1. INTRODUCTION

Time flies! It has been 3 years since I wrote the editorial “In the Shadow of Giants: Challenges and Opportunities for the New Editor of Physiological Reviews” (1). It has been an incredible honor and a solemn responsibility to be selected as the Editor-in-Chief of Physiological Reviews by the Publications Committee of the American Physiological Society. It also has been great fun to work with the editorial team, consisting of some of the best-known scientists in the world. Together, we strove to maintain the excellence of Physiological Reviews and to increase its impact on the scientific community. I was extremely pleased and honored when I was informed that my term as Editor would be extended for another 3 years, starting on January 1, 2021. The purpose of this brief editorial is to highlight the accomplishments made and the challenges during the last term and to outline our plans for the second term.

2. STATUS OF PHYSIOLOGICAL REVIEWS IN THE SCIENTIFIC COMMUNITY

We publish comprehensive, authoritative, nonbiased, and informative reviews, in all areas of biomedical research. Our audience includes physiologists, neuroscientists, cell biologists, biophysicists, and clinicians with special interest in pathophysiology of disease. During the last 3 years (1/1/2018 to 12/31/2020), we published 134 invited reviews, 1 editorial, 4 Letters to the Editor, and 1 Corrigendum. The outstanding team of Associate Editors proposes topics and authors. Our Senior Editorial Assistant, Ms. Amy McEver, circulates the proposals to the Associate Editors attending our biannual meetings. All proposals are discussed in detail with particular emphasis being given to the excellence of the proposed author and her/his recent contributions to peer-reviewed literature, the importance of the topic, and the likelihood that the review will have a considerable impact on the field. It is our hope and expectation that each review will provide an in-depth coverage of an important field and highlight what needs to be done to reconcile major differences of opinion. All articles undergo in-depth peer evaluation by members of our Editorial Board and guest reviewers. The Editor, in consultation with the Associate Editor, then makes a decision as to whether the article meets our high standards. During the last 3 years, a number of articles were withdrawn or rejected because they could not address the comments of the reviewers in a satisfactory fashion.

Our journal is held in high esteem by members of the scientific community as shown by the following: 1) the large number of citations of published articles; 2) the increase of its impact factor from 24.014 in 2017, to 24.250 in 2018, and to 25.588 in 2019; 3) the 70% acceptance of invitations to submit reviews by the most outstanding scientists in the world; and 4) the fact that Physiological Reviews is ranked consistently as the most impactful journal in physiology.

Below, we provide a brief summary of major accomplishments and outline some of the plans the Deputy Editors and I have to increase the excellence and impact of Physiological Reviews.

3. MAJOR ACCOMPLISHMENTS

3.1. New Editorial Features

In addition to in-depth discussion of basic mechanisms, we expect each review to highlight the translational and
possibly clinical implications of the subject matter. This has increased interest and citations considerably. Examples include the outstanding articles on the following: 1) the pathophysiology of migraine (2); 2) mechanisms of insulin action and resistance (3); 3) new insights into the mechanisms of aging; 4) the origins of metabolic diseases (4); and 5) mechanisms of insomnia (5). To highlight the translational and clinical implications at a glance, authors are now requested to include a call-out-box-for-clinicians, highlighting why physician scientists, clinicians, and even the public may find a review worthwhile to read.

It is true that some topics may not have obvious translational implications, but they still are of interest to members of our scientific community. We continue to solicit and publish reviews on these topics, assuming that the Associate Editors make a strong case that they will move a field forward. Alexander Fleming never imagined the impact that penicillin would have on public health when he discovered it in 1928.

Two additional new features are worth mentioning: the first is the inclusion of a graphical abstract, summarizing the main concepts of the review at a glance. We have been to numerous presentations at scientific meetings in which we have seen the graphical abstract presented as an introduction to a talk. In addition, a well-constructed graphical abstract catches the attention of a reader who then wants to find out more about the topic. We also use graphical abstracts to highlight all published articles in Twitter (@physiolrev) and Facebook (https://www.facebook.com/physiolrev/) as well as for journal covers (FIGURE 1). In addition, the Editor and Deputy Editors use the graphical abstracts in their lectures to residents and graduate and medical students. We hope that they will be incorporated in the lectures of all members of Physiological Societies around the world.

However, our most important initiative was the launch of Publication-Ahead-of-Print (Articles in Press; https://journals.physiology.org/toc/physrev/0/0). Previously, it took an average of 4 months from the time an article has been accepted until it was available online. This has allowed us to make articles available more quickly to our subscribers, and the Associate Editors can then make decisions about the articles on the basis of the feedback they receive.

FIGURE 1. Left: elevated plasmin in vulnerable people may cleave the spike proteins of SARS-CoV-2 to enhance the invasion into host cells via the surface receptors. The new furin site of the S proteins could be proteolytically cleaved by plasmin as it does in the epithelial sodium channels (ENaC). ACE2, angiotensin-converting enzyme 2. Cover of July 2020 of Physiological Reviews (from Ref. 9). Right: CRISPR tools are currently revolutionizing molecular approaches in life science. The new possibilities go far beyond mere gene editing. Gene activities, transcription factors, and chromatin marks can be locally manipulated by using CRISPR approaches, enabling one to influence cellular behavior, to manipulate disease-associated gene expression, and to replace cells lost during disease. PAM, protospacer adjacent motif. Cover of January 2021 of Physiological Reviews (from Ref. 7).
was accepted for publication to the time it was published in print and appeared in PubMed. Since the launch of Articles in Press, accepted articles have been published on our website within 2 weeks (https://journals.physiology.org/toc/physrev/0/0) and appear in PubMed as submitted shortly after (assuming that no copyright issues are identified). Thanks to this feature, two of our reviews appeared in PubMed, before the topics were chosen by the Nobel Prize committees in the last 2 years: Dr. Taylor’s article on the mechanisms and consequences of oxygen and carbon dioxide sensing in mammals (6), and Dr. Stricker’s article on CRISPR tools for physiology and cell state changes (7). Currently, >85% of authors are choosing to make use of Articles in Press. We encourage all authors to submit manuscripts with figures and legends incorporated into the text to increase their readability online.

3.2. Establishment of the Board of Associate Editors and the Editorial Board

The European and North American Boards were integrated into a single Board of Associate Editors consisting of 20–25 leading scientists with significant editorial experience (https://journals.physiology.org/physrev/edboard). The increased interaction among Associate Editors on our biannual meetings improved the quality of proposed review topics and provided valuable feedback on new ideas of how to improve the impact of our journal. The biannual meetings are vibrant events, and one cannot help but be proud of being part of these great gatherings of scholars.

Drs. Carol Ann Remme (Amsterdam University Medical Center, The Netherlands) and Willis K. Samson (Saint Louis University School of Medicine, St. Louis, MO) were appointed Deputy Editors, effective January 1, 2021. They are replacing Dr. Barbara Cannon, who has served Physiological Reviews for 12 years as the Chair of the European Board and as Deputy Editor. Our most sincere thanks go to Dr. Cannon, as well as to Drs. Kim Barrett, Pierangelo Geppetti, Lora Heisler, Helle Praetorius, Giulia Taraboletti, Gary Westbrook, and Richard Ye for their service as Associate Editors during the last 9–12 years.

One of the difficulties encountered in the past was the identification of reviewers with the necessary expertise willing to spend the time and effort to provide valuable feedback to authors of submitted manuscripts. To expedite this process, we established an Editorial Board (https://journals.physiology.org/physrev/edboard) consisting of 60–70 outstanding scientists, asked to review two to three manuscripts per year. The creation of the Editorial Board has increased the visibility of Physiological Reviews and facilitated the review process. The time to first decision (~60 days) is considerably longer than the average time of most research journals but necessary because of the length, complexity, and comprehensive nature of these manuscripts. Associate Editors also reach out to guest reviewers so each article receives the benefit of at least two reviews. We want to express our sincere thanks to members of our Editorial Board and our Guest Reviewers for their service to our journal and scientific community.

3.3. Scientific Symposia and Webinars

We started organizing a 1-day scientific symposium, held just before the biannual meeting of Associate Editors. This was designed to enhance the visibility of Physiological Reviews among the international community and to highlight the scientific contributions of junior and senior scientists of the International Physiological Societies cohosting one of our biannual meetings. The first symposium entitled “Physiological Homeostasis in Health and Disease” was held in Athens, Greece in 2019 and featured presentations by Associate Editors, as well as senior and junior members of the Hellenic Physiological Society. A second symposium was to take place before the 2020 meeting in Florence, Italy, which unfortunately was cancelled because of COVID-19 pandemic-travel restrictions. Instead, Dr. Samson, organized a very well-attended Webinar on “Modern Approaches to Research in Physiology” (https://www.physiology.org/detail/event/2020/06/18/default-calendar/webinar-modern-approaches-to-research-in-physiology?SSO=Y), featuring talks by Drs. Remme (“Preventing Cardiac Arrhythmias”), Galliano (“Flipping the Switch Genetically to Understand Neural Circuity”), and Yosten (“Sniffing out Paracrine Interactions”). The emphasis of all talks was on presenting state of the art techniques, which would help young scientists elevate the quality and impact of their science. ~150 junior and senior scientists from all over the world attended. Additional webinars, featuring our distinguished Associate Editors and members of our Editorial Board, are being planned the coming year.

3.4. COVID-19 Mini-Reviews

In 2018, Physiological Reviews published an authoritative review on “Integrative Physiology of Pneumonia” by Drs. Wuinton, Walkey, and Mizgerd (8). Among viral agents, rhinoviruses and influenza were listed as accounting for 50% of the cases. A few years later, when pneumonia became a dreaded complication of the SARS-CoV-2 virus infection, this review became a must read document and prompted us to solicit mini-reviews on all aspects of SARS-CoV-2 virology, immunology, and physiology as well as on public health impact of
COVID-19 disease. The entire collection of these articles can be found in our webpage (https://journals.physiology.org/topic/physrev-collections/covid19?seriesKey=physrev&tagCode=). This collection is updated as additional mini-reviews and letters to the Editor are accepted.

Submitted papers underwent thorough but rapid reviews and when accepted were published in final (copy-edited) mode within a few weeks from acceptance; they were also made available free of charge to the public and members of the scientific community. To date (1/12/2020), we have published five mini-reviews (downloaded 48,817 times) and three letters to the Editor (downloaded 4,365 times). It is remarkable that at the time the first review was posted (April 2020), there were nearly 3 million people worldwide diagnosed with COVID with 200,000 deaths. As of January 2, 2021, there were 85,897,728 COVID cases worldwide, with 1,842,164 deaths (https://www.worldometers.info/coronavirus/?utm_campaign=homeAdvegas17). Below we highlight three of the most cited reviews and provide brief discussions of their findings.

The first mini-review by Ji et al. (9) was published in April 2020. The authors summarized existing evidence showing that patients with hypertension, diabetes, cardiovascular diseases, and other comorbidities, known to have worse clinical outcomes when infected with SARS-CoV-2, have higher levels of plasmin, which enhances the virulence and infectivity of SARS-CoV-2 virus by cleaving its spike protein. It has been downloaded more than 30,000 times and been cited 137 times (https://journals.physiology.org/doi/full/10.1152/physrev.00013.2020). Shortly after its publication, clinicians proposed a clinical trial to investigate whether tranexamic acid, an agent that prevents the conversion of plasminogen to plasmin, reduces the severity of COVID (https://clinicaltrials.gov/ct2/show/NCT04338126). In addition, a number of physician-scientists, at the forefront of COVID patient care, have written letters to the Editor concerning the use of tranexamic acid in the early stages of COVID-19 (10).

The second article by Dr. Romagnoli (“SARS-CoV-2 and COVID: From the Bench to the Bedside”), a leading Italian physician involved in taking care of COVID patients in Italy, described the three phases of COVID, the rationale for various treatments (including Remdesivir and corticosteroids) and detailed the impact of COVID on public health in Italy (11). This review has been downloaded 7,218 times and has been cited 85 times.

In another very interesting review by Dr. Chritchley (“Pregnancy and COVID-19”) (12), the authors pointed out that the risk of severe COVID disease in pregnancy may be higher than in the general population. They brought attention to the establishment of the COVIPREG database by the International Federation of Gynecology and Obstetrics for the collection of data on COVID in pregnancy and in the postnatal period (https://www.figo.org/covid-19-data-collection-your-contribution-needed). Finally, the authors mentioned that pregnant women were excluded from practically all therapeutic trials at the time that this article was written. This review has been downloaded 4,635 times and received 2 citations.

3.5. Established Guidelines and Procedures for the Submission on Nonsolicited Proposals

As mentioned above, most of the published reviews are proposed by our Associate Editors. However, the Editor welcomes suggestions from the scientific community. Actually, during the last year (2020) we received 33 nonsolicited article suggestions. If there is consensus among the Editor, Deputy Editors, and at least one Associate Editor as to the scientific excellence of the team and the likelihood that the review will have a major impact in the field, we ask for a preproposal to be discussed at the biannual meetings. The Editor makes the final decision, based on the outcome of the discussion, whether or not to issue an invitation for a review.

4. CHALLENGES AND OPPORTUNITIES FOR THE NEXT 3 YEARS

4.1. Maintain the Exceptional High Quality and Timeliness of Published Reviews

This is challenging due to the ever-increasing demands on the times of the very busy outstanding scientists asked to contribute reviews. It takes on average 3 years from the original invitation until the review is submitted. Approximately, 30% of invited reviews are abandoned by the authors for various reasons.

4.2. Increase Interactions with Physiology Research Journals

Drs. Samson and Remme will lead an initiative to increase our interactions with the research journals sponsored by the American and European Physiological Societies. We will solicit and publish brief editorials integrating information on recent review articles published in Physiological Reviews with articles on the same topic published in a research journal. As an example, please see the editorial in the American Journal Physiology-Regulatory, Integrative and Comparative Physiology by Dr. Samson (13) based on a review on food intake after bariatric surgery published in Physiological Reviews (14) and various
research articles published on this topic published in American Journal Physiology-Regulatory, Integrative and Comparative Physiology.

4.3. Record Podcasts on the Most Impactful Articles

There is concern that many researchers, especially our junior colleagues, are suffering from “information overload.” It has been suggested that graduate students, postdoctoral fellows, and junior faculty may not have the time to read and assimilate the in-depth information in each of our published authoritative reviews. Podcasts have been used by a number of journals to highlight important findings to both scientists and the public (who may not have access to the full article). The Editor and Deputy Editors will contact authors of Trending Research/Most Read/Most Cited Articles published in Physiological Reviews (see homepage at https://journals.physiology.org/journal/physrev) and request that they help generate 10-min podcasts, which will appear on our webpage as well as in our Facebook page. This may be a great opportunity to bring attention to recent publications in research journals on the same topic.

Possible examples of podcasts include the reviews by the following: 1) Quinn and Kohl (15) on “Cardiac Mechano-Electric Coupling,” an excellent example of integrative physiology with a clear translational impact. The review is highly informative and provides an excellent, in-depth overview of the intracardiac feedforward and feedback loops between electrical and mechanical behavior, its molecular mechanisms, and its impact on cardiac electrical activity and arrhythmogenesis. Importantly, the review also addresses the clinical implications of mechanoelectric coupling for arrhythmia formation in the setting of different diseases and resulting potential therapeutic approaches; 2) Hoffman et al. (4) on “Developmental Origins of Metabolic Diseases,” which details the physiological mechanisms that increase the risks of obesity, fatty liver disease, hypertension, and diabetes; and 3) Ray et al. (16) on “Precision Medicine in Asthma,” which details how one can integrate omics data with the results of animal experiments and molecular and cellular studies to identify new biomarkers to allow patients with asthma to receive maximum benefits from medical treatment; and the various articles on COVID cited previously.

4.4. Publish Systematic Reviews

A systematic review is a research summary that addresses a focused question in a structured, reproducible manner. Well-conducted systematic reviews “identify, select, assess, and synthesize” the evidence that makes clear what is known and not known about drugs, devices, education and training methods, and healthcare practices. Writing of a systematic review with a meta-analysis is an arduous and time-consuming task requiring a team of authors and an expert librarian to search a number of databases in addition to PubMed. However, it can answer important questions on controversial topics (17). We plan to commission at least two systematic reviews during the next 3 years. We stress that the large majority of reviews will adhere to the existing format.

4.5. Establish a Junior Editorial Board

We will solicit nominations from the Associate Editors for 20 junior scientists with outstanding credentials and significant potential of developing into independent productive investigators to be appointed to our Junior Editorial Board for a 3-year term. Associate Editors will assign two submitted manuscripts per year to each member of this board (in addition to at least two senior reviewers) and provide constructive criticisms on their reviews. This will allow our junior colleagues to interact with leaders in the field and gain valuable experience on how to write helpful and constructive reviews.

5. CONCLUDING REMARKS

Physiological Reviews is in great shape thanks to the hard work of the Deputy and Associate Editors, the Editorial Board, our Senior Editorial Assistant (Ms. Amy McEver), the Journal Supervisor (Mr. Sean Boyer), the Publications Director, Editorial and Production (Dr. Audra E. Cox), and the many dedicated staff in the APS Editorial Office (https://journals.physiology.org/physrev/edboard). Some people look in the future and see challenges. We see opportunities to increase its impact and improve its quality. The best years are ahead of us.

CORRESPONDENCE

Correspondence: S. Matalon (smatalon@uabmc.edu).

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.
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