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ESE News

The newsletter of the European Society of Endocrinology

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The future is now!

Applying new discoveries in endocrinology

Also in this issue

Highlights from ECE 2018

The best endocrine reads of 2017

European Society of Endocrinology

In this issue

This document is available on the ESE website, **www.ese-hormones.org**

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European Society of Endocrinology

Editorial

This issue of *ESE News* celebrates our remarkable Congress in Barcelona. Also, like ECE 2018, it specifically looks to the future of our discipline and our exciting progress in managing endocrine disease, across basic, translational and clinical science.

Of course, 'the future' always remains just beyond our reach. While we continue to stride towards this distant horizon, it is important to note that many of the developments that seemed inconceivably remote just a few years ago are now within touching distance.

So it is with the translation of the considerable research on gene polymorphisms from basic science into clinical reality. On page 8, André Uitterlinden and his colleagues look at the application of DNA arrays in practice and the huge benefits they will bring with them in enhancing our understanding of individual patients.

Tumour organoids offer the promise of a similarly individualised understanding of patient needs. Talya Dayton from Hans Clever's laboratory has been working on this potential new tool for basic and translational research on neuroendocrine neoplasms. On page 10, you will discover that organoids have already been generated from tumours of many different tissues, with the aim of creating preclinical models.

It is almost 100 years since Banting and Best's pioneering work on the use of insulin to treat diabetes. Now, 'the artificial pancreas' is set to revolutionise the management of this disease in ways we could only have dreamt of until recently. Roman Hovorka and Gianluca Musolino explain on page 11 how real-time monitoring, an insulin pump and a carefully crafted computer algorithm are combined to reduce the burden of treatment.

Sometimes the most fundamental things make the greatest difference. The rise in the prevalence of chronic disease presents a huge challenge to the future of healthcare. On page 9, we welcome an article from the ESE Nurses' Working Group, examining patients' crucial role in leading the management of their own diseases.

The future of our food is as important to a healthy existence as anything else. On page 14, Wouter de Herder casts his eyes over a huge fish – only to discover that it isn't acromegalic, or even giant. It is, however, an example of a practical application of endocrinology. But the question remains whether it will tempt people's taste buds.

Inevitably, of course, the shape of endocrinology's future will be determined by our young colleagues, though their education is the responsibility of us all. On pages 6 and 7, you can learn how ESE is working hard to enhance educational opportunities in clinical endocrinology.

Finally, for those of you, like me, still recalling the excellence of ECE 2018, look no further than page 3 for the highlights and page 15 for some photos – or relive the experience via ECE On Demand (see page 6)!

AJ van der Lely
ESE President
Co-Editor of *ESE News*

Sizzling science in the sunshine:

Highlights of ECE 2018

Barcelona, Spain, 19–22 May 2018

ECE 2018 was another success for the international endocrinology community. With over 3500 attendees, more than 70 sessions and 1750 submitted abstracts, the Congress offered access to the best basic and clinical endocrinology, with opportunities to meet colleagues and plan future collaborations.

During the Congress, the Barcelona International Convention Centre bustled with excitement, skies were blue and the mood was always light and convivial. Delegates were readily immersed in the atmosphere of scientific enquiry, yet able to make the most of any opportunities to relax and network.

The Opening Ceremony saw ECE 2018 off to a great start, with delegates enjoying a warm welcome from AJ van der Lely (President), Márta Korbonits (Programme Organising Committee Chair) and Manel Puig Domingo (Local Organising Committee Chair), along with a piano recital and a little opera.

Two award lectures then set the high standard of the sessions to come. As Manel Puig Domingo commented, 'Christos Mantzoros (USA)'s Geoffrey Harris Award Lecture, on the neuroendocrine mechanisms involved in energy homeostasis and metabolism, was comprehensive, comprehensible and precise. The following talk, by *European Journal of Endocrinology* Award Lecturer Filip Knop (Denmark), discussed the secretion of glucagon in the gut. It was very enlightening and clarified previous research that was not easy to interpret.'

On Sunday, Stavroula Kousteni (USA)'s plenary lecture 'Bone regulates the brain' was a clear favourite, with a busy auditorium. Márta Korbonits applauded the talk, saying, 'The lecture was a prime example of basic, translational and clinical science. It covered the action of lipocalin 2 (a newly discovered protein secreted by bone) in the hypothalamus, where it suppresses appetite. This is a truly novel concept.'

That same day, Maria Chiara Zatelli (Italy) and Mónica Marazuela (Spain) discussed whether receptor profiling is useful for predicting the outcome of pharmacological therapy in pituitary disease, during one of the six debates at ECE 2018. The session started with the audience mostly in favour of molecular profiling. However, towards the end, the majority agreed that the data are not ready to be transferred to clinic. Delegate Zhanna Belaya (Russia) found the debate very exciting: 'Both presenters really put their hearts into it. It was a real, interactive discussion that went beyond just presenting opposing views.'

Rafael Simó (Spain) presented his findings on diabetic retinopathy to a captivated audience on day 3. His research indicates that certain retinal pathways may be inactive in diabetic patients and contribute to the development of cognitive impairment. Manel Puig Domingo reflected on the talk's importance, 'This work shows not only that the retina could offer useful biomarkers to identify diabetic patients at risk of developing Alzheimer's disease, but also that reactivating retinal pathways may contribute to preventing cognitive decline in diabetes.'

The plenary lecture 'The link between insulin resistance and fatty liver', delivered by world expert Gerard Shulman (USA), highlighted the biochemical pathways that can lead to fatty liver disease, and why insulin resistance in the liver should be addressed urgently. As session chair Jens Otto Jørgensen (Denmark) commented, 'We used to focus our insulin resistance research on skeletal muscle, but there is no doubt that hepatic insulin resistance is even more important. It is associated with fatty liver disease, which can lead to various fatal illnesses.' Manel Puig Domingo added, 'This issue is reaching pandemic proportions. It was a forgotten problem that needed to be addressed, as it affects about 40% of the population. It also complicates the metabolic scenario for diabetes and obesity patients, and makes treatments ineffective.'

The Congress received the attention not only of those working in the field, but also of the international media. The press releases that were sent to journalists (see **www.ese-hormones.org/publications/press-releases**) led to the media's active interest in the event, generating over 400 news articles worldwide, including several in major publications such as *The Guardian* and *Forbes*.

We thank all participants, including of course the delegates, without whom the event would have lacked its amazing energy and atmosphere. You will find photographs of the many award recipients on page 15.

ECE 2019 will take place on 18–21 May in Lyon, France.

ESE endorses recommendations for FP9

Alliance for Biomedical Research in Europe

As a member of the Alliance for Biomedical Research in Europe (BioMed Alliance), ESE recently endorsed that organisation's detailed recommendations for FP9 (the EU's ninth Framework Programme for Research and Innovation).

The Framework Programmes are important in establishing a coherent, internationally competitive European research landscape. EU funding has huge potential to add value in health research. However, research in this field is often too complex to be effectively managed at the national level. The BioMed Alliance is therefore calling for more robust EU support for health research, through increased funding under FP9 and development of a long term strategy involving the creation of a European Council for Health Research.

You can read the recommendations at **www.biomedeurope.org/eu-policy-actions.html.**

New Executive Committee members

ECE 2018 saw Mónica Marazuela (Spain, pictured above top) become the new Secretary of ESE, while Riccarda Granata (Italy, pictured above) took on the role of Chair of the Congress Committee. We congratulate both of them on their new roles and thank retiring Secretary Manuela Simoni (Italy) and Chair of the Congress Committee Susan Webb (Spain) for their hard work and dedication on behalf of ESE.

European Survey on Sexual Health Training

Members of the European Young Endocrine Scientists (EYES) recently took part alongside young psychiatrists, gynaecologists and urologists in a European survey, to assess the coverage of sexual health within postgraduate training programmes. In total, 366 completed surveys were gathered from 40 countries. While almost 80% of respondees considered sexual health training to be important or very important, almost two-thirds had not received such training. Trainees felt more confident in managing patients with sexual health problems when the topic was included in their postgraduate training.

Find out more in Kristufkova *et al.* 2018 *Sexual Medicine* doi: 10.1016/j.esxm.2018.04.001.

40% discount for members

Open access ESE journal *Endocrine Connections* publishes original quality research and reviews in all areas of endocrinology, with a focus on papers relevant to related disciplines and biomedicine in general. Its coverage includes basic, translational and clinical studies. Remember that ESE members are entitled to a 40% discount on the article publication charge. Find out more at **www.ese-hormones.org/publications/journals.**

Further insight into Egil's mystery

You may recall that our 'Did you know?' column in *ESE News* issue 35 featured the bone disease of Viking poet Egil Skallagrímsson (c 910–990). We thank István Takács (Budapest, Hungary), who recently contacted us to say that the disorder suffered by Egil was unlikely to be Paget's disease as we suggested, but more probably sclerostosis (van Buchem's disease).

From the ESE Office

It seems incredible that ECE 2018 in Barcelona is over. Organising a congress of its size and complexity began 5 years ago, when the location was chosen – and 2 years ago the ESE Office, Congress Team and Programme and Local Organising Committees really got to work to bring this event to reality.

We depend on our wonderful and inspiring faculty, our supportive sponsors and, of course, the people who attend and learn from the Congress to make it such a success.

Every Congress has its own flavour; in Barcelona, the words 'sunshine and passion' sprang to mind. Sunshine because, well, the sun shone (much appreciated by those of us from the UK), and passion because the atmosphere was full of excitement.

Whether people were first-time presenters or seasoned professors, whether delegates had never been to ECE before or had been every year since it began, there was a feeling that things were just getting better and better. Was this the effect of my rose-tinted spectacles or do you agree? I'd love to know your thoughts.

You can catch up on anything you missed at **www.eceondemand.org**, where a very high proportion of the speakers have agreed to publish their webcasts (see page 6). You will also discover many new interviews, plus abstracts, e-posters and more.

Finally, do renew your membership and continue to be part of our expanding community, which has seen a greater than 10% rise in members in the past year – the biggest increase ever. The more we grow, the better we can build our services and represent you.

Helen Gregson
Chief Executive Officer, ESE
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Africa welcomes ICE 2018

Cape Town, South Africa, 1–4 December 2018

www.ice2018.org

The International Society of Endocrinology (ISE) and the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) will host the first global gathering of endocrinologists on the African continent, when the 18th International Congress of Endocrinology (ICE) is held jointly with the 53rd Annual SEMDSA Congress in December!

The Programme Organising Committee, led by Shlomo Melmed (Los Angeles, CA, USA), has organised a programme focusing on global health priorities, including diabetes, obesity, reproduction and ageing. Academically excellent, it will also appeal to the entire endocrinology community of clinicians, scientists, nurses and allied health professionals, and provide valuable opportunities to meet face-to-face with colleagues from around the world.

Visit **www.ice2018.org** to find out more. ESE members who are also members of ISE National Societies are eligible for the ISE member registration rate (a $150 discount), and up to 100 Travel Grants are available to support participation by early career researchers from outside South Africa.

Key dates for ICE 2018

Early bird registration deadline:
31 July 2018

Submission of late-breaking abstracts:
1 September – 1 October 2018

22nd Postgraduate Course on Clinical Endocrinology

Visegrád, Hungary, 22–25 February 2018

The beautiful medieval city of Visegrád, Hungary, was the setting for the 22nd ESE Postgraduate Training Course on Clinical Endocrinology, Diabetes and Metabolism.

The programme covered a wide range of topics, including diabetes, the pituitary, endocrine tumours, adrenal and thyroid disease, reproductive endocrinology, and calcium and bone disorders. Other highlights included a symposium dedicated to hormone resistance syndromes, as well as a discussion of some of ESE's new guidelines.

The 152 participants had travelled from 23 countries across Europe and as far away as Australia and Brazil. They enjoyed the beautiful surroundings of Visegrád's medieval fortress and the River Danube, with a backdrop of snow-covered hills, as well as a musical component to the social programme.

The 23rd Postgraduate Course takes place in Minsk, Belarus, on 8–10 November 2018. Save the date now!

Márta Korbonits and **Miklós Tóth**

10th ESE Clinical Update

Abu Dhabi, UAE, 12–13 January 2018

The 10th ESE Clinical Update focused on endocrine problems, in particular medullary thyroid cancer, testosterone-related disorders, thyroid storm in Graves' disease and the management of female infertility, with a keynote presentation on adrenal failure and replacement strategies.

It was organised in conjunction with the Imperial College London Diabetes Centre (ICLDC; **www.icldc.ae**), the region's largest 'one-stop shop' for treatment, prevention, awareness, research and education regarding diabetes and related conditions. World experts delivered in-depth presentations on the latest trends in endocrinology and best practice, as well as workshops based on clinical case studies and Q&A sessions.

The workshops were a stimulating environment for learning and focused on low risk thyroid cancer, testosterone and glucocorticoid therapy and adrenal suppression.

The Clinical Update is accredited by the Abu Dhabi Department of Health and is part of the ICLDC's renowned Education Series, promoting the sharing of medical experience and practice, to develop a cadre of highly qualified experts across the region.

Next year's event is on 11–12 January 2019.

Mapping the future of postgraduate clinical training

From the ESE Education Committee

Much is happening within ESE's Education Committee, and one of our major activities concerns the written curriculum for endocrinology, diabetes and metabolism. The need for this was identified by our National Affiliated Societies, and it aims to define, harmonise and raise the standard of what young endocrinologists across Europe need to know in order to best help our patients.

ESE's Postgraduate Training Courses on Clinical Endocrinology, Diabetes and Metabolism are the flagship of our educational training programme, and we are actively working to implement the curriculum within them. We aim to cover the whole curriculum in a balanced way over three courses; we felt it would not be possible to implement it across a smaller number. Every course will also have an ESE guideline talk and cover one or more rare endocrine diseases.

Additional online resources are being developed, as it is obviously not possible to cover the whole curriculum in detail over three courses. These will include an online interactive curriculum as well as online interactive cases and questions.

To make the ESE Postgraduate Course training accessible to those young endocrinologists who are unable to travel to the specific event(s) they would prefer, we have also started work on plans to make the courses available online. Further details will follow.

On page 7, you can read about the new European Board Examination: naturally, our postgraduate training will play an important role in preparing young European endocrinologists for this exciting new qualification.

Camilla Schalin-Jäntti
Chair, Education Committee

ESE Postgraduate Training Courses on Clinical Endocrinology, Diabetes and Metabolism

Aimed at endocrine specialists, including those in training, these courses focus on the most relevant aspects of clinical endocrinology, but also cover related basic research and molecular endocrinology.

If you are interested in the next course on **8–10 November 2018 in Minsk, Belarus**, contact **info@euro-endo.org**.

The courses are sponsored by an unrestricted education grant from Novo Nordisk.

ESE also runs **Basic Science Courses, Clinical Update Courses** and **Themed Courses and Workshops**. To find out more about all ESE's courses see **www.ese-hormones.org/education/educational-courses**.

ECE On Demand

If you need a reminder of what you enjoyed – or missed – at ECE 2018, then ECE On Demand can provide you with access to a huge amount of Congress content:

- Plenary and prize lectures
- Debates
- Invited symposia
- ESE guideline updates
- Meet the Expert sessions
- plus other sessions, interviews, abstracts, e-posters and much else besides

We are pleased to present the webcasts of most of the speakers from the meeting!

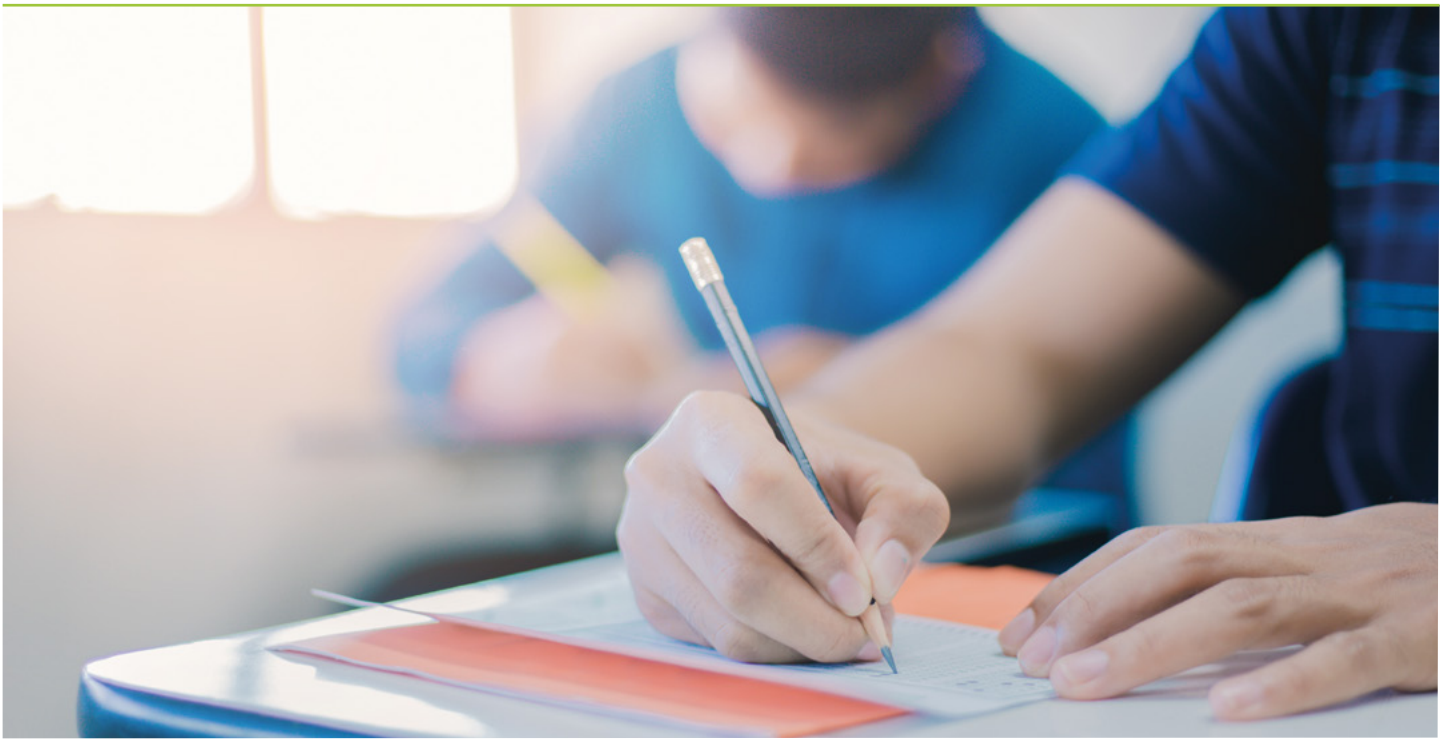
ECE On Demand is available to all ECE 2018 delegates and ESE members – you just need to log into **www.eceondemand.org** on your computer, tablet or phone using your registered email address. The app is also available to download from the App Store and Google Play – search for 'ECE On Demand'.

NEW for 2018:

ECE On Demand is also available to ESE Guest Users. Share the link to **www.eceondemand.org** for your colleagues to enjoy free access to:

- Selected highlights of ECE 2018 until 1 September 2018
- All ECE 2018 content after 1 September 2018
- The full ECE 2017 archive

ECE On Demand:
www.eceondemand.org



First candidates sit new European Board Examination

The first European Board Examination in Endocrinology, Diabetes and Metabolism took place on 6 June 2018.

This examination, established by ESE in collaboration with the European Union of Medical Specialists (UEMS), forms part of wider efforts towards harmonisation of education in clinical endocrinology across Europe. Its development followed requests by members of ESE and of our National Affiliated Societies for improved, internationally standardised, recognition of their clinical expertise.

Importantly, it will provide candidates with an opportunity to measure their knowledge and to effectively communicate this to potential employers.

Developing the exam

When forming an internationally standardised assessment of knowledge, consideration must be given to the adequate differentiation of candidates based on their abilities, rather than through luck or otherwise. For an examination to function properly, each component part must strengthen rather than detract from this differentiation process.

The development of the European Board Examination, from the generation of new questions, through to the marking system and the setting of the pass marks, took into consideration how effectively it would work to identify stronger candidates based on their answers.

Question writing

Questions for the European Board Examination are developed through a rigorous process of drafting followed by several stages of review and modification, until they are deemed suitable for use in the examination.

Question writers are trained in the processes involved before they are asked to submit a number of draft questions. These questions are collated and reviewed by all of the question writers at a question writing meeting, where the writers collectively debate, amend and agree or reject questions based on their suitability. Once agreed, questions are entered into a question bank for consideration in future examinations.

Choosing the questions

A selection of questions, based on the examination blueprint (which is available on the examination website at **www.ebeedm.eu**), is sent to the Examination Board.

The Examination Board meets to review the questions and consider them further for accuracy, fairness and difficulty. Questions considered appropriate in the wider context of the individual examinations are then compiled together to form the examination draft. This draft is then reviewed and approved before being sent to the Standard Setting Group.

Setting the pass mark

The pass mark is established individually for each examination.

The Standard Setting Group is made up of experienced clinical endocrinologists with an understanding of the examination processes and aims. Before each examination, the Group reviews and assesses the difficulty of each question. Consideration is given to the expected level of knowledge of the candidates using a procedure known as the modified Angoff method.

These scores are used to determine a criterion-referenced pass mark, which is in turn modified using the Hofstee compromise – taking into account all of the candidates' marks and adjusting the pass mark accordingly.

The process of marking

The European Board Examination is a two-paper test delivered on-screen in computer-based format (referred to as CBT). Each of the two papers is 3 hours in length, and consists of 100 'best-of-five' questions.

The marking system for the examination is as follows:

- one mark (+1) is awarded for each correct answer
- no mark is deducted for an incorrect answer (i.e. there is no negative marking)
- no mark is awarded or deducted if a question is left unanswered.

Any candidate who achieves the pass mark or above will be deemed to have passed the examination.

Why you should take the exam

Don't miss out on this, the first opportunity for European trainees to gain international certification, which we envisage will become the recognised standard across Europe and beyond.

For more information, including how to apply, see **www.ebeedm.eu**. You will find sample questions, information about what to expect and answers to frequently asked questions.

Genetics: the new face at the bedside

Are the large scale endeavours associated with DNA analysis actually delivering in clinical practice? The answer is 'Yes – big time!'

All human diseases and phenotypes have a 'genetic component' that contributes to explain the phenotypic variance, and ranges between 20 and 100%. This explained variance can be large, as in rare Mendelian diseases, or modest, as in the so-called common 'complex' diseases. Technology associated with DNA analysis has discovered the underlying causative DNA variants for many of these diseases, which holds promise for treatment and diagnostics.

The Human Genome Project and its successors have shown that the DNA sequence varies at numerous places between people, ranging from single nucleotides to very large chromosomal variations. These variations can be rare (e.g. mutations in Mendelian disease) to very frequent in the population (e.g. single nucleotide polymorphisms in common disease). We estimate that ~5% of all 3.3 billion nucleotides in the human genome vary and that each human differs at millions of places in their genome compared with their fellows.

The application of technology

DNA analysis technology now makes it possible to analyse millions of DNA variants in millions of DNA samples. Whereas next generation sequencing technology is a tool for some targeted purposes (it is expensive and generates too great a volume of overly complex data), pre-composed DNA arrays will be the tool for robust, comprehensive, cost-effective DNA diagnostics in large scale applications.

In particular, the recent introduction of very cheap DNA arrays (costing <€30 per sample) with a very rich content of ~900,000 DNA variants (such as the GSA array from Illumina (San Diego, CA, USA) and the PMRA array from Affymetrix (Santa Clara, CA, USA)) has accelerated large scale application. The genotyping of more than 25 million DNA samples has taken place. Importantly, this has been mainly outside the traditional research arena of biobanks and cohort studies.

Such genetic studies have led global collaborative consortia of investigators to execute optimal scientific experiments, including replication of discoveries in the same collaborative study and resulting publication. This new solid and efficient culture in research sets an example to be followed by all scientific and medical disciplines.

By applying this to large longitudinal cohort studies and biobanks, genome-wide association studies (GWAS) have resulted in the identification of >60 000 genetic factors (a number that is still growing!) for common diseases, traits and risk factors. Together with the ~150 000 known Mendelian mutations, such genetic factors are now beginning to find their way into clinical, forensic and societal practice.

Clinical genetics in practice

Historically, over the past 60 years, the field of clinical genetics has developed to focus on rare and family-based Mendelian disorders. However, our much increased knowledge of the genetics of complex diseases is now starting to enter practice across all clinical disciplines. Applications include pharmacogenetics, genetic risk scores and particular variant tests for patient stratification, guiding treatment as well as differential diagnostics.

The low cost of DNA arrays allows us to do this effectively and comprehensively across clinical disciplines at an institutional level.

High-throughput generation of genotypes at the Human Genotyping Facility, Erasmus MC. © JMH Verkerk

It also calls for a new vision regarding the role of clinical genetics outside that of classical Mendelian disease patient management.

In forensics, the newly discovered GWAS variants for visible traits (such as eye, skin and hair colour) and ancestry have already been used in court cases to solve crimes, making these genetic GWAS discoveries relevant to society.

Genetic tests are now also increasingly offered commercially (e.g. by direct-to-consumer (DTC) companies such as 23andMe (Mountain View, CA, USA)). These tests are based on the many known GWAS and Mendelian variants and help to empower the individual with health-related knowledge and enable an informed healthy life course. Needless to say, that there are many societal, ethical and economic issues surrounding this development. However, the substantial global sales of the DNA arrays, especially DTC tests, testify that this development is happening and that citizens and patients are interested.

We propose that clinicians and (academic) hospitals should have a leading role in this development, to help citizens and patients make informed decisions based on their genetic profile, and to guide politicians and society in when, how and for whom information from such genetic testing should be applied.

AG Uitterlinden, F Rivadeneira, JMH Verkerk and **JBJ Van Meurs**
Department of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands

Letting patients take charge

The future of healthcare will increasingly see patients steer their own chronic endocrine disease management.

The widespread growth and financial cost of chronic diseases have been well-documented. In Europe, 86% of deaths are related to chronic conditions.[1] Indeed, most patients we see in endocrine clinics live with a chronic health condition, which may be common (e.g. type 2 diabetes) or rare (e.g. genetic endocrine disorders).

Regardless of prevalence, chronic disease management is expensive and poses significant challenges for health systems globally. Importantly, patients provide >95% of the care for chronic health conditions themselves.[2] They face many choices and must make daily decisions about managing their health. Patients are the ones who decide whether or not to get a prescription filled, to take medication, to follow lifestyle modification recommendations, to make appointments with healthcare providers, or to come to appointments. And they are the first to note a change in their health status.

The activated patient

Patient education has long been viewed as an essential component of promoting patient self-care. Indeed, therapeutic education has been shown to effectively improve patient comprehension of disease management practices. However, as noted in the voluminous literature on medication adherence, knowledge alone is insufficient to change behaviour.

Patient activation and empowerment are critical levers to improve self-efficacy: one's motivation and confidence to effectively perform self-care activities. An empowered, activated patient is one who is engaged in shared decision-making and negotiates treatment objectives with healthcare providers. This is a radical change from the traditional hierarchical medical delivery model – yet financial, political and social pressures are making this transformation a reality.

In 2016, an European Commission expert panel on effective ways of investing in health identified four key disruptive opportunities for meeting European health needs: (a) transfer of skills (i.e. patient self-management), (b) an individualised approach to managing chronic disease, (c) new models of person-centred care (i.e. shared decision-making), (d) technology (i.e. web-enabled mobile health).[3] However, some of these concepts are not exactly new.

Since the 1990s and across numerous chronic conditions, Kate Lorig and colleagues have demonstrated the clinical effectiveness and cost savings of patients coaching other patients for self-management.[4] The internet provides novel avenues for peer-to-peer support for patients with rare diseases, who by definition are geographically dispersed. Web-enabled connectivity is critically important for the rare disease community, as it provides the opportunity to lift the 'veil of isolation' many patients feel living with an orphan disease.[5]

Moreover, while we as healthcare providers understand the pathophysiology, genetics and pharmacology related to many rare conditions, patients understand what it is like to live day-to-day with a rare disease. Thus, the web not only provides a source of peer-to-peer support, it also provides a platform for crowd-sourcing solutions where patients can learn about treatment options and share information on the latest therapeutic developments. In addition, it allows healthcare providers to directly connect with patients about their needs and to provide value in care.

The role of patients in R&D

Empowered patients have also changed the paradigm of research funding. Patient advocacy groups and internet-based crowd-funding (e.g. GoFundMe) have financed research calls for particular conditions of interest. In such citizen research, patient voices are clearly heard. Patient communities explicitly express their desire for attention and investigation into issues that matter most to them.[6]

Further, empowered patients are engaging in do-it-yourself hacks to solve problems they face in managing chronic conditions. Perhaps the most striking example is John Costik, a software engineer and father of a child with type 1 diabetes. Costik developed Nightscout – a digital solution for transmitting glucose data from a sensor to a cloud-based system that he and others could access from anywhere. He made this code open source and freely available for other parents to use, bypassing the traditional avenues of drug/device development.[7]

The examples of empowered patients self-managing their chronic conditions, funding research and bringing new ideas to the healthcare arena are disruptive opportunities for addressing the public health challenge of chronic diseases. Some may see this as an exciting and transformative movement. Others may consider the emergence of such trends as threatening and fraught with worrying ethical concerns.

Independent of one's personal viewpoints on the empowered patient, this grassroots movement is a powerful reminder to physicians, nurses and others in the care team of the growing patient demand for clear communication and shared decision-making. This type of inclusive approach is a hallmark of patient-centred care.

Andrew A Dwyer, on behalf of the **ESE Nurses' Working Group**
Boston College, MA, USA, and University of Lausanne Institute of Higher Education and Research in Healthcare, Switzerland

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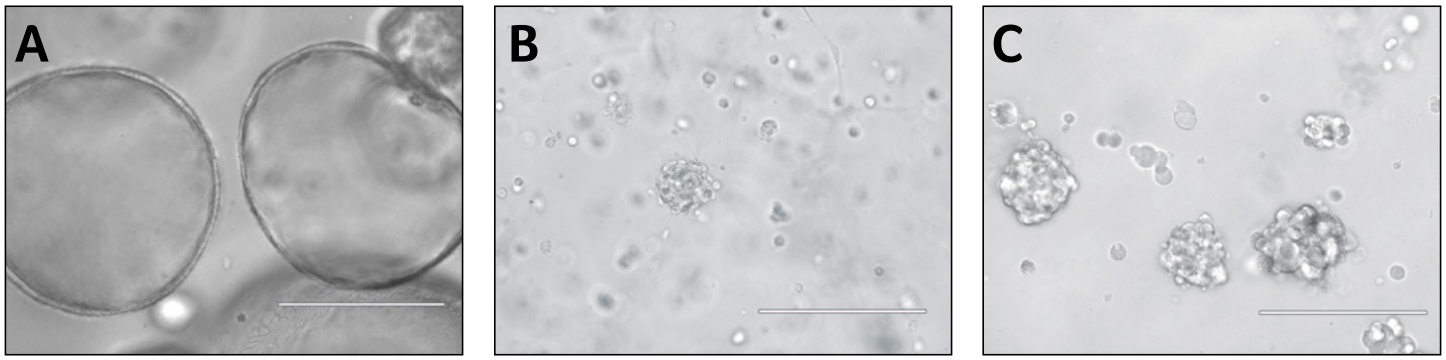
Tumour organoids: a new frontier

In the future, will we routinely use patient-derived organoids to determine individualised treatment?



Human organoid cultures established from primary resected normal pancreas tissue (A) and pancreatic NEN tissue (B and C). Scale bars 200µm. © T Dayton

Neuroendocrine neoplasias (NENs) are rare tumours that show features of neuroendocrine differentiation and are therefore thought to arise from the cells of the diffuse neuroendocrine system. Neuroendocrine cells are found in many different organs throughout the body, such as the pancreas, small intestine and lung, and thus NENs can arise in all of these organs. Due to the high degree of heterogeneity of neuroendocrine cells, the resulting tumours vary vastly in their underlying biology and clinical behaviour.

Generally, NENs can be subdivided into high grade neuroendocrine carcinomas (NECs) and low-to-intermediate grade neuroendocrine tumours (NETs). Despite very distinct differences with regards to clinical presentation, proliferation rate, and time to progression, NECs and NETs are both difficult to treat and represent a significant clinical problem. NECs are highly metastatic and, despite a relatively indolent clinical course, 60–80% of NET patients present with advanced disease.

A number of large-scale sequencing and expression studies on NENs from different anatomical sites have improved our understanding of these tumours at the genetic level. However, there are still many unanswered questions about the pathways and mechanisms that drive NEN formation and progression, and the heterogeneity and relatively low incidence of NENs have made these tumours particularly difficult to study.

The need for effective models

To gain insight into the biology of NENs and to uncover therapeutic vulnerabilities that can be exploited for treatment, one needs experimental models that faithfully recapitulate the features of this disease. Until recently, the options for preclinical models were limited to genetically engineered mouse models (GEMMs), tumour-derived cell lines, and patient-derived tumour xenografts (PDTXs).

While each of these systems has contributed significantly to our understanding of most cancers, they have been difficult to apply to the study of NENs. Although GEMMs of high grade NECs, including high grade insulinomas and small cell lung cancer, and of genetic NEN predisposition syndromes (e.g. *MEN1*) have contributed significantly to our understanding of these diseases, little is known about disease progression, and relatively few studies have been performed on human cells. These tumours have proved to be difficult to grow *ex vivo* and there are only a handful of NEN cell lines and PDTXs.

There is a clear need for the development of novel experimental systems to help us study this cancer type.

Enter the organoids

As a postdoctoral researcher in the lab of Hans Clevers, I would argue that organoids are a promising new tool for basic and translational research on NENs. The organoids developed in our lab represent a technology that allows for the *in vitro* growth of 'mini-organs' derived from adult stem cells. Organoids maintain the 3D organisation and cell type composition of the tissue from which they are derived, and can be expanded without limitations.

Organoids have opened the door to being able to study normal and tumour cells *in vitro*, and we have successfully utilised this system to grow primary human tumour tissue from many kinds of primary tumour.

Tumour organoids accurately represent the primary tumours from which they are derived, at both the genetic and the phenotypic levels. We find that the culture conditions can support growth of both low and high grade clones and tumour types. To date, we and others have generated large biobanks of human organoids derived from tumours of the colon, pancreas, oesophagus, stomach, liver, endometrium, breast and prostate.

In collaboration with the University Medical Centre in Utrecht and the Netherlands Cancer Institute in Amsterdam, we are currently building a biobank of NEN organoids derived from low and high grade pancreatic, intestinal and lung NENs and matched adjacent normal tissue. Our current success rate for establishing NEN organoids is close to 50%, and we are actively working on optimising culture conditions to improve this number.

While much work remains to be done, we believe that NEN-derived organoids will prove to be an important preclinical model for these diseases, as has been shown for other cancer types.

One particularly important application is the use of organoids to perform drug screening studies. To date, the results of such studies on tumour organoids from other tumour types have uncovered tumour-specific vulnerabilities to different therapies, suggesting that tumour organoids are a promising tool for personalised medicine. One might imagine a future where patient biopsies are routinely used to generate organoids and identify the appropriate course of treatment for each individual patient.

Talya L Dayton
Hubrecht Institute, Utrecht, The Netherlands

Using numbers to change lives

The artificial pancreas is set to transform the lives of patients with type 1 diabetes.

The burden of type 1 diabetes

Type 1 diabetes results from immune-mediated destruction of pancreatic β-cells in genetically predisposed individuals and is associated with life-long dependency on insulin administration.It is one of the most common chronic conditions in childhood; its incidence is increasing worldwide at an estimated overall annual rate of approximately 3%, including in the youngest age group.[1] Insulin treatment strategies include either multiple daily insulin injections or continuous subcutaneous insulin infusion (so-called insulin pump therapy).

The emergence of innovative technologies, including sensor-augmented pumps, has significantly shaped the management of type 1 diabetes over the past decade, providing new opportunities to improve metabolic outcomes.

The use of insulin pumps is increasing, particularly in the paediatric population. Real-time continuous glucose monitoring enables greater understanding of glucose excursions. It provides low and high glucose alarms and facilitates accurate insulin dose adjustments.

Despite these advances, achieving recommended glycaemic control without hypoglycaemia remains a challenge for people of all ages and for healthcare providers. The majority of youths fail to meet treatment guidelines for target glycated haemoglobin below 7.5% (58.5 mmol/mol).[2]

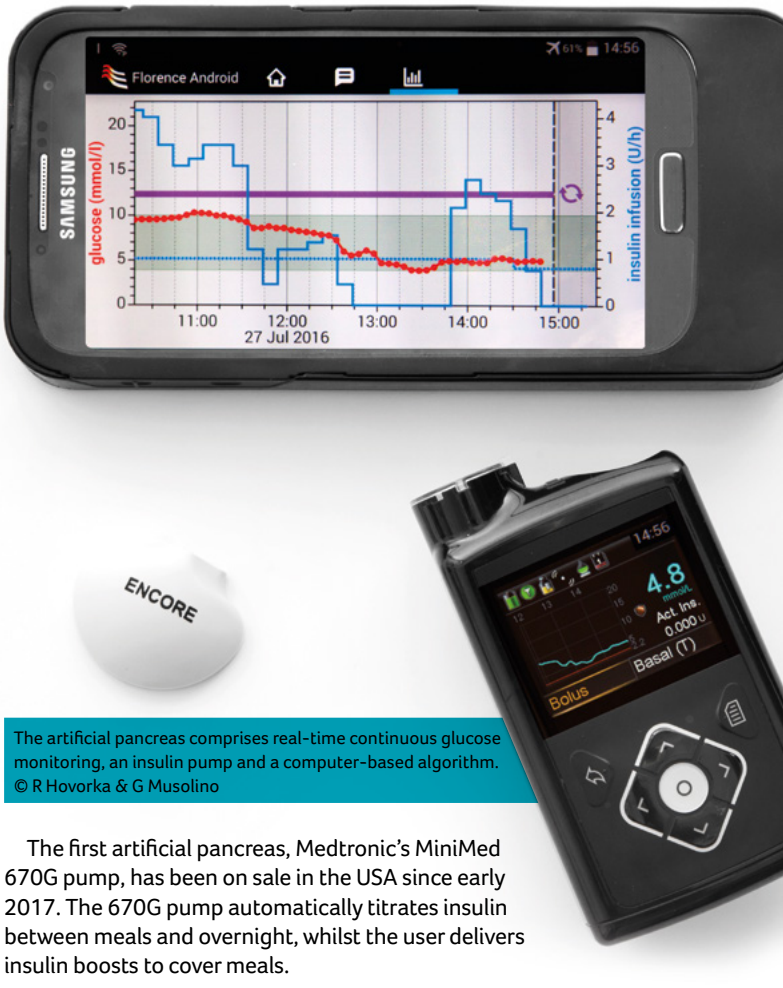
The artificial pancreas: technical (r)evolution

The 'artificial pancreas' is an emerging technology promising to transform management of type 1 diabetes.[3] It combines real-time continuous glucose monitoring with insulin pump therapy to achieve glucose responsive subcutaneous insulin delivery mimicking β-cell function as much as possible. The vital component of the system is a computer-based algorithm that is able to translate, in real-time, the information it receives from the glucose sensor and to compute the amount of insulin to be delivered by the insulin pump.

Use of this technology can reduce the burden for patients by automatically adjusting the amount of insulin entering the body on the basis of sensor glucose levels.

A recent meta-analysis[3] of randomised controlled trials in adults, children and adolescents compared the artificial pancreas systems with other insulin treatments. According to the data, the use of the artificial pancreas was associated with significant benefits in terms of increased time in the near normoglycaemic range and reduced time in hypoglycaemia and hyperglycaemia.

The team in Cambridge.



The artificial pancreas comprises real-time continuous glucose monitoring, an insulin pump and a computer-based algorithm. © R Hovorka & G Musolino

The first artificial pancreas, Medtronic's MiniMed 670G pump, has been on sale in the USA since early 2017. The 670G pump automatically titrates insulin between meals and overnight, whilst the user delivers insulin boosts to cover meals.

Increasing experience and collaboration

The University of Cambridge and collaborators have gathered considerable experience of investigating the artificial pancreas in individuals of all ages. Since 2012, we have enrolled over 250 subjects in randomised clinical trials of free-living artificial pancreas use, lasting from 1 week to 2 years.[3] Our clinical trials have shown the artificial pancreas to improve glycaemic control and to reduce the burden of hypoglycaemia.

Our team is currently co-ordinating longer term studies with investigators in the EU and USA.

The KidsAP project, funded by the European Commission's Horizon 2020 Framework Programme with additional funding by the charity JDRF (the Juvenile Diabetes Research Foundation), will assess the ability of the artificial pancreas to improve glucose control in the most vulnerable population with type 1 diabetes, children aged 1–7 years.

The CLOuD (Closed Loop from Onset in type 1 Diabetes) project is designed to assess the impact of the closed loop approach on preservation of C-peptide residual secretion in newly diagnosed adolescents with type 1 diabetes characterised by higher residual C-peptide secretion at diagnosis.

A bright outlook

The artificial pancreas is a primary example of how technology can change people's lives. Research progress made over the last two decades will result in the artificial pancreas becoming the standard of practice in type 1 diabetes care in the near future.

Roman Hovorka and **Gianluca Musolino**
University of Cambridge, Wellcome Trust–MRC Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, UK

REFERENCES

1. Patterson *et al.* 2012 *Diabetologia* **55** 2142–2147.
2. Wood *et al.* 2013 *Diabetes Care* **36** 2035–2037.
3. Bekiari *et al.* 2018 *British Medical Journal* **361** k1310.

The best reads of 2017

In this special feature, Hans Romijn, Editor of *European Journal of Endocrinology*, reviews some of the most downloaded papers from ESE journals in 2017.

Growth and growth hormone therapy in short children born preterm

This review by da Silva Boguszewski and de Andre Cardoso-Demartini examines the effects of being born preterm on childhood growth and adult height.

The World Health Organization defines preterm birth as birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of a woman's last menstrual period. They estimate that, in 2010, 11.1 % of babies were born prematurely. In cases of premature birth, babies are deprived of the intense intrauterine growth phase, and postnatal growth failure might occur. Some children born prematurely will remain short at later ages and in adult life. The risk of short stature increases if the child is also born small for gestational age.

Approximately 70–80% of children born preterm will have adequate height, weight and head circumference by 3 years of age. However, when growth restriction remains during infancy and childhood, children born prematurely are of increased risk of short stature. Those who are short at 2 years of age are unlikely to reach normal height during childhood, so careful follow-up is recommended. If further catch-up growth is not observed, these children might be candidates for recombinant human growth hormone treatment.

See *European Journal of Endocrinology* **176** R111–R122

Potential role of ER–mitochondria contact sites in metabolic disease

Cellular metabolism is closely regulated and compartmentalised within distinct subcellular organelles. Mitochondria and endoplasmic reticulum (ER) play a crucial role in these processes. ER–mitochondria contact sites, defined as mitochondria-associated membranes, start to emerge as important signalling hubs that integrate nutrient and hormonal stimuli and adapt cellular metabolism.

This review by Tubbs and Rieusset summarises the established structural and functional features of mitochondria-associated membranes and focuses on the latest breakthroughs, highlighting a crucial role of organelle crosstalk in the control of metabolic homeostasis.

Recent studies highlight that ER–mitochondria miscommunication in the liver could contribute to metabolic diseases, though these observations are clearly still in the initial stages. Future studies should determine whether ER–mitochondria miscommunication is a cause or a consequence of metabolic disease, and whether this also applies to humans.

See *Journal of Molecular Endocrinology* **58** R87–R106

Hormonal and metabolic effects of a single light exposure at night

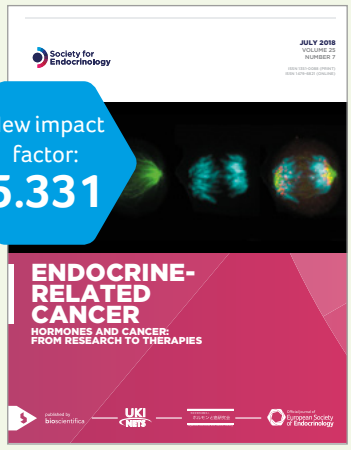
Albreiki *et al.* conducted the first study in humans to assess the influence of bright light exposure (room light) at night on metabolic and hormonal responses in healthy young participants.

Bright light exposure was associated with significantly higher glucose and insulin levels, suggesting glucose intolerance and insulin insensitivity. In addition, dim light was associated with elevated free fatty acid levels prior to the test meal.

The mechanisms underlying the endocrine and metabolic effects of bright light exposure cannot be explained with certainty, but may include effects of light through the retino-hypothalamic tract, e.g. on melatonin levels. The results of this study support the notion that light exposure per se, such as in night shift work, alters metabolic regulation.

See *Endocrine Connections* **6** 100–110

Glycosylation is a global target for androgen control in prostate cancer cells



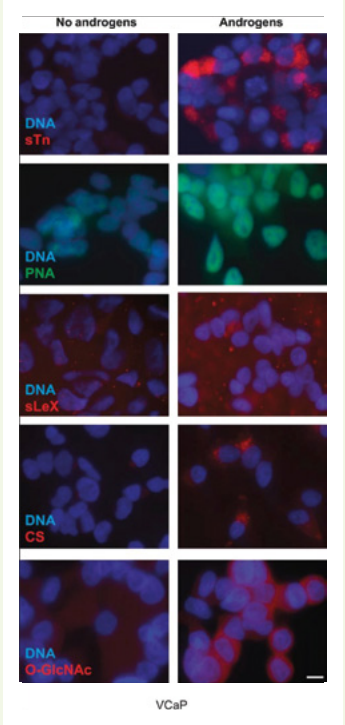
New impact factor: **5.331**

Glycosylation has a key role in many important biological processes in cancer, including cell adhesion, migration, interactions with the cell matrix, immune surveillance, cell signalling and cellular metabolism.

Munkley and co-workers have recently identified glycosylation as a global target for androgen control in prostate cancer cells and further defined a set of eight glycosylation enzymes, which are also significantly upregulated in prostate cancer tissue. These eight enzymes are under direct control of the androgen receptor.

These results suggest that alterations in patterns of glycosylation via androgen control might modify some or all of these processes in prostate cancer. Emerging data have the potential to improve risk stratification and therapeutic strategies in prostate cancer patients.

See *Endocrine-Related Cancer* **24** R49–R64



Immunofluorescent detection of cancer-associated glycans in VCaP prostate cancer cells, grown with or without 10nM R1881 (androgens) for 72h. Glycans were detected using antibodies in the case of sTn (sialyl-Tn), sLeX (sialyl Lewis X), CS (chondroitin sulfate) and O-GlcNAc (O-N-acetylglucosamine), whereas PNA (peanut agglutinin) lectin was used to detect the Tn antigen (GalNAc linked to serine or threonine). Scale bar 10μm. (Reproduced from *Endocrine-Related Cancer* **24** R49–R64 by permission.)

New impact factor: **4.012**

A causal role for hyperinsulinaemia in obesity

Insulin plays a fundamental role in maintaining energy homeostasis. In this review, Templeman and colleagues discuss new evidence demonstrating that modest reductions in circulating insulin prevent weight gain, with sustained effects that can persist after insulin levels normalise.

Importantly, evidence from long term studies reveals that a modest reduction in circulating insulin is not associated with impaired glucose homeostasis, meaning that body weight and lipid homeostasis are actually more sensitive to small changes in circulating insulin than glucose homeostasis in these models.

Collectively, the evidence from new studies on genetic loss-of-function models forces a re-evaluation of current paradigms related to obesity, insulin resistance and diabetes.

See *Journal of Endocrinology* **232** R173–R183

Euglycaemic diabetic ketoacidosis: a diagnostic and therapeutic dilemma

Euglycaemic diabetic ketoacidosis (EDKA) is a clinical triad comprising increased anion gap metabolic acidosis, ketonaemia or ketonuria and normal blood glucose levels <200mg/dl. This condition may be a diagnostic challenge as euglycaemia disguises the underlying diabetic ketoacidosis.

Rawla *et al.* present two patients on regular insulin treatment who were admitted with a diagnosis of EDKA. The first patient had insulin pump failure and the second had urinary tract infection and nausea, thereby resulting in starvation. Both were aggressively treated with intravenous fluids and insulin drip as per the protocol for the blood glucose levels till the anion gap normalised, and the metabolic acidosis reversed.

This case series summarises the aetiology, pathophysiology and treatment of EDKA.

See *Endocrinology, Diabetes & Metabolism Case Reports* **2017** 17-0081

Endocrinology, Diabetes & Metabolism
CASE REPORTS

The future of food

Could a genetically engineered 'giant' fish help feed the planet and save the environment?

Size comparison of an AquAdvantage® Salmon (background) versus a non-transgenic Atlantic salmon sibling (foreground) of the same age (~12 months). © AquaBounty Technologies

Genetically engineered (GE) mice have been produced since the late 1970s. Now, almost four decades later, many different species, including those traditionally consumed as food, have been engineered with various recombinant DNA constructs.

The combination of continued overfishing, habitat destruction and warming oceans has dramatically reduced the world's salmon populations. As an example, the Atlantic salmon (*Salmo salar*) population fell by more than 75% between 1984 and 2001.

The AquAdvantage® salmon is a GE Atlantic salmon that grows nearly twice as fast, on less food, than its comparator. Researchers Choy Hew and Garth Fletcher developed the salmon in the late 1980s. They introduced a growth hormone (GH) gene from a Chinook salmon (*Oncorhynchus tshawytscha*) into an Atlantic salmon. In 2015 it was approved by the US Food and Drug Administration (FDA). The AquAdvantage salmon is currently farmed and marketed by the company AquaBounty Technologies, Inc. (Maynard, MA, USA; **www.aquabounty.com**).

The underlying biology

This GE salmon contains a construct for expression of the GH of the Chinook salmon under the control of a promoter from the ocean pout (*Zoarces americanus*). The ocean pout is a fish which inhabits the chilly depths off the coast of New England and eastern Canada.

Triploid hemizygous, all-female Atlantic salmon bear a single copy of the α-form of the opAFP-GHc2 rDNA construct at the α-locus in the EO-1α lineage. This genetic code acts like an 'on' switch to activate GH.

The sterile transgenic female GE salmon are first produced as eggs for grow-out in the company's hatchery at Bay Fortune on Prince Edward Island, Canada. Subsequently they are raised in land-based tanks inside steel buildings equipped with multiple redundant physical barriers to escape.

Neither 'giant' nor 'acromegalic'

The GE AquAdvantage salmon are more than twice the size of their comparators at 12 months of age. This equates to around 1kg (2.2lb) compared with 300–400g (0.7–0.9lb) for the regular salmon.

The genetic gain of the GE salmon is, however, only their *rapid* growth: they grow year-round instead of only during spring and summer like the regular salmon. Therefore, the GE salmon grows to market size in 16–18 months rather than 3 years. The mature GE salmon are ultimately a normal size and NOT acromegalic giants.

There was no statistically significant difference between the mean insulin-like growth factor-1 (IGF-1) levels of the GE and the non-GE salmon, though the range of values for the GE salmon exceeded that for the non-GE salmon by more than 10%. The FDA concluded that exposure to the IGF-1 levels in these fish would be well within levels of exposure from other dietary sources of salmon, and would pose no additional risk. Furthermore, no direct food consumption hazards were found.

The future of food?

GE fish could provide a solution to the extinction of wild fish, by meeting the huge demands of the food sector and taking the pressure off wild stocks. They could also reduce energy requirements and carbon emissions.

However, in a 2013 poll by *The New York Times*, 75% of respondents stated that they would refuse to eat GE fish. Other polls have shown that consumer knowledge level is limited and often at odds with the facts. A report from Health Canada in August 2017 concluded that Canadians' views of genetically modified organisms (GMOs) were shaped by 'confusion, misinformation and generally low awareness/understanding'. The (political) movement opposed to GMOs in general and to GE 'Frankenfish' in particular is still very active.

AquaBounty sold 4.5 tonnes of AquAdvantage salmon in Canada in June 2017 and further small tonnage sales are planned for 2018. Due to a limited production capacity while new facilities are being constructed, continuous sales are not anticipated in the USA and Canada until early 2020. AquaBounty has no plans to sell AquAdvantage salmon in Europe but have ongoing field trials in Brazil and Argentina.

So, we must wait to see if fast-growing GE fish will become a staple part of the human diet.

Wouter W de Herder
Erasmus MC, Rotterdam, The Netherlands

The help of Dave Conley of AquaBounty Technologies in the preparation of this article is very much appreciated.

Celebrating success at ECE 2018

Honorary Membership of ESE was awarded to **Vera Popovic** (Serbia, left) and **Pia Burman** (Sweden, right) by ESE President AJ van der Lely

Left–right: Wouter de Herder (The Netherlands), **Jens Bollerslev** (Norway) and **Christian Strasburger** (Germany) received Special Recognition Awards from ESE President AJ van der Lely

Award Lecturers

Christos Mantzoros (USA)
Geoffrey Harris Award

Filip Knop (Denmark)
European Journal of Endocrinology Award

Ilpo Huhtaniemi (UK/Finland)
European Hormone Medal

Philippe Chanson (France)
Clinical Endocrinology Trust Award

New Award

Valeriya Lyssenko (Norway)
Jens Sandahl Christiansen Award

Raúl Luque (Spain)
Jens Sandahl Christiansen Award

Young Investigator Award winners

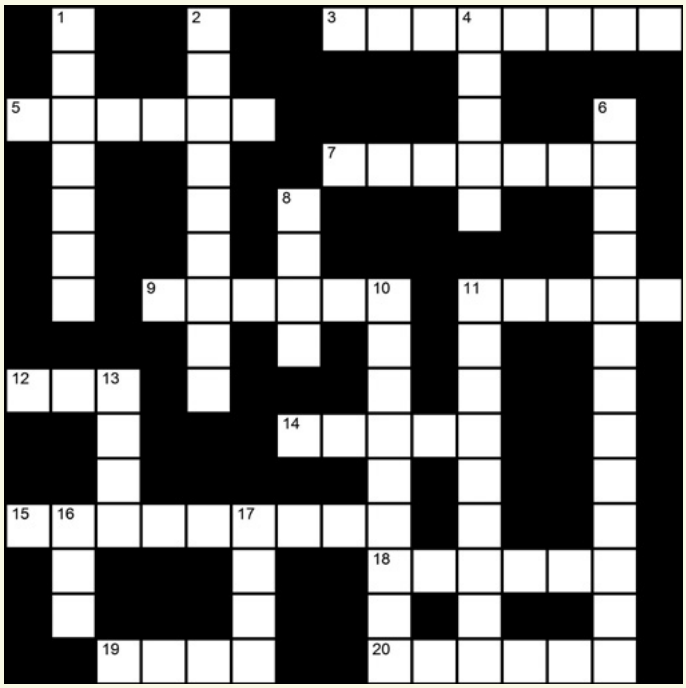
Alexandre Buffet (France), **Edward Buitenwerf** (The Netherlands), **Albert Cano Palomares** (Spain), **Simona Chisalita** (Sweden), **Beatriz Violeta Heras Domínguez** (Spain), **Iva Jakubikova** (Czech Republic), **Patimat Khandaeva** (Russia), **Torres Moreno** (Spain), **João Sérgio Neves** (Portugal), **Michiel Nijhoff** (The Netherlands), **Karina Sarkisova (Russia)** and **Sun Wook Cho** (Korea), seen here with the Co-Chairs and Chair of the Programme Organising Committee (POC): **Barbara Obermayer-Pietsch, Raúl Luque** and **Márta Korbonits**

Poster Prize winners

Maximilian Bielohuby (Germany), **Sofie Bliddal** (Denmark), **Miguel Chenlo** (Spain), **Marcin Chruściel** (Finland), **Simona Frunza-Stefan** (USA), **Kateryna Kondratiuk** (Ukraine), **Alberto Stefano Tresoldi** (Italy) and **Isabel Weigand** (Germany). **Kateryna, Alberto** and **Simona** are seen here with with the Co-Chairs and Chair of the Programme Organising Committee (POC): **Raúl Luque, Barbara Obermayer-Pietsch** and **Márta Korbonits**

The Endo Crossword

Send us your solutions to this topical puzzle for your chance to win one of three €20 Amazon vouchers! Let us have your answers, along with your name and email address, by emailing them to **info@euro-endo.org** or faxing them to 0044 1454 642222.



Congratulations

Our winner from issue 35 was Jakub Radocha (Czech Republic).

Answers to the puzzle in issue 35

Across 1. Domenechi, 5. Flavins, 6. Asn, 9. Seven, 10. Metre, 12. *E. coli*, 15. Cortisol, 16. Tunica, 17. Carnation

Down 2. Montaner, 3. Hercules, 4. Montjuïc, 7. Lallotja, 8. Lee-Boot, 11. Eighteen,13. Urea, 14. MRI, 15. Cava.

Across

3 See 15 across
5 **and 14 across** FRS who envisaged organ transplantation 350 years ago (6,5)
7 Gut hormone stimulating appetite and promoting fat storage (7)
9 **and 11 across** Serbian-American engineer who predicted WiFi and mobile devices in 1909 (6,5)
11 See 9 across
12 Collective term for symptoms such as acne, tiredness and mood changes seen monthly in women of child-bearing age (abbrev.) (3)
14 See 5 across
15 **and 3 across** Italian anatomist who first described the ducts from the ovaries to the uterus (9,8)
18 See 17 down
19 Antibiotic-resistant 'superbug' (abbrev.) (4)
20 S American plant, source of artifical sweetener shown to lower blood glucose (6)

Down

1 Literal meaning of the prefix in 6 and 10 down (7)
2 One of the visible symptoms of 8 down (9)
4 Type of pioneering eye surgery broadcast on TV from London's Moorfields Hospital in 1965 (5)
6 Medical condition where frenulum fails to recede (13)
8 More commonly used name for Stein-Leventhal syndrome (abbrev.) (4)
10 Joint stiffening due to fusion of bones (9)
11 Amino acid encoded by all codons starting 'AC' (9)
13 Hardened covering of dried secretions (4)
16 Hormone used to estimate ovarian reserve (abbrev.) (3)
17 **and 18 across** Yale University President who, in 1700s, accurately predicted US population in 1900s (4,6)

Did you know?

Flushed with pride

Forget that activity tracker on your wrist. The next must-have accessory may well be a smart toilet.

Rob Knight (San Diego, CA, USA) is co-founder of the American Gut Project: a crowd-sourced citizen science project to characterise the human microbiome. He says that, for directly health-relevant traits, studying your 1.5kg of gut microbes is more relevant than your genes. For instance, your microbial DNA can indicate whether you're lean or obese with 90% accuracy, compared with only 58% accuracy using your human DNA.

Professor Knight predicts that toilets of the future will analyse your stool and summarise your health, giving advice for improving your microbiome. Predictive modelling could anticipate the likely benefits after 10–20 years of taking your toilet's advice...

Save the date

For more information about any ESE event see **www.ese-hormones.org/events-deadlines.**

6th European Young Endocrine Scientists (EYES) Meeting
31 August –2 September 2018
Poznań, Poland

43rd Symposium on Hormones and Cell Regulation (ESE)
10–13 October 2018
Mont Ste Odile, France

EndoBridge 2018
25–28 October 2018
Antalya, Turkey

23rd ESE Postgraduate Course on Endocrinology, Diabetes and Metabolism
8–10 November 2018
Minsk, Belarus

Europit 2018
14–17 November 2018
Annecy, France

ECE2019
21st European Congress of Endocrinology
18–21 May 2019
Lyon, France

Deadlines

3 September 2018
EndoBridge Clinical Cases
Submission deadline

18 September 2018
43rd Symposium on Hormones and Cell Regulation (ESE)
Registration deadline

30 September 2018
ESE Small Meeting Grant
Application deadline

30 November 2018
ESE Short-Term Fellowship
Application deadline