XLV JCET LECTURE, 07.11.2014, 9.00

H2S Donors and H2S synthesis inhibitors: basic pharmacology and translational opportunities

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Hydrogen sulfide (H_2S) regulates smooth muscle tone, cell metabolism and growth, apoptosis and migration. It has, thus, been implicated in a plethora of physiological and pathophysiological processes including angiogenesis, cardioprotection, atherosclerosis, inflammation and cancer. H_2S is produced by cystathionine beta synthase (CBS), cystathionine gamma lyase (CSE) and 3-mercaptopyruvate sulfur transferase (3-MST). Aminoethoxyvinylglycine (AVG), ß-cyano-L-alanine (BCA) and propargylglycine (PAG) selectively inhibit CSE over CBS and 3-MST. All of them, exhibit limited potency and block other PLP-dependent enzymes, too. It should be emphasized that no selective CBS or 3-MST inhibitors are currently available. As CBS has been shown to be up-regulated in colon cancer, potent and selective CBS inhibitors could be of translational value.

The available H2S donors can be divided based on their chemical nature and rate of release to inorganic vs organic compounds and fast vs slow releasers. The most widely used inorganic compounds to generate H_2S are NaSH and Na_2S. These compounds dissociate rapidly in solution leading to immediate H_2S formation. The organic donors available can be divided according to their source of origin into naturally occurring and synthetic. Contrary to inorganic salts, the organic donors release H_2S more slowly; the rate of H_2S liberation may differ substantially depending on the absence or presence of biological material. Mitochondrial-targeted donors and hybrid molecules between known drugs and H_2S-releasing moieties are special subclasses of H_2S donors. During the second part of the presentation data on signaling, pharmacological profiles and biological activities in the context of cardiovascular disease of different classes of H_2S-generating compounds will be analyzed.

Curriculum Vitae

Andreas Papapetropoulos received his bachelor's degree in Pharmacy from the University of Patras (Greece) and earned his PhD in Pharmacology with distinction at the Medical College of Georgia (Augusta, GA). After completing his graduate training he moved to the Department of Pharmacology and the Boyer Center for Molecular Medicine at Yale University as a postdoctoral fellow. In 1999, he joined the Faculty of the University of Athens as Assistant Professor. From 2003-2013 he served as Associate and later as Professor and Director of the Laboratory of Molecular Pharmacology at the Department of Pharmacy at the University of Patras. He is currently Professor of Pharmacology at the School of Pharmacy (University of Athens) with a secondary appointment in the 1st Department of Critical Care and Pulmonary Services and Affiliated Investigator at the Biomedical Research Foundation of the Academy of Athens. During his academic career in Greece, he has held visiting positions and adjunct professorships at McGill University, the University of Dentistry and Medicine in New Jersey, the University of Texas Medical Branch at Galveston and Maastricht University.

Prof. Papapetropoulos serves on the Editorial Board of the British Journal of Pharmacology, The Journal of Pharmacology and Experimental Therapeutics and Arteriosclerosis, Thrombosis & Vascular Biology. He is board certified in Pharmacy and an Expert at the European Medicines Agency, where he has served as national delegate on the paediatric committee. He is also a Fellow of the American Heart Association and a Fellow of the British Pharmacological Society.

Prof. Papapetropoulos' research focuses on cardiovascular and, to a lesser extent, pulmonary pharmacology, studying the role of various receptors and signaling pathways as therapeutic targets. The work of his group extends from the molecular mode of drug action, to in vivo drug testing in animal models of disease. He chairs the European Network of Gasotransmitters, a network of 200 scientists from 24 European countries funded by the European Science Foundation. His research is funded by intramural, national, European and international agencies and he has published 121 papers in peer-reviewed journals which have received >11,000 citations.

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