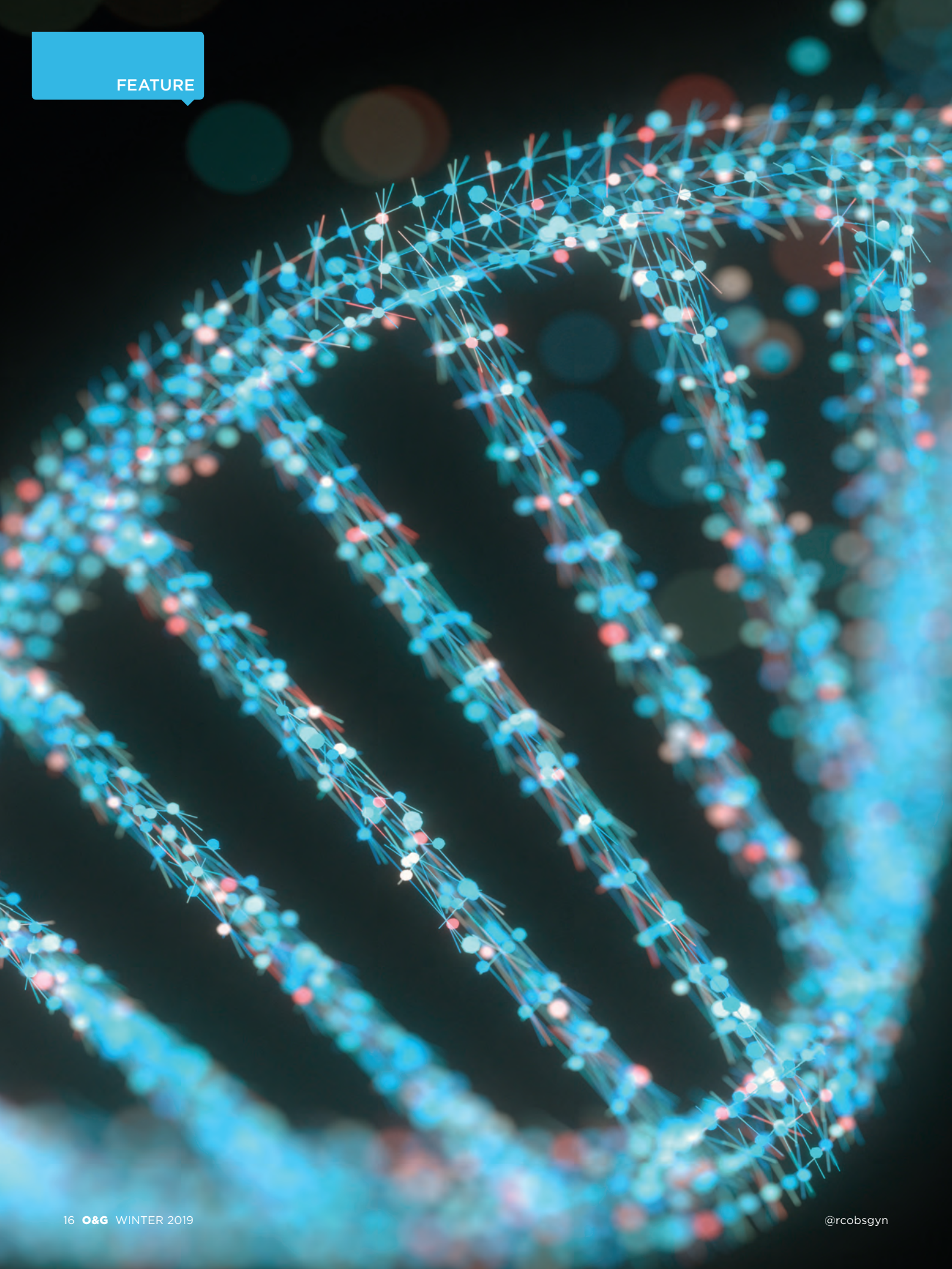

THE FUTURE IS HERE, NOW

Genomics – the study of genes and their function – is transforming medicine. It's time the O&G profession embraced it, says **Professor Peter Braude**

THE POTENTIAL FOR genomics to contribute to clinical care has been long anticipated and written about both in the lay and medical press, says Professor Peter Braude, an expert on preimplantation genetic diagnosis. However, the pace of defining the benefits and risks of incorporating genomic findings into medical practice has been relatively slow. Here he answers our questions on genomic medicine and the imperative to make it part of O&G practice.

"Chief among the causes for delay is the erroneous belief that genomic medicine is still some way into the future"

Q WHAT'S THE WIDER CONTEXT OF GENOMIC RESEARCH?

In December 2018, the extraordinary 100,000 Genomes Project sequenced its 100,000th genome. Its aim, as its name suggests, was to sequence over 100,000 whole human genomes through public participation, with a goal of harnessing whole genome sequencing (WGS) technology to uncover new diagnoses and improved treatments for patients with rare inherited diseases and various forms of cancer. Now not only have more than one in four volunteer participants who have children with previously undiagnosed syndromes received a diagnosis for the first time, it has provided potential actionable findings in up to half of cancer patients where there is now an opportunity to take part in a therapeutic trial or to receive a targeted therapy. As a result of this NHS initiative, seven Genomic Medicine Centres have been established in England, two in Scotland and one each in Wales and Northern Ireland. Each is associated with the Genomic Laboratory Hub that will facilitate centralised receipt and reporting of samples for genetic diagnosis.

ABOUT PETER

PETER BRAUDE ***is Emeritus Professor of Obstetrics and Gynaecology at Kings College London.***
He was formerly head of the Department of Women's Health and directed the Centre for Preimplantation Genetic Diagnosis for the Guy's and St Thomas' NHS Foundation Trust until 2011. He has been involved in assisted reproduction and embryo research in Cambridge and London for over 40 years. He was a member of the HFEA (1999–2004), chair of the RCOG Scientific Advisory Committee (2004–2007), and a member of the Nuffield Council on Bioethics working group that considered the ethics of Novel Techniques for the Prevention of Mitochondrial DNA Disorders. He was awarded an OBE in 2015 for his services to Reproductive Medicine.

"To many of our members, genomics may seem rather remote from our daily need. But nothing is further from the truth"

HOW ARE OTHER SPECIALTIES REACTING TO GENOMICS?

Several of our Royal Colleges have started the process of educating and implementing genomics into routine clinical care pathways, but the process has not been easy. Chief among the causes for delay is the erroneous belief that genomic medicine is still some way into the future, and to a large degree in the realm of research rather than daily practice. It is believed only to be mainstream in certain branches of clinical medicine such as oncology, ophthalmology, cardiology, diabetes and clinical genetics.

In conjunction with Health Education England and Genomics England, the RCGP has provided a series of easily understandable genomics podcasts and webinars which deal with key areas relevant ways to GPs. The RCN has also done something similar (see 'Further reading', below, for links).

The Royal College of Physicians, the Royal College of Pathologists and British Society for Genetic Medicine have formed a Joint Committee for Genomics in Medicine whose mission is to help to integrate genomics into mainstream clinical practice *(www.phgfoundation.org/clinical-champions)*. The RCOG will be contributing a member to this group.

WHY DO OBSTETRICIANS AND GYNAECOLOGISTS NEED TO UNDERSTAND GENOMICS?

To many of our members, genomics may seem rather remote from our daily need. But nothing is further from the truth: our College is unique. It is the only one dealing day-to-day with transgenerational genomics.

A substantial part of the obstetric workload revolves around preconception counselling and prenatal testing for genetic disease, diagnosing morphological abnormalities in utero by ultrasound and trying to predict the outcome for the fetus through mass or targeted prenatal screening. The carrying-out of prenatal procedures for diagnosis is in our hands, as is specialist intervention to prevent transmission, or to ameliorate disease in utero.

HOW IS GENOMICS CHANGING O&G?

New cellular and genomic technology has made testing easier and more reliable through non-invasive prenatal testing, and further advances in genomics and stem cell technology are likely to make diagnostic intervention less frequent, but in utero intervention on the fetus for early genetic modification more likely.

Since 1990 preimplantation genetic diagnosis (PGD) being carried out in a limited number of IVF centres to avoid transmission of serious genetic disorders by the selection of unaffected embryos has been added to these prenatal interventions. This now includes modification of the egg or embryo for those carrying mtDNA genetic disorders using mitochondrial replacement therapy (MRT). With the significant recent change in our ability to edit the genome through CRISPR and allied technologies, it is likely that sooner or later genome editing will be incorporated within or as an alternative to PGD, with the prospect of transgenerational genetic change either

Further reading

- Genomics England (information packages for practitioners) www.genomicsengland.co.uk/understanding-genomics
- The 100,000 Genomes project www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project
- Genomics in nursing (with RCN) www.genomicseducation.hee.nhs.uk/genomics-in-healthcare/genomics-in-nursing
- Courses and resources from Health Education England www.genomicseducation.hee.nhs.uk/education
- Consent and Confidentiality in Genomic Medicine (report of the Joint Committee on Genomics in Medicine) tinyurl.com/consent-genomics-jcgm
- RCGP genomics podcasts tinyurl.com/rcgp-genomics

The RCOG Genomics Taskforce

THE FIRST MEETING of the genomics taskforce was in May 2019, bringing together experts in fetal medicine, clinical genetics, urogynaecology, gynaecological oncology, reproductive medicine, obstetric medicine, endometriosis, fibroids, and molecular biology, ethics and genomics education. At this meeting it became clear that the a distinction needed to be made between research needed to advance genomics, and genomics of immediate import to O&G practice.

Professor Andrew Horne will be leading on the research aspects of genomics through the Academic Committee. Brianna Cloke and Prof Peter Braude will lead the integration of genomics into mainstream care as Genomic Champions for the RCOG. Genomics will feature as part of the next Blair Bell Research Society meeting in February, and the restructured taskforce will be rolling out our genomics training and education programmes during 2020.

"Being at the cutting edge of many of the most controversial aspects of genomic testing, the RCOG's role is unique"

incidentally as a result of intervention in the early embryo, or possibly as the ethical climate changes, through editing of gametes prior to fertilisation.

In common with other surgical specialties, oncology is central to much of our care in gynaecology including preventative testing, diagnosis and immunisation against vulval and cervical cancers, and surgical treatment and oncological therapy for uterine and ovarian tumours. But, genomic research is also opening up new areas in benign gynaecology improving prospects for diagnosis and treatment of uterine fibroids, dysfunctional uterine bleeding, endometriosis and irritable bladder.

Q WHAT IS THE RCOG'S ROLE?

Being at the cutting edge of many of the most controversial aspects of genomic testing – non-invasive prenatal diagnosis and its consequences, assisted conception and the possibility of germline editing, and neonatal testing with the prospect of replacing a diagnostic heel prick with whole genome sequencing – our role is unique. The RCOG must now engage fully with the changes that genomic medicine is likely to produce.

To this end the RCOG has established a taskforce (see box, above) with a clear purpose of understanding the need for genomics education among our membership, and to provide learning packages and educational meetings to help them achieve genomic competence at a level commensurate with providing best advice and service as this rapidly expanding field develops and becomes a routine part of O&G practice.

As Sir John Burn, Professor of Clinical Genetics in Newcastle, said in his 2018 interview for BBC Radio 4's The Life Scientific: "The term genomic medicine will soon disappear. It will just be called medicine as it will be in all branches of our work."