



Editorial

Endothelin XIII

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ARTICLE INFO

Available online 28 September 2014

ABSTRACT

Twenty-five years ago, a groundbreaking paper from Tsukuba University in Japan was published, identifying the sequence of the endothelin gene and peptide (Nature 332, 411–415, 1988). This work opened the way for the discovery of the endothelin receptors and the development of orally active endothelin receptor antagonists (ERAs). Today, ERAs are part of medical therapy of patients around the world for the treatment of pulmonary arterial hypertension. Since the discovery of endothelin, about 1000 papers per year have been published, with more than 27,000 articles available today. Many important and break-through findings presented in the endothelin conferences have been published in the conferences' proceedings. Endothelin XIII is the proceedings of the Thirteenth International Conference on Endothelin, held at Tokyo Campus of Tsukuba University, Japan, in September 2013. At the conference, the 25th anniversary of endothelin's discovery was celebrated and articles produced from data presented at the conference are compiled in this Special Issue of Life Sciences. Endothelin XIII includes more than fifty articles, including review articles by experts in the field and numerous original research articles. As the Editors of this special issue, we are proud to present Endothelin XIII and wish the field continued growth for the benefit of patients and for the advancement of biomedical science.

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Over the past 25 years, the International Conferences on Endothelin have contributed to the development of endothelin research by providing the place to share the most recent and up-to-date information on endothelin (Emoto et al., 2014b). Also, the conferences have developed into meetings where young researchers and senior scientists from the most diverse disciplines and from all regions around the world come together to meet and to discuss and share their recent findings (Emoto et al., 2014b). The First International Conference on Endothelin was launched as the “First William Harvey Workshop on Endothelin” in December of 1988 and chaired by Sir John Vane, Ph.D., FRS, in London, U.K. (Vane et al., 1989), less than nine months after the

publication of the molecular structure of the endothelin gene and peptide (Yanagisawa et al., 1988). Since then, the International Conferences on Endothelin have been held every other year and many of the scientifically important advances of the field were published in the conference proceedings (Barton, 2012; Battistini et al., 2000; d'Orleans-Juste, 2010a, b; d'Orleans-Juste et al., 2008a, b; Emoto, 2014; Kohan, 2006; Miyauchi, 2004; Vane et al., 1989; Vane et al., 1991, 1993, 1995, 1998; Webb, 2002).

Coinciding with the 25th anniversary of the discovery of Endothelin (Emoto and Yanagisawa, 2014), the Thirteenth International Conference on Endothelin (ET-13) took place in September 2013 on the Tokyo Campus of the University of Tsukuba in Tokyo, Japan (Emoto et al., 2014b). The articles published in the proceedings of ET-13 are compiled in Endothelin XIII, a special issue of the multidisciplinary journal *Life Sciences*, and include more than 50 articles spread over [000] pages, which makes it the most comprehensive endothelin conference proceedings volume of the past decade (Emoto, 2014).

In celebrating 25 years of the discovery of endothelin, the Endothelin XIII issue opens with a summary of the meeting, scientists who delivered invited lectures and an overview (Emoto and Yanagisawa, 2014),

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followed by an article describing the history of endothelin research, conference highlights, including all the haikus (Japanese poems) presented by young investigators, and an outlook on the next generation of endothelin researchers (Emoto et al., 2014b). The recipient of *The Second Tomoh Masaki Award*, Katsutoshi Goto, Ph.D., of Tsukuba University is honored with an article which summarizes his scientific achievements in the field of endothelin research (Emoto et al., 2014a). This first section of the journal concludes with an article summarizing the scientific career of Wolfgang Kiowski, M.D., who unexpectedly passed away in late 2012 during the planning stages for the ET-13 conference (Barton and Schiffrin, 2014). Dr. Kiowski had been one of the foremost clinician-scientists in endothelin research. Twenty years ago, he published a study reporting the first-in-man use of endothelin antagonists in patients (Kiowski et al., 1995). He had actively participated in many of the past endothelin conferences, including being a member of their scientific advisory boards (Barton and Schiffrin, 2014).

The second section of Endothelin XIII comprises a total of nine in-depth review articles, both from the area of basic sciences as well as clinical medicine, that have been provided by leaders in their field. In a comprehensive review article, Matthias Barton, M.D., Zurich, who also celebrated an anniversary that year, discusses the important role of the endothelin system in aging, and how mechanisms of disease and the aging process are closely related, and how people can actively contribute to age healthily (Barton, 2014). Mahalia Desruisseaux, M.D., and her colleagues from New York give an extensive review of the literature highlighting the pathological role of ET-1 in infectious disease processes and discuss the promising new results suggesting a potential application of ERAs for infectious disease such as malaria (Freeman et al., 2014). In his article “End O’ The Line Revisited”, which summarizes parts of his Honorary Chair Lecture, Paul M. Vanhoutte, M.D. Ph.D., Hong Kong, discusses the roles of endothelin-1 on vascular tone in the light 50 years of vascular biology research and 25 years of endothelin research. He also provides his view on the most recent data on the subject (De Mey and Vanhoutte, 2014). Takayuki Matsumoto, Ph.D., Tokyo, and Rita C. Tostes, Ph.D., Ribeirao Preto, and colleagues provide an overview on how to link the beneficial effect of current therapies in diabetes to the endothelin system (Matsumoto et al., 2014). The interplay between endothelin and life-threatening ventricular arrhythmias in myocardial infarction is discussed by Theofilos Kolettis, M.D. Ioannina (Kolettis, 2014). Berthold Hocher, M.D., Berlin, contributed a review article which discusses in detail the many pitfalls that have encountered the development of endothelin receptor antagonists (ERAs) for patients with chronic kidney disease and proposes alternatives for the design of future clinical trials (Reichetzedler et al., 2014). The clinically important role of endothelin in obesity and diabetes and the therapeutic potential of endothelin antagonism for related disorders are discussed by Carmine Cardillo, M.D., Rome, and colleagues (Campia et al., 2014). Fernando Rodríguez-Pascual, Ph.D. Madrid, and colleagues provide an extensive overview discussing the controversies about the ambiguous roles of endothelin in profibrotic diseases and the clinical implications associated with it (Rodríguez-Pascual et al., 2014), an area also discussed in the review article about the role of endothelin in aging (Barton, 2014). Finally, the recipient of the ET-13 Best Presentation Award for best oral presentation, Johannes Backs, M.D., Heidelberg, was invited to submit a review article, which gives an excellent and fascinating overview on the role of endothelin-1 in the sympathetic nervous system in the heart (Lehmann et al., 2014b). The data on which his oral presentation was based (Backs et al., 2013) have been recently published elsewhere (Lehmann et al., 2014a). The invitation to publish a review article is part of the award which was introduced in 2012 and has since been co-sponsored by Elsevier publishers (Barton and Pollock, 2012).

These articles are followed by a large number of high-quality, original research articles that reflect the complexity of endothelin biology

and at the same time the vitality of this research field. In these articles, data from basic research and clinical studies are presented from the fields of nephrology (Certikova Chabova et al., 2013; Heunisch et al., 2014; Ogura et al., 2014), autoimmune disease (Tajiri et al., 2014), infectious disease (Naito et al., 2014; Seki et al., 2014), ophthalmology (Finzi et al., 2014), and cardiac, pulmonary, and vascular research (Backs et al., 2013; Baretella et al., 2014; Kolettis et al., 2014; Van Hung et al., 2014), cell biology (Jacobs et al., 2014), physiology (Donato et al., 2014; Meyer et al., 2014), and oncology (Cianfrocca et al., 2014), among others. How micro-RNAs might regulate endothelin expression in different organs and pathological situations is presented by Cain et al. (Jacobs et al., 2014). The hopes for the treatment of hypertension raised by novel ERAs are presented by Iglarz et al. (Iglarz et al., 2014), while Tajiri’s results show that an increased inflammatory response might be caused by such an antagonist under certain disease conditions (Tajiri et al., 2014). Rosano et al. describe the molecular events underlying the potential therapeutic benefit of endothelin antagonism in cancer (Caprara et al., 2014; Cianfrocca et al., 2014). Many more translational discoveries were presented in these proceedings that we were honored to present as part of Endothelin XIII.

All manuscripts have been rigorously peer-reviewed by at least three international experts, including members of the Endothelin XIII Editorial Board. All manuscripts went through at least one to up to three revisions before they could be accepted. The Guest Editor decided to continue the format of the proceedings from those introduced with the preceding conference proceedings, Endothelin XII (Barton, 2012), particularly with regard to the following points: We are publishing the ET-13 Conference Proceedings in *Life Sciences*, a highly respected and interdisciplinary journal published with Elsevier, who also agreed to publish all conference abstracts in an online version of the journal (Emoto, 2013). All conference abstracts and articles of Endothelin XIII are published Open Access™ to facilitate the global dissemination and to allow access for scientists from all over the world (Emoto, 2013). Video recordings of the conference presentation were available in the online version for many articles published in Endothelin XII (Barton, 2012; Barton et al., 2012), and we have continued this tradition publishing articles with corresponding videos, which are freely accessible on the publisher’s website (Emoto, 2014). Also, recordings of most of the presentations at the conference are available as HD video and can be accessed via the ET-13 conference program pages of Endothelin XIII (Conference Program). Finally, as a first, each conference abstract has received a digital object identifier (DOI) and is citable like a regular article is (Emoto, 2013). We are confident that this new feature will facilitate exchange of knowledge in the endothelin field and beyond.

We thank all authors for their contributions to this Special Issue of *Life Sciences*. We also thank all members of the *Life Sciences* Endothelin XIII Special Editorial Board and all of the many reviewers. We thank them for their enormous efforts put into reviewing the abstracts and manuscripts submitted, for their tenacity, and for providing insightful and stimulating comments. We also express our appreciation to Takashi Miyauchi, M.D. Ph.D., Tsukuba, ET-13 Co-Chair, the entire conference faculty of ET-13, and the members of *Endothelin International Advisory Board* (ET-IAB) of the International Conferences on Endothelin for their support. We are particularly grateful for the assistance provided by Nicolas Vignon-Zellweger, Ph.D. for his energy and his administrative talent. We are indebted to Anne Marie Pordon, Ph.D. of Elsevier as the publisher of *Life Sciences* for her professional support. We thank Loren Wold, Ph.D., Columbus, OH, Editor-in-Chief of *Life Sciences*, for his trust in this project, and Christine Kisthardt and Ruthie Hewitt at *Life Sciences*, for their sensational support through the whole process of publishing the proceedings. We also wish to thank all participants, sponsors, and the musicians Dimitri and Vovka Ashkenazy for their concert performance on occasion of the 25th anniversary of the discovery of endothelin in Tokyo.

We hope that you will enjoy this ET-13 Special Issue of *Life Sciences* and look forward to meeting you again in 2015 at ET-14 which will be held in Savannah, Georgia.

August 2014



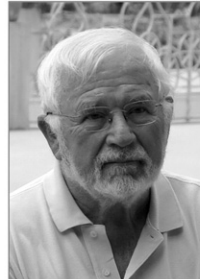
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Conflict of interest

None.

Appendix A. Supplementary data

Supplementary video to this article “Highlights of ET-13 - Professor Masashi Yanagisawa's summary of the conference” can be found online at <http://dx.doi.org/10.1016/j.lfs.2014.09.021>.

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