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EDITORIAL

Pharmacology of the 'gasotransmitters' NO, CO and H_2S: translational opportunities

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The current themed issue collates a number of reviews and original papers on the pharmacology of NO, CO and H_2S. These three molecules have been grouped together to form a family of signaling mediators that has become known as '*gasotransmitters*'. Authors of the articles in this issue are members of ENOG- the European Network On Gasotransmitters (COST Action BM1005, www.gasotransmitters.eu). ENOG currently numbers more than 200 researchers from 24 European Countries and is funded through the European Science Foundation. Work from ENOG researchers and colleagues around the world have contributed to the understanding of the role of these molecules in physiology and disease initiation and progression. In addition, substantial progress has been made in recent years in the pharmacology of CO and H_2S with the development of several CO- and H_2S-donors.

The NO field is more than 3 decades old, but readers can find in this issue reviews on novel aspects of NO/cGMP signaling and on the therapeutic usefulness of components of this pathway in cardiovascular diseases (Papapetropoulos *et al.*, 2015) with or without co-morbidities, such as metabolic diseases (Pechánová *et al.*, 2015). Sexual dysfunction (Yetik-Anacak *et al.*, 2015) and male infertility (Buzadzic *et al.*, 2015) are additional fields where modulation of NO signaling bears therapeutic potential. S-nitrosation, a NO-induced post-translation modification of proteins is discussed by Santos *et al.* (2015) in the context of neuronal plasticity.

The H_2S field has recently experienced a booming interest as evidenced by the exponentially increasing number of published articles in the field. Papers on the role of H_2S in ischaemic diseases (Bos *et al.*, 2015), as well as blood pressure regulation and hypertension (Snijder *et al.*, 2015; Brancaleone *et al.*, 2015) can be found in this issue. Interactions of H_2S with myeloperoxidase are reported in an original paper by Pálinkás *et al.* (2015); the inhibitory effect of H_2S on myeloperoxidase is expected to contribute to the actions of H_2S in the context of inflammation.

CO is a unique gasotransmitter, as its specific molecular targets are still not known and it is a more stable molecule as compared to NO or H_2S. However, the strong affinity of CO for metal centers can guide us in the search for the putative cellular targets. E.g. mitochondria rich in haeme-iron proteins are potential candidates for molecular targets for CO. This concept is discussed in the review of Queiroga *et al.* (2015) in the context of the role of endogenous and exogenous CO in pathologies of the central nervous system. In addition, ion channels have been recognized as possible effectors of CO signaling and it appears that modulation of the activity of channel proteins is part of the mechanism contributing to the physiological and therapeutic actions of CO (Peers *et al.*,

2015). Comprehensive and conceptually challenging reviews in this issue also summarize the anti-inflammatory and tissue protective activity of CO in specific conditions, such as acute gastrointestinal inflammation (Babu *et al.*, 2015) and preeclampsia (Ahmed and Ramma, 2015), where both H_2S and CO exert anti-angiogenic properties.

The interaction of NO, H_2S, and CO at the cellular level can be observed in several pathologies, such as ischaemic heart disease and hypertension, allowing several pharmacological approaches for modulation of these gasotransmitters in order to protect the ischaemic heart with or without co-morbidities (Andreadou *et al.*, 2015) and to regulate blood pressure (Wesseling *et al.*, 2015). Cardiovascular co-morbidities may alter cardioprotective signaling including gasotransmitters, therefore, co-morbidities have to be taken into account when developing cardioprotective therapies as reviewed recently elsewhere (Ferdinandy *et al.*, 2014).

The current issue also contains practical guides for scientists just entering into the interesting field of gasotransmitter research, including technical guidelines to measure NO in biological samples (Csonka *et al.*, 2015), basic guidelines for H_2S pharmacology (Papapetropoulos *et al.*, 2015), and the chemical characteristics and biological behaviors of CO-releasing molecules (Schatzschneider, 2015).

The editors of this themed issue hope that the papers gathered here will be useful for established researchers already involved in gasotransmitter research, as well as for young scientists just planning to enter the field, and for teachers and students interested in the physiology, pathology, and pharmacology of NO, H_2S and CO.

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