 2023
25th European Congress of Endocrinology
Istanbul, Turkey

18–21 June 2023
ESE Summer School 2023
Innsbruck, Austria

8–10 September 2023
EYES Annual Meeting 2023
Würzburg, Germany
INTERVIEW

What drew you to endocrinology and your current research? It actually started a bit more than 20 years ago. I was doing research for my Master’s, and I worked on the response of genes to hormones, which was mostly based on cell culture systems. It was quite tedious, but I really got hooked by the excitement and complexity of endocrinology as a whole.

Then I did my PhD on gene regulation, at the University of Clermont in France, under the supervision of Marie and Antoine Martinez. There, I started using mice and rats to do comparative endocrinology. That sounds very old-fashioned these days but, by comparing gene responses between these two species, we managed to find response elements that were specific to one species or the other, and explained the response to androgens and adrenocorticotrophin (ACTH).

From there, I decided I really wanted to do in vivo research. So, after graduating, I went for a postdoc in London, UK. I stayed for about 4 years at the Institute of Cancer Research, under the supervision of Amanda Swain. I studied embryonic development, mostly of adrenal glands and gonads, which share a common progenitor. It was heavily based on genetics and crossing multiple backgrounds together, to try to understand how the adrenal and gonads were forming, early in life.

At the end of my postdoc, I started applying for a full-time researcher position in France, at the CNRS (Centre National de la Recherche Scientifique), which was pretty competitive. I succeeded after quite a few attempts, and I think this is quite important to say that you must be persistent. Getting a position rarely just happens the first time you try, unless you are very lucky! Eventually I was successful, and I started working more in adult adrenal physiology, but still with the idea that physiology, disease and development are all intertwined, and that the pathways which are involved in embryonic development and deregulated in tumours are also important for differentiation of the tissue.

After working as a researcher, I was fortunate enough to establish my own group at iGReD in Clermont–Ferrand, France. We work heavily on adrenal tumours with a very strong focus on mouse models.

Overall, you can think of this as a fairly linear journey, but nothing was quite that simple and I encountered a number of hurdles on the way. But, if you know what you want, have a bit of luck and are ready to fight for it, you will get there eventually.

Do you recall your first ever publication? It was a paper describing the regulation of a gene that was pretty obscure at the time, called AKR1B7. It turned out to be quite an important gene in zona fasciculata, at least in mice. The ‘story’ was about how it was responding to androgens and ACTH. This was a very basic paper, but it dealt with transcription factors like SF1, which is a key factor for steroidogenesis, and also C/EBP and CREB, which are all very endocrinology-related. It was published in Endocrinology.

The experience was rather a long process, with lots of tedious cell culture experiments and many obstacles. I remember going through multiple phases, first getting excited, then getting depressed and then getting excited again. It really was like a constant roller coaster, but eventually it went through. Endocrinology was pretty old-fashioned around that time (2002), as most journals were already starting web submission, but Endocrinology wanted you to submit your work as a printed paper, which took forever to sort out!

What do you think of the modern publication process? Well, the online submission process has clearly improved. But, of course, the requirements for getting a good paper accepted have increased dramatically over the last 20 years. These days things go faster, but journals want a lot more data to confirm what you’re claiming. Overall, I think it’s still really hard work to get a paper published.

‘Overall, you can think of this as a fairly linear journey, but nothing was quite that simple and I encountered a number of hurdles on the way. But, if you know what you want, have a bit of luck and are ready to fight for it, you will get there eventually.’

Pierre Val, Group Leader, iGReD

Amazing careers: Meet Pierre Val

Pierre Val is Group Leader at the Genetics, Reproduction and Development Institute (iGReD) in Clermont–Ferrand, France. His research focuses on the field of adrenal development and sexual dimorphism. Here, he tells Antoan Stefan Šojat about his career so far and his tips for success based on his experience.
‘You can have all kinds of good theories, but you just have to face the fact that sometimes the data do not agree with your hypotheses. You then have to think “out of the box” to try understanding what’s going on. It may seem frustrating, but these moments are also great opportunities to find completely novel things!’

What are some of the key moments in your career?
I think it was going from a PhD student to being a postdoc and moving to London. You start being independent; you start applying for money, designing elaborate experimental schemes...

You also start realising that – well – you can have all kinds of good theories, but you just have to face the fact that sometimes the data do not agree with your hypotheses. You then have to think ‘out of the box’ to try understanding what’s going on. It may seem frustrating, but these moments are also great opportunities to find completely novel things!

This is how we established that the PKA and WNT signalling pathways were antagonising each other to allow normal cortex functional zonation, when we initially set out to prove that the two pathways were synergising to form tumours! It took a lot of time to figure out how it was working, but we eventually published it in *Nature Communications*, which was a really nice achievement for us. I really think it is essential to be prepared for surprises and to think inventively in this career!

And what have been some of your greatest challenges?
Well, adversity is everywhere in science, obviously. Now, I think that the biggest challenge is to get funding for your projects, which allows you to hire talented and motivated people to embark on novel adventures. There are lots of talented people out there, and lots of exciting problems to tackle, but clearly not enough money for research! I also had multiple failures. You really have to confront failure and get back on your feet. This is really challenging sometimes; it’s easy to get depressed. But if you gather the energy to move on, you always gain something form these moments!

What is the most important work done by ESE, and specifically the EYES community?
I think ESE are doing a tremendous job of organising all kinds of events and activities for young endocrinologists in Europe, enabling them to interact with other endocrinologists, especially their peers. This is a very active area of ESE, and I think it should really be encouraged. The only thing I see, and this is a bias for all endocrinology societies, is that basic science is not as well represented. But I guess this is also because the discipline is very medically oriented. So, I think the one thing that ESE should think about is trying to involve more basic scientists in the process. But I know it’s complicated and we don’t always speak the same language, although we pretty much work on the same questions.

Who or what has inspired you, and continues to do so?
I was very lucky to meet great people along my career path. My supervisors were really great people, very curious and thorough scientists, with really good ethics. They really inspired me and set very high standards from the beginning of my career. If you don’t have high moral standards in research, it’s very easy to start doing the wrong things to try to get into the big journals. Of course, there’s pressure to publish and, yes, everybody would like to publish in *Science* or *Nature*, but I don’t think this should be a goal. You should always think about the next exciting question you want to address, not the next big paper you may or may not publish.

I also get lots of inspiration and stimulation from daily chats with students, postdocs and colleagues – and from animated, sometimes conflictual, scientific discussions with my girlfriend, who also happens to be a scientist. I really think it is very important to have supportive family and friends, as this job can really take its toll!

In addition, I think it’s essential to have some spare time, away from the lab. It may sound weird somehow, but I think I never have my best ideas when I’m stuck in the lab, working hard on a project or writing a paper. They usually come when I’m wandering around, driving my car or just sitting in the garden, initially thinking about something else. I suddenly start connecting the dots, and the things that seemed incomprehensible in the lab just become crystal clear!

And tell us, what hobbies do you have that are unrelated to science?
The only serious hobby that I have is being a licensed amateur radio operator. I communicate with people throughout the world through radio waves. It may seem unusual, but it is somehow science-related because you get to build your electronic equipment in order to communicate, which I find really stimulating!

What was it like to be a part of ESE Summer School?
I think it was absolutely gorgeous. People were very relaxed, but still very into it. I was very impressed by the young people asking lots of very clever questions! That really was a refreshing experience in a stunning environment. There were very good discussions and really good vibes between people.

What are your top tips for success?
I would say you have to be excited and positive about what you’re doing. Also refrain from thinking about getting the next big paper or the next big grant. Try to stay excited, try to answer questions, try to solve problems, try to see how things work. Eventually, you realise that it will all work out! You’ll get that nice publication, you’ll get that big grant and you’ll get your career. Be very open-minded, and be prepared to fail. Failure is not really failure. It’s just a step in the process.
Artificial intelligence: a short dictionary

Artificial intelligence (AI) can be viewed as research done by algorithms, which is increasingly an option, now most medical data is digitised.

The algorithms take data input from the real world (a series of measurements) and make decisions or estimations as an output. Here is a short dictionary of terms for researchers and clinicians, to get you started in understanding AI techniques:

**Machine learning (ML)** – a family of algorithms that learns by induction – they scan the input data and discover general knowledge.

**Training** – the process whereby an algorithm observes the input data and creates a map between input and output.

**Supervised learning** – a training strategy where the algorithm observes input–output pairs and learns a function that maps from input to output.

**Unsupervised learning** – a training strategy where the algorithm finds patterns in the input dataset without any explicit output values (e.g. clustering).

**Pattern recognition** – a type of ML problem where an algorithm needs to assign a label (class) to a set of input measurements (e.g. early atrial fibrillation detection).

**Regression** – a type of ML problem where an algorithm needs to assign a number to a set of input measurements (e.g. prediction of direction and rate of change of blood glucose levels).

**Deep learning** – a family of ML techniques based on early work that tried to model networks of neurons in the brain with computational circuits, often called neural networks (McCulloch & Pitts 1943), used for visual object recognition, machine translation, speech recognition, etc.

**Data mining** – extracting useful, previously unknown information from large sets of data (e.g. healthcare management, improvement of patient care).

**Computer vision** – the branch of AI that develops algorithms for automatic extraction, analysis and understanding of useful single image or video information (e.g. detection of abnormal structures, such as colonic polyps, in medical scans).

**Natural language processing** – the branch of AI that develops algorithms that can use natural language to communicate with humans and learn from written input (e.g. extraction of information from textual medical records).

AI is a dynamic field, where new algorithms and techniques are constantly being developed. It can be hard to navigate its ever-changing landscape, and a good understanding of the basic concepts can significantly ease the use of new algorithms and ideas.

**Bogdan Dugić**
Serbia

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**Dosing algorithms enable closed-loop insulin delivery**

Closed-loop systems for glycaemic management are set to transform healthcare in type 1 diabetes mellitus (T1DM).

T1DM is a chronic disease caused by the interaction of genetic determinants and environmental factors, resulting in the autoimmune destruction of pancreatic β cells. Intensive insulin therapy, aimed at good glycaemic control, significantly reduces microvascular and macrovascular complications. However, hypoglycaemia remains the major barrier to achieving glycaemic targets. More than 70% of people with T1DM do not achieve targets despite advances in insulin analogues, educational programmes, insulin pumps and glucose sensors.1

‘We are entering a new era for the management of patients with type 1 diabetes mellitus.’

Closed-loop insulin delivery systems are recent technologies that automate insulin pump delivery based on glucose sensor readings and a dosing algorithm. Several groups have developed dosing algorithms for automated insulin delivery systems. Some of them have been compared with sensor–augmented pump therapy in randomised day and night clinical trials.

The Cambridge algorithm was tested in several trials, including participants with suboptimal and good glycaemic control. It consistently showed improvements in glucose control. The University of Virginia’s algorithm was also tested in several clinical trials and showed improvements in glucose control, although the benefits were lower when the algorithm was embedded in a phone as opposed to a pump.1–3 The Medtronic first generation dosing algorithm was tested in several non-randomised trials. Their second generation algorithm was recently tested in a 4-week randomised trial and also showed improvements in glycaemic control.4

A recent randomised trial compared a closed-loop automated insulin delivery system with sensor–augmented pump therapy in outpatient, unsupervised and free-living conditions, with no remote monitoring. The system used the iPancreas platform and a model predictive control algorithm. It was shown that the automated insulin delivery system increased time spent in the target glucose range and reduced time spent in hypoglycaemia. The benefits were observed during both day and night. Moreover, treatment satisfaction was increased with the automated insulin delivery system, in line with patients’ expectations regarding the prospective use of automated closed-loop insulin delivery systems.5

In conclusion, recent data from clinical trials confirm that closed-loop automated insulin delivery improves glycaemic control, even when compared with sensor–augmented pump therapy. It seems that we are entering a new era for the management of patients with T1DM.

**Stavroula A Paschou**
Greece

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**REFERENCES**


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**FURTHER READING**

Towards personalised medicine in adrenal disease

Machine learning and multi-steroid profiling offer new opportunities for the treatment of patients with adrenal conditions.

Machine learning techniques are being increasingly used within biomedical and research domains. Able to identify, learn and extrapolate intrinsic patterns within high-complexity data, these techniques provide a powerful tool to meet the demand for ‘big data’ analysis and for increasingly sophisticated diagnostic and prognostication techniques within a wide range of medical fields.

Types of machine learning algorithms
Various definitions and categories of machine learning algorithms have been proposed. Unsupervised learning (used for clustering or dimension reduction) and supervised learning (used for classification or regression) are common terms. Unsupervised learning algorithms find intrinsic patterns, correlations and relationships within unlabelled data. They should be considered when the aim is to explore the characteristics of an undefined dataset, the information contained in the data is unknown, or the aim is to reduce dataset complexity. Supervised learning algorithms learn by example. They are provided with a defined, labelled dataset and are trained to recognise characteristic patterns or correlations to correctly classify or predict data outcomes. The aim is to create models able to make accurate decisions which are generalisable to a wider, unseen population. They can be extremely useful in biomedical research to predict outcomes such as diagnosis, prognosis and treatment response.

The need for transparent and accountable models
Using models that are accountable in terms of how they make decisions, easy to interpret, robust and fair promotes trust, improves understanding and protects against unjust outcomes. Furthermore, considering interpretability as a driver in designing machine learning methods can aid acceptability and facilitate a wider implementation. Interpretability within a model helps with bias detection, and so ensures impartiality in decision making. It provides robustness to the method and acts as insurance for the method, by being able to ensure model reasoning comes from meaningful variables inferring the output.

Machine learning to understand adrenocortical diseases
An individual’s entire steroid hormone output, including precursor steroids, can be accurately quantified through multi-steroid profiling in urine and blood by mass spectrometry methods. This generates a considerable amount of data, which can be often challenging to interpret using traditional methods. For this reason, machine learning is ideally suited to investigate inherited and acquired adrenocortical diseases.

Improving diagnosis and management of adrenocortical cancer
In 2011, Arlt et al. combined comprehensive urine multi-steroid profiling by mass spectrometry with supervised machine learning analysis (i.e. urine steroid metabolomics; USM) to differentiate malignant from benign adrenal tumours.1 Using 32 urine steroid metabolites, the method was able to discriminate adrenocortical carcinomas (ACC) from adrenocortical adenomas with high accuracy. In a large follow-on prospective validation study, USM combined with adrenal tumour size and computed tomography tissue attenuation was confirmed to accurately detect ACC and reduce the number of false positives observed when relying on imaging alone.2 An extension study proposed that USM could also be used to detect early ACC recurrence after surgical resection.3

Improving outcomes in inborn disorders of steroidogenesis
Wilkes et al. investigated whether machine learning could be used to approximate human expert interpretation of urine multi-steroid profiling for a range of suspected diagnoses, including congenital adrenal hyperplasia (CAH) and 5α-reductase deficiency.4 Baranowski et al. further explored this concept for the differential diagnosis of inborn disorders of steroidogenesis, using a data-driven approach with urine steroid metabolome data collected from individuals with genetic confirmation of disease.5 Another potential application of machine learning in this context is patient stratification for more personalised treatments. In 2020, Kamrath et al. aimed to identify steroid fingerprints to explain variability in response to glucocorticoid treatment in patients with CAH due to 21-hydroxylase deficiency.6 They identified four distinct fingerprints, defined by differing urine steroid metabolome patterns, which represented patients who were adequately treated, over-treated, under-treated, or did not adequately respond to treatment (representing either non-compliance or the need for a different dosing regimen).

Dissecting cortisol excess in adrenocortical tumours
Prete et al. recently applied USM in a large cohort of patients with benign adrenocortical tumours and varying degrees of cortisol excess.7 They found steroid fingerprints that accurately characterise mild autonomous cortisol secretion and Cushing’s syndrome, and that can also be used to predict an increased cardiometabolic risk.

Identification and subtype classification of primary aldosteronism
Eisenhofer et al. recently combined plasma multi-steroid profiling with machine learning in patients tested for primary aldosteronism.8 They found that this approach may facilitate the diagnosis of primary aldosteronism, as well as the identification of unilateral adenomas carrying somatic KCNJ5 mutations, who are most likely to benefit from adrenalectomy.

Conclusions
The examples described here show the potential of applying machine learning to the wealth of information from multi-steroid profiling. This approach provides mechanistic insights into adrenocortical diseases and holds promise for translation to routine clinical practice. Collaborative working is required between clinicians, statisticians, mathematicians and computer scientists to develop strategies for comprehensive analysis leading to accurate, fair and generalisable outputs.

Alessandro Prete and Elizabeth Baranowski
UK

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Steroid ‘fingerprints’ of adrenocortical diseases can be generated by means of multi-steroid profiling and machine learning techniques.
Artificial intelligence and male reproduction

Over the past 20 years, the use of artificial intelligence (AI) in medicine has attracted considerable interest, but is there a ‘knowledge gap’ in its application to male reproduction?

In reproductive endocrinology, many trials have applied AI to predict the fertility of women, and the quality of oocytes and blastocysts, as well as decision-making algorithms for ovarian stimulation.

In male reproduction we see fewer studies, with most focusing on the examination of seminal fluid. Several trials have presented image recognition systems for morphological classification of sperm, determining their motility, or selection of gametes with reduced DNA damage for assisted reproduction technique (ART). Although very effective, these tools are not yet found in daily clinical practice and cannot be used in the general population.

Nevertheless, AI can find other targets in the field of male infertility. One interesting approach concerns radiomics. By use of image analysers, we try to make objective ultrasound parameters operator-dependent, for instance regarding the ecostructure and echogenicity of the testicular parenchyma. In a pilot study conducted by the University of Modena, classification of these two parameters on an objective basis using radiomics correlated with semen quality and circulating levels of androgens and gonadotrophins.1 Although preliminary and not yet usable in clinical practice, these data lead the way for new objective parameters, beyond the calculation of testicular volume, for an increasingly widespread and relatively low-cost examination.

With a similar purpose, a predictive model that uses hormonal, clinical and seminal baseline data was developed to predict the outcome of varicocelectomy in terms of improving seminal parameters.2

Another field of application of AI in andrology has been highlighted by researchers at the University of Münster, who have created a predictive model based on machine learning for the identification of patients with Klinefelter syndrome from subjects with idiopathic azoospermia. This predictive model has a sensitivity of 100% and a specificity >93% for the identification of subjects with the 47,XXY karyotype.3 A benchmarking analysis against 18 andrologists experienced in diagnosing and treating subjects with Klinefelter syndrome showed the superiority of this predictive model. So, while the uses of AI in male fertility almost all address analysis of the characteristics of spermatozoa, especially for ART, the possible uses are many. Use of AI should be aimed at providing tools to improve diagnostic accuracy and predict treatment outcomes.

Settimio D’Andrea
Italy

Can AI discover fractures better than humans?

New techniques and software to properly address skeletal health and fragility are in high demand in clinical practice.

Dual X-ray absorptiometry (DXA) is the gold standard for the diagnosis of osteoporosis. However, this method has many technical limitations and the parameters derived by its use need careful interpretation by clinicians. A multitude of studies are starting to investigate the role of AI models in application to diagnostics in osteoporosis and bone metabolism disorders – some of them are achieving intriguing results.

Radiomics involves the conversion of images to higher dimensional data and the subsequent mining of these data for improved decision support.1 This approach is able to extract many features from traditional medical imaging (computed tomography/magnetic resonance imaging scans) and make these features (e.g. greyscales) available for further processing and analysis. In the setting of osteoporosis, this technique could be crucial in overcoming some of the limitations of DXA and in elucidating the texture and spatial heterogeneity of bone, with potential great improvement in diagnostic accuracy.

One example of its application to osteoporosis is offered by the machine learning model that Rastegar et al. are developing, with promising results.2 They are starting to identify the radiomics/DXA-derived parameters with higher predictive role, for a new and more precise classification of normal bone versus osteopenia/osteoporosis.

Vertebral fractures (VF) are considered the hallmark of osteoporosis, yet the correct approach and methodology to investigate and define fragility VF are still highly debated. Could a computer be as precise as the human eye? Apparently, we are getting closer to this. In a recently published study, Biamonte and colleagues described an AI-based radiomics model using computed tomography-derived images of the lumbar spine, which was able to identify bone textural features independently associated with the presence of VF, and could also correctly identify and characterise skeletal fragility.3

These are only some of early experiences from the application of highly advanced technologies to the field of bone health, and more work will be necessary before these tools can become part of clinical practice but, clearly, we are on the right track.

The future of AI as clinical aid for the management of bone disease seems to be bright … or possibly just greyscale.

Walter Vena
Italy

REFERENCES
Artificial intelligence and the thyroid gland

Artificial intelligence (AI) is an emerging technology which is increasingly being used in thyroid medicine, enabling the transition from population-based to individualised medicine. In the era of personalised medicine, risk stratification before, during and after treatment is important. It is a combination of technologies that mimic human interaction — it corresponds to human perception.

At the same time, thyroid ultrasonography (TUS) is increasing worldwide, resulting in the identification of more thyroid nodules, and a growing number of fine needle aspirations (FNA). There are several problems in the care of patients with thyroid nodules: inconsistent assessment by the ultrasonographer, uncertainty in cytopathologic diagnosis, difficulty in differentiating follicular neoplasms, and inaccurate prognosis. Therefore, the final step in characterising a thyroid nodule is pathohistological analysis, which is sometimes unnecessary.

Application of AI in TUS

TUS is the recommended imaging modality for patients with thyroid nodules, because it is inexpensive, effective and does not require radiation. Several features on TUS indicate an increased risk of malignancy: solid composition, hypoechogenicity, irregular margin, microcalcification, and a shape that is taller than it is wide. However, these features cannot confirm or exclude a diagnosis of thyroid cancer.

AI uses TUS images, cell smears and tissue sections to extract morphological, textural and molecular features. This information is fed into the AI classifier to improve its performance and optimise the workflow of thyroid cancer diagnosis and treatment. AI applications are of increasing interest in reducing the number of invasive clinical procedures.

Application of AI in cytopathological evaluation of FNA

FNA is one of the most important preoperative examinations for the evaluation of thyroid nodules. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is a state-of-the-art decision-making tool for clinicians. In clinical practice, 15–30% of thyroid nodules continue to be classified as indeterminate nodules. Recent studies showed excellent agreement between machine learning models and cytologists in predicting malignancy (malignancy risk of TBSRTC III determined by machine learning was much lower than manual classification: 4.2 versus 18.8%). Morphological and genetic classifications supported by AI models are quite accurate in distinguishing malignant from benign thyroid nodules. AI as a second opinion reduced the number of FNA procedures by 27%.

‘AI applications are of increasing interest in reducing the number of invasive clinical procedures.’

Conclusion

AI systems learn on a case-by-case basis. Because human tissue is characterised by high heterogeneity and variability between and within subjects, no finite training set can fully represent the diversity of cases that may occur in clinical practice.

Extensive research is still needed to improve the generalisability and accuracy of AI-based models (the major limitation being the small amount of data used to develop and validate predictive models). Therefore, the use of AI applications alone for diagnosis in clinical practice should continue to be avoided. However, AI applications can improve the accuracy of thyroid diagnosis, especially for physicians in training. AI applications may be integral to the procedure and should be interpreted according to routine clinical practice.

Karin Zibar Tomšić
Croatia

FURTHER READING
After a long gap of 3 years, the 9th EYES Meeting took place in person in Zagreb, Croatia, on 2–4 September 2022.

Set in the historic centre of this picturesque capital city, the meeting welcomed over 150 participants from 22 countries. The EYES Annual Meeting 2022 aimed to encourage young doctors and scientists to introduce their research, and 81 abstracts were presented on topics spanning the ESE Focus Areas.

**Interacting with the experts**
As well as learning from their peers, attendees could meet diverse experts in endocrinology. We were delighted to host Ljiljana Marina (Serbia) who talked on premature ovarian insufficiency, and Daniele Santi (Italy) who spoke about male infertility.

Local experts included Tina Dušek, who discussed the endocrine treatment of transgender individuals, Mirsala Solak, who lectured on thyroid disease in pregnancy, and Ivana Kraljević, who led a workshop on insulin pumps. Tamara Sladoljev-Agejev, a Senior Lecturer in English, gave helpful tips on academic writing.

**Networking together**
The meeting was enhanced by numerous social events, including a sightseeing tour of Zagreb which left us in awe of this charming and lively city and its turbulent history. We enjoyed a live concert by the band Dijagnoze (Diagnoses), a group of medical doctors from the city of Rijeka who are also musicians. This was followed by an excellent party which lasted until the first rays of dawn!

Delegates also had a chance to test their general knowledge in a pub quiz. We congratulate the ‘Mediterranean’ team who kept maintained their concentration despite the delicious Croatian food, and won first place! On the final afternoon, we visited the medieval castle of Medvegrad, in a nature park rising above Zagreb.

**Our award winners**
We congratulate our winners, who presented the two most outstanding abstracts. James Wilmouth Jr (France, pictured) won first place for ‘Ablation of Znrf3 and Trp53 induces metastatic adrenocortical carcinoma in mice’, receiving free registration for ECE 2023. Alessandro Prete (UK) came second with ‘Combining steroid and global metabolome profiling by mass spectrometry with machine learning to investigate metabolic risk in benign adrenal tumours with mild autonomous cortisol secretion’.

He received a place at the Croatian Society for Endocrinology and Diabetology’s 2023 Annual Meeting.

Our grateful thanks
We thank the Croatian Society for Endocrinology and Diabetology, ESE and the EYES community, the Bioscientifica Trust, the Open Medical Institute, the European Network for the Study of Adrenal Tumors and Harmonisation for their support, as well as all the sponsors. We are grateful to the Local Organising Committee for putting in the extra effort. Last, but not least, we thank all the lecturers, moderators and participants for ‘staying hungry’ and pursuing continuous improvement.

We look forward to seeing you at EYES 2023 next September. Watch out for further information!

Karin Zibar Tomšić
Croatia
Working in harmony on adrenal tumours

Harmonisation seeks to provide a multidisciplinary network, harmonising clinical care and research on adrenal tumours throughout Europe. This framework will additionally help develop a new generation of real-time and real-life randomised clinical trials, which will be federated and registry-based.

Harmonisation is a COST (Co-operation in Science and Technology) Action (CA 20122). As such, it is an interdisciplinary research network funded by the EU, which brings researchers and innovators together to investigate a topic of their choice for 4 years. It is focused on COST Inclusiveness Target Countries. The COST Action funds the organisation of meetings, training schools, short scientific exchanges and other networking activities.

Harmonisation is arranged in five Working Groups:

• Harmonising clinical practice for adrenal tumours
• Harmonising adrenal tumour research and -omics practice
• Harmonising information technology (IT)/artificial intelligence (AI) tools towards a standardised registry
• Harmonising the ethical and legal framework required for federated European trials
• Communication, dissemination, and inclusiveness.

Currently, there are 174 members, from 31 countries, with an excellent gender balance (56% female participants) and target country inclusion (37%), and a great proportion of early career investigators (56%) spread among the five working groups. Active and interested eligible experts with a clinical, basic, IT or ethics background would be welcomed as members.

COST Harmonisation Adrenal Tumour Masterclass

Harmonisation held a very successful Masterclass online between 23 and 25 March 2022. Clinical, translational and basic topics were represented equally in the programme. An impressive number of attendees registered (>400), with 270 active participants. They enjoyed some very insightful talks and great discussions, including the following topics:

• Diagnosing and treating adrenocortical carcinomas (Martin Fassnacht)
• Co-morbidities in patients with adrenal incidentalomas (Ljiljana Marina)
• Diagnosis of subtypes of primary aldosteronism (Felix Beuschlein)
• Management of phaeochromocytomas (Henri Timmers)
• Dealing with variants of unknown significance (Mercedes Robledo)
• Cases of phaeochromocytoma and paraganglioma cases with variants of unknown significance (Joakim Crona)
• Organoids in adrenal tumour research (Michaela Luconi)
• Omics platforms (Fátima Al-Shahrour).

The audience gave stellar reviews for the event, with >60% rating it as excellent and 70% of attendees saying they were very likely to attend the next masterclass.

What does the future hold?

We are excited by the prospect of future developments, such as the first results from our working group surveys.

‘We are excited by the prospect of future developments, such as the first results from our working group surveys.’

We’re on our way to Istanbul

Hey, hey! Another European Congress of Endocrinology is coming your way!

Take note: ECE 2023 will be held in Istanbul, Turkey, on 13–16 May 2023. As usual, among the list of brilliant sessions that attendees can enjoy, you will also find our beloved EYES Symposium.

On behalf of the EYES Committee, it is my great honour to invite you all to the 2023 EYES Symposium, entitled ‘Feeding the endocrine-related cancers: weight matters’. There is increasing evidence linking obesity and tumour development and progression, especially in endocrine-related cancers. I can assure you that anyone joining our session will therefore enjoy outstanding basic and clinical research talks on a really hot topic, given by bright young scientists from around the world.

Please follow us on Twitter and Facebook for updates (see page 2 for details of EYES on social media). I can’t wait to see you all there!

Juan Manuel Jiménez Vacas
UK

Find out more at www.goharmonisation.com and www.cost.eu/actions/CA20122. Please work with us by joining our working groups.

Darko Kaštelan, Croatia
Ljiljana Marina, Serbia
Antoan Stefan Šojat, Serbia

ECE 2023
25th European Congress of Endocrinology

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Some of the participants at the Masterclass
ESE membership has so much to offer!

Don’t forget all the benefits that ESE provides to you, our early career members. And, importantly, remember to tell your colleagues and friends too, so they don’t miss out.

Making your voice heard
The EYES community within ESE has been growing quickly in recent years and is an attractive ‘home’ for young researchers. Representation by ESE gives you a voice in the world of endocrinology. The members of the EYES Committee represent early career colleagues on the other ESE Committees, allowing their views to inform the breadth of ESE activities. The Society also enables early career investigators to connect in multiple ways with an incredibly wide and heterogeneous network of colleagues (medical doctors, biologists, nurses) spread across Europe and around the globe.

Learning opportunities
ESE provides you with a range of learning opportunities (see www.ese-hormones.org/education and www.ese-hormones.org/events-deadlines), allowing young researchers and clinicians to easily engage with experts in endocrinology, through a diverse selection of in-person meetings and online events. These include our very own EYES Annual Meeting, the ESE Summer School and the ESE Postgraduate Training Courses in Clinical Endocrinology, Diabetes and Metabolism, as well as ESE Clinical Updates, ESE Talks and Spotlight on Science, amongst others.

Training resources
Early career members have access to an enormous number of resources, including clinical practice guidelines and other articles in the ESE journals, European Journal of Endocrinology and Endocrine Connections, as well as content from previous meetings and events, via ESE On Demand. The ESE Online Curriculum provides educational materials relating to the ESE Curriculum of Specialisation (www.ese-hormones.org/education/ese-curriculum-of-specialisation/ese-online-curriculum). These materials enable you to expand your knowledge without being limited by your physical location.

Financial support
ESE Membership gives you access to sources of financial support. Many grants and awards are available to early career members (see www.ese-hormones.org/grants-and-awards), including the Clinical and Research Observership Programmes, which allow applicants to visit highly specialised centres for career advancement. Members are also eligible for reduced price registration for ECE and other events.

The latest news and views
You will also regularly get to hear about the latest developments in the field, through features, interviews and insights in Endocrine Views (ESE’s forum for opinion and debate) and EYES News, as well as monthly email news alerts.

All in all, the sea of opportunity is here, within your reach; make sure you dive in!

Antoan Stefan Šojat, EYES Co-Chair
Walter Vena, EYES Committee member

EnGiO meet in Rome

After a difficult few years due to the pandemic, the highly anticipated 2nd National Conference of Endocrinologia Giovane Italiana (EnGiO; the Italian Young Endocrinologists) took place in Rome on 23–24 September 2022. EnGiO is the early career branch of Italian Society of Endocrinology.

Over 100 people attended the conference, with 2 days of energetic collaboration between young endocrinologists and biologists interested in clinical and translational research. We enjoyed interactive sessions on the diagnosis of andrological and gynaecological diseases, open debate on the latest guidance regarding newly patented treatments for diabetic disease, meet the expert sessions, and an incredible oral session, enriched with the most up-to-date Italian research, presented by those who will be the endocrinologists of the future. All of this was squeezed into a programme which encompassed all the advances in endocrinology in a bench–to–bedside fashion.

The scientific committee included young delegates from the most important early career societies in Italy, encouraging the sharing of knowledge between different the areas that endocrinology encompasses. Lots of ongoing projects and an enthusiastic environment fed the insatiable appetites of these participant in endocrinology’s future.

Moreover, at the end of the session, many young participants enjoyed a social event which allowed networking to create informal bonds and share direct research and clinical experience, in the beautiful surroundings of Italy’s capital city.

Riccardo Pofi
on behalf of the EnGiO Committee

You and your colleagues can find out more about membership and join ESE at www.ese-hormones.org/membership
EYES: working for you

EYES Committee members bring you up to date as your representatives on the ESE Committees. They tell you about their roles, and what ESE is doing for the EYES community.

WALTER VENA, ITALY
Education Committee

Being part of the ESE Education Committee is a challenging ‘mission’ for a youngster like me, and I don’t need to hide that it feels like a big responsibility. Also, at the same time, I can say I’m really proud to be part of it and of ESE as an organisation, because I feel that including young members on all ESE Committees is crucial and brings fresh energy around the Society’s major fields of action. Indeed, amongst the Education Committee’s goals is to ensure that ESE remains interesting, attractive and welcoming to early career members.

One big challenge for me is to maintain continuous communication with young ESE members and gather feedback, in order to truly be the voice of the early career members, ensuring proactive participation and a broader interest.

Beyond the activities aimed at young members, the Education Committee works on a lot of interesting tasks, some internal to ESE and others in collaboration with other international organisations.

The Committee’s remit includes delivery of ESE’s postgraduate education programme, with both physical and online educational events and resources. It also manages the ESE Clinical Update series, maintaining its high quality and relevance to clinical practice across the breadth of endocrinological diseases.

There is also a fundamental role to collaborate with UEMS (the European Union of Medical Specialists) to develop and maintain the European Board Examination in Endocrinology, Diabetes and Metabolism. This requires close co-ordination with Europe’s most important organisation in endocrinological education.

I’m sure this will be another crucial experience along my career path. I hope my contribution will be relevant, especially, but not exclusively, to young members. Much work and effort will be needed, and I can’t wait to give my best to make things work and collaborate with all the other Committee members.

JUAN MANUEL JIMÉNEZ VACAS, UK
ECE 2023 Programme Organising Committee

ECE 2023 will take place in Istanbul, Turkey, on 13–16 May 2023. Being the EYES representative on the Programme Organising Committee (POC) for the Congress is an absolute honour.

The POC’s main task is to develop and organise the scientific programme, taking into consideration the suggestions of the ESE members. In this way, it is responsible for the event’s high scientific quality, and follows a strategic approach to ensure that the content is relevant and topical, and that the speakers are worldwide experts in their different fields. In addition, the POC ensures a balance of basic and translational science as well as clinical interest, so that all the ESE community is engaged by our beloved Congress.

I have already attended several meetings where suggestions for speakers and sessions from the POC members have been discussed, along with suggestions received from our endocrine community.

Importantly, the POC also evaluates the submitted abstracts − within the specified timeframe, using the specified criteria − to take key decisions such as their inclusion in the programme as a presentation or poster and the winners of the Young Investigator Awards and Poster Awards.

My specific role as EYES representative is to try my best to ensure that a significant number of young basic and clinical researchers are selected as speakers, so that young investigators are represented in the final Congress programme. In addition, I am in charge of the organisation of the EYES Symposium, as well as collaborating with the Local Organising Committee to organise the EYES social event for ECE 2023. I take this opportunity to invite you all to both events!

From a personal point of view, I am glad to have been able to contribute to the EYES community by being part of the POC for ECE 2023. This role has taught me how to organise the scientific programme of a top-class international congress, by getting advice from worldwide experts.

I must share with you and emphasise the huge commitment of all the POC members to programme development. It is a pleasure to have been able to work alongside this outstanding group of people. And there is still so much work ahead of us!

‘One big challenge for me is to maintain continuous communication with young ESE members and gather feedback, in order to truly be the voice of the early career members, ensuring proactive participation and a broader interest.’

‘I am in charge of the organisation of the EYES Symposium, as well as collaborating with the Local Organising Committee to organise the EYES social event for ECE 2023. I take this opportunity to invite you all to both events!’
ESE: helping you financially

As an ESE Member, you can apply for a range of grants and are eligible for other support to help you financially. Check www.ese-hormones.org/grants-and-awards/grants to see if you could benefit.

ESE-SEEDER-EU Programme – this provides consultancy support to help you choose and apply for grants from EU funding schemes. It is available to individuals and consortia. You can apply at any time.

Meeting Grants – these grants of €400 support attendance of ESE events, including Postgraduate Training Courses, ECE, the ESE Summer School and the EYES Annual Meeting.

Basic Science Meeting Grants – also worth €400 each, these grants specifically support attendance of ECE by ESE Members who work in basic research.

Short Term Fellowship Grants – intended to promote scientific collaboration between ESE members, these grants provide up to €2500 towards short research visits for early career members. Apply by 31 May and 30 November each year.

EYES Observership Programmes (Clinical and Research) – these allow early career investigators to undertake a 1-month stay in a European endocrine centre of special interest. Applications open in November 2022 for awards in 2023 (see below).

Clinical Update returns for 2023

The next ESE Clinical Update is on Obesity and Female Reproduction and takes place online on 10–12 January 2023. Topics to be covered span new developments in non-pharmacological approaches, pharmacotherapy and endocrine aspects of bariatric surgery.


Save the dates

Early notice of two important dates for 2023...

18–21 June 2023
ESE Summer School 2023
(Innsbruck, Austria)

19–22 November 2023
EuroPit 2023 (Annecy, France)

EYES Observership Programmes

It will soon be time to apply for the next round of EYES Observership Programmes.

The programmes are currently supporting 6 early career investigators who are already learning new clinical and lab skills from the best mentors, with 22 more in line to embark on this journey, across 18 European countries.

We have worked hard this summer, so that we can provide even more centres (in addition to those on the map, right) and facilitate more collaborations, thus enabling even more people to get a chance to do what they are passionate about. We will announce more details about how you can apply shortly, so stay tuned.

Find out more at www.ese-hormones.org/eyes-cop-and-rop.

Antoan Stefan Šojat
EYES Co-Chair
COP/ROP Co-ordinator

Germany welcomes EYES 2023

We are excited to announce that the EYES Annual Meeting 2023 will be held in Würzburg, Germany, on 8-10 September 2023. We look forward to seeing you there!

Your chance to host EYES 2024

A call for bids to host the 2024 EYES Annual Meeting will open on 11 November 2022 and close on 7 April 2023. Watch out for further information at www.ese-hormones.org/eyes-meeting-bids-2024.
ANIDEN: early career colleagues in France

ANIDEN (the Association Nationale des Internes de Diabetologie, Endocrinologie and Nutrition) is an organisation for French residents (junior doctors) in endocrinology, diabetology and nutrition (EDN). It was created in 2013 to promote solidarity and communication between members, improving their working conditions and their training, representing them nationwide, fostering continuous education and scientific research, and promoting the field among other healthcare professionals and students.

The organisation provides a hub to help residents navigate through the changing educational landscape. Indeed, in recent years, residency training has undergone significant changes in France: residents gain autonomy earlier in their training and nutrition has become an integral part of the residency. ANIDEN has developed alongside these changes, and has acted as a mediator between residents and higher authorities.

Increasing visibility and information

ANIDEN has enhanced the visibility of the EDN field among medical students. It helps future residents make key decisions about their residency. In France, medical students choose their specialisation after 6 years of combined theoretical teaching and hospital training, in the form of internships. Unfortunately, the number of internships is limited, and not all students have the opportunity to discover EDN before choosing their specialty. This year, with the help of passionate residents from across France, we launched a social media campaign to promote our discipline and detail the opportunities and type of jobs on offer. This approach got excellent feedback from students and teachers.

Nearly 100 medical students per year specialise in EDN. After choosing their field, they must then select the region in which they will work for the next 4 years. Each has its own organisation and training opportunities. ANIDEN provides detailed information about each region and connects medical students with residents.

Enhancing training opportunities

Another aim of ANIDEN is to improve training and create new learning opportunities. It achieves this in three ways:

• We are fortunate to have many pre-existing training courses. ANIDEN does its best to make them accessible to all residents, enabling them to easily take the ones they need in order to thrive. We frequently communicate about upcoming events and courses on ANIDEN’s website (www.aniden.fr) and social media.

• Moreover, we negotiate reduced prices for courses, congresses and subscriptions to scientific newspapers. In 2022, we organised a webinar with rheumatologists about common issues (namely surgical complications of bariatric surgery). We plan to repeat the experience with other specialists.

• Another current project is the creation of an application about diabetology. It will contain a summary of algorithms, treatment recommendations and emergency management solutions to help residents and doctors in their day-to-day practice. It should be available shortly, and we’re really looking forward to sharing it with our colleagues. We hope to extend this facility to endocrinology and nutrition very soon.

Encouraging communication

Finally, ANIDEN helps foster communication and collaboration among residents. In France, residents write their medical thesis during the first 3 years of residency. In recent years, they have had the opportunity to present their work at the congress of the French Society of Diabetology. This is a rewarding moment for them, as they get the chance to share their ideas and meet future colleagues.

ANIDEN is a young association that cannot wait to evolve and improve. We are tirelessly working on our current projects and are optimistic about future collaborations with other similar European organisations. Please get in touch!

Amina Attia, France

With thanks to Jérôme Bertherat for facilitating communication between EYES and ANIDEN.

‘ANIDEN is a young association that cannot wait to evolve and improve.’
Celebrating Summer School

Innsbruck, Austria, 17–20 July 2022

Summarising the 2022 ESE Summer School in a few words is not an easy task, as many activities took place during those very rewarding days!

Our marvellous location was TBI-Grillhof, the Tyrolean Education Institute, which has unique panoramic views of the Nordkette and Serles, some of the most imposing mountains of the Alps. This contributed to a relaxed yet concentrated learning environment. It was the perfect place to deepen our knowledge and skills as well as to have fun – the best combination to support learning!

We enjoyed brilliant, interactive talks on fascinating topics, covering all the ESE Focus Areas, from clinical and basic research perspectives. We were privileged to learn from outstanding experts in their respective fields, who extensively reviewed the most important findings related to their topic, and showed impressive novel data, leaving our mouths open in awe. During the ‘group work breakout sessions’, attendees discussed their ideas on a given topic face-to-face with international experts.

But, hey, not everything was about work! The EYES Committee had organised many recreational and sporting activities for the attendees. These extended from going for a dip in the Lanser See Lake to a range of football and table tennis activities. I will never forget how shocking it seemed, to be able to look at the snow in the mountains while having a calm swim... And what’s not to like about a karaoke session?! I found singing together was a very good way to get to know each other a bit better.

Last, but not least, I would like to thank the Scientific Organising Committee on behalf of the EYES Committee and the ESE Summer School 2022 attendees: Professor Josef Köhrle and Professor Martin Fassnacht did such a fantastic job. We can’t wait for the next Summer School; more details will follow soon!

Juan Manuel Jiménez Vacas
UK

My highlights from Summer School 2022

I really appreciated Professor Ljiljana Marina’s discussion of progesterone and its link with the breast: from the physiology of the menstrual cycle to insights into natural and synthetic progesterone. To sum up: not all progestins are the same, pay attention!

Professor Franz Jakob’s explanation of the deep connection between muscles and bone health also caught my attention, including the major role of high impact exercise in the prevention of fractures, and how mechanical stimuli can result in hormone release.

Dr Ulrich Dischinger explained the role of gut hormones in non-alcoholic fatty liver disease, and how some well known drugs for diabetes, such as glucagon-like peptide-1 (GLP1) receptor agonists, may reduce inflammation and ameliorate liver function. The new gastric inhibitory peptide−GLP1 dual agonist may boost the hormonal network of these patients.

I also learnt about things I have never heard of before, like ‘tanyocytes’ (I know you will Google it) or the skill of salamanders to regenerate their body parts endlessly.

One of the best aspects was the chance to get to know other young researchers from across Europe and beyond. It was a really great experience, even if it made me realise that I am not as good at tennis table as I thought...

Lorenzo Marinelli
Italy

Due to the wide variety of topics presented in the poster sessions, I could experience scientific progress in a multi-dimensional way, which helped me to develop a new idea for improving my experimental screening set-up.

Critical considerations regarding endocrine disruptors which may be present in laboratory equipment supported my ‘outside the box’ thinking. Talks were structurally organised to show how ideas evolved from the first experiments into final conclusions demonstrating how to coherently manage a scientific project.

I was eager to find the answer to one question that I had specifically asked myself before joining the Summer School, namely ‘how does the endocrine system function on a systemic level?’ Through participating in the School, I discovered how many functions of thyroid hormones are mediated through co-ordinated and synergistic interactions with the sympathoadrenal system. In pathological states, where either the sympathoadrenal or the thyroid system is fixed at a high or a low level, co-ordination is lost, with disruption of the physiology and development of symptoms. Emerging evidence suggests that disrupted interactions between the sympathoadrenal system and thyroid hormones contribute to explain metabolic variability. Finally, we saw recent studies, suggesting that the gut is an important reservoir for thyroid hormones and that it may also influence regulation of hormone activity.

Sanas Mir-Bashiri
Germany