

## Introduction

# Major advances in physiology: celebrating a centenary of contributions by women

2015 is the 100th anniversary of women becoming members of The Physiological Society. To celebrate this important anniversary, this issue of *Experimental Physiology* comprises invited review articles by distinguished women physiologists, all of whom have delivered either the Joan Mott Prize Lecture or one of the other prestigious Prize Lectures awarded by the Society.

The Physiological Society was established in 1876 by 19 men, most of them Fellows of the Royal Society, physicians or surgeons. They were responsible for developing the new academic discipline of physiology in the UK so that it became part of teaching in medical schools, with the movement spreading throughout the British Empire and USA. A particular concern was the increasing number of animal experiments carried out to study physiological processes, which was attracting agitation from anti-vivisectionists. The UK Government set up a Royal Commission to develop legislation to regulate procedures on animals, which included senior physiologists, and those working in physiology were keen to have a formal grouping that could offer advice to the Commission.

With this background, the Rules of The Physiological Society included promoting the advancement of physiology and facilitating intercourse between physiologists. Membership was initially limited to 40 men, all to be working physiologists, while ‘Men of distinction in Science . . . were eligible for election as *Honorary Members*’. Minutes of the Society over this period make little mention of women except as guests at the dinner that was associated with each Scientific meeting (Sharpey-Schafer, 1927*a*).

In 1913, the proposition was made that women should be eligible for membership. The motion was carried by 16 votes to 13, but an amendment that the membership should be circulated for their opinion was lost. In 1914, the proposition was considered again. This time, a poll of the membership was carried out by postcard. It delivered a clear majority that women should be admitted on the same terms as men, rather than the alternatives of associate membership with no right to attend Society dinners, or no change in the Rules. The Committee changed the Rules in January 1915, and in June 1915 six of the eight newly elected members were women. There was a steady increase in women members over the following years, and in 1920 the first woman was elected to the Committee (Sharpey-Schafer, 1927*b*).

Since then, women have played a full role in The Physiological Society; many have been elected to the Committee or Executive Committee, held Officer roles and chaired Sub-Committees. In parallel, many women have become nationally and internationally recognized for their contributions to science and to physiology in particular. One of these was Joan Mott who, after graduating in 1943 with a first class degree in Zoology at Newnham College, Oxford, took an Assistant Lectureship at Royal Holloway College, London, investigating methods of preventing barnacles from colonizing ship hulls. She later returned to Oxford and was awarded a DPhil for pioneering work using cine-angiography on the circulation of eels. Her interests in the circulation flourished, developing into a passion to understand reflex regulation of the cardiovascular system in neonatal mammals. She became Foundation Fellow of Wolfson College in 1966 and secretary of the newly formed Neonatal Society from 1963 to 1967. At meetings of The Physiological Society, she was known for her direct questions and forthright views. However, she always showed an interest in the work of young physiologists. It was therefore fitting that when she died in 1995 and left a bequest to the Society, the Committee decided to award a Prize Lecture biennially, to be

particularly relevant to young physiologists, with the aim of enhancing the profile and significance of women within the discipline.

Most of the women who have delivered the Joan Mott Prize Lecture and several who have delivered one of the other Prize Lectures have contributed a Review to this issue of *Experimental Physiology*, some reviewing progress in the topic of their Prize Lecture, others reviewing with colleagues the recent advances in their current research area. Given the origins of The Physiological Society, it is noteworthy that several of the reviews demonstrate the continuing importance of *in vivo* experiments on animals to investigate important physiological questions. It is also significant that several clearly show how today's physiologists are embracing the techniques of molecular biology and genetics to understand fundamental physiological mechanisms and investigate ways of treating disease. Several of the reviews reflect Joan Mott's legacy and interests.

Maria Fitzgerald gave the first Joan Mott Lecture in 1998. Here, she reviews recent and current studies on brainstem and cortical neurocircuitry in developing newborn mammals that have greatly improved understanding of the recognition and treatment of pain in infants (Fitzgerald, 2015).

Susan Wray takes us back into pregnancy and discusses the functioning of the myometrium, particularly in preterm birth and dysfunctional labour. She reviews the findings of genomic studies from normal and abnormal pregnancies and argues that whilst genomic studies are informative, physiological studies will continue to be necessary to advance understanding of dysfunctional labour (Wray, 2015).

Abigail Fowden, with colleague Alison Forhead, reviews current understanding of the roles of maternal and fetal glucocorticoids in fetal development and maturation. They also consider emerging evidence on the epigenetic mechanisms by which excess glucocorticoids during pregnancy adversely affect postnatal development (fetal programming) and lead to cardiometabolic diseases in adult life (Fowden & Forhead, 2015).

Lucilla Poston and colleagues focus on the globally important issue of maternal obesity. Epidemiological evidence suggested an association with obesity and cardiometabolic disease in the offspring, but they demonstrate that animal models provided the essential cause–effect evidence and are revealing the underlying mechanisms and effects of intervention. This has led to the exciting prospects of a multicentre, randomized controlled trial involving dietary and physical activity intervention in pregnancy and follow-up in childhood (Patel *et al.* 2015).

Janice Marshall reviews advances in our understanding of how local dilator and sympathetic vasoconstrictor influences interact at cellular levels to regulate oxygen distribution within skeletal muscle during acute hypoxia. Knowledge of the adaptations induced by chronic hypoxia is patchier, but recent evidence indicates that chronic hypoxia *in utero*, as well as chronic hypoxia in adult life, leads to blunted sympathetic vasoconstriction and systemic hypertension; identifying the underlying mechanisms is a key challenge (Marshall, 2015).

Dame Nancy Rothwell and her colleagues discuss recent evidence that inflammation is a major contributor to the consequences of acute brain injury caused by haemorrhagic stroke or brain trauma. Studies on rodents, including genetically modified mice, have implicated multimolecular inflammasomes and interleukin-1. These important preclinical studies have formed the basis for ongoing clinical trials testing the therapeutic potential of interleukin-1 receptor antagonism (Brough *et al.* 2015).

The tools available to access the genome-wide data sets containing cell-specific information on exon usage that allow discrimination of proteins generated as splice isoforms are reviewed by Diana Lipscombe and colleagues. They show how such information has helped to establish the physiological significance of isoforms of genes encoding voltage-operated  $\text{Ca}^{2+}$  channels and neuronal  $\text{Na}^{+}$  channels, and discuss the potential of strategies to normalize splicing events associated with various diseases (Lipscombe *et al.* 2015).

Kay Davies and colleagues review Duchenne muscular dystrophy, an example of a devastating X-linked genetic disorder caused by lack of the cytoskeletal protein dystrophin and dysfunction of the associated protein complex in skeletal, respiratory and cardiac muscle. They discuss understanding gained from animal models of the disease and the preclinical studies of various gene-replacement and gene-modification strategies that have led to the first clinical trials (Guirard *et al.* 2015).

Holly Shiels and colleague Rebecca Sitsapesan review excitation–contraction coupling in the fish heart, which functions at low temperatures that arrest mammalian hearts. They focus on recent evidence that the open–closed state of the fish ryanodine receptor (RyR2), the sarcoplasmic reticulum  $\text{Ca}^{2+}$ -release channel, is temperature sensitive and regulated by  $\beta$ -adrenergic stimulation. Elucidating these mechanisms should provide insight into processes fundamental to the environmental distribution of fish and to evolution of the mammalian heart (Shiels & Sitsapesan, 2015).

In their review, Daniela Riccardi and colleagues discuss the functioning of extracellular calcium-sensing receptors (CaSRs), which are well known for their involvement in whole-body  $\text{Ca}^{2+}$  homeostasis. Here, they focus on new findings that CaSRs in gut, respiratory airways and vasculature are implicated respectively in nutrient movement and tumour repression, in asthma and in blood pressure regulation; they discuss strategies to develop cell-specific CaSR modulators for therapeutic use (Lopez-Fernandez *et al.* 2015).

Finally, Hannelore Daniel, who delivered the 2015 Joan Mott Prize Lecture, reviews with Tamara Zietek, the recent evidence that membrane transporters in the gut not only transport monosaccharides and amino acids but also function as sensors, triggering release of hormones from enteroendocrine cells, which then promote insulin output. This is a beautiful example of research on species ranging from nematodes to genetically modified mice and to rats and humans that is opening the door to new ways of regulating metabolic control (Daniel & Zietek, 2015).

Taken together, these Reviews clearly provide only a sample of the outstanding contributions made by women physiologists. They also show some of the major advances in important physiological topics over recent years and hint at the exciting issues that remain to be explored.

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