

MEETING ABSTRACT

Open Access

sGC redox regulation and asthma

Dennis J Stuehr^{1*}, Arnab Ghosh¹, Cynthia J Koziol-White², Kewal Asosingh¹, Georgina Cheng¹, Lisa Ruple¹, Jennifer Rodgers¹, Dieter Groneberg³, Andreas Friebe³, Johannes-Peter Stasch⁴, Reynold A Panettieri², Mark A Aronica^{1,5}, Serpil C Erzurum^{1,5}

From 7th International Conference on cGMP Generators, Effectors and Therapeutic Implications Trier, Germany. 19-21 June 2015

Asthma is defined by airway inflammation and hyper-responsiveness, and contributes to morbidity and mortality worldwide. Although bronchodilation is a cornerstone of asthma treatment, current bronchodilators become ineffective with time and with worsening asthma severity. We investigated an alternative pathway for bronchodilation that involves activating the airway smooth muscle enzyme, soluble guanylate cyclase (sGC).

The pharmacologic sGC stimulator BAY 41-2272 or a NO donor each triggered a dose-dependent bronchodilation in precision cut human lung slices from healthy donors and in mouse tracheal rings, whereas BAY 60-2770 was a less effective bronchodilator in these circumstances. Neither NO nor BAY 41-2272 relaxed tracheal rings obtained from sGC^{-/-} mice. This established the NO-sGC pathway can trigger bronchodilation in healthy airway. In live animal studies, a single intra-tracheal administration of either BAY 41-2272 or BAY 60-2770 reversed the airway hyper-responsiveness that had developed in mice with allergic asthma and restored their normal lung function. The sGC recovered from the mouse asthmatic lungs displayed three hallmarks of oxidative damage that render it NO-insensitive, and identical changes were found to occur in sGC obtained from human lung slices or from cultured cells that had been exposed to low chronic NO. Our findings reveal how allergic inflammation in asthma, and its resulting airway inflammation and excessive NO production, impede the natural NO-sGC-based bronchodilation pathway, and suggest that pharmacologic sGC stimulants or activators can provide a novel therapeutic approach to achieve bronchodilation despite this loss.

Authors' details

¹Department of Pathobiology, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio 44195, USA. ²University of Pennsylvania Medical Center, Pulmonary, Allergy, and Critical Care Division, Philadelphia, PA 19104, USA. ³Institute of Vegetative Physiology, Universität Würzburg, D-97070 Würzburg, Germany. ⁴Bayer Pharma AG, Aprather Weg 18a, D-42096 Wuppertal, Germany. ⁵Respiratory Institute, Cleveland Clinic, Cleveland, Ohio 44195, USA.

Published: 2 September 2015

doi:10.1186/2050-6511-16-S1-A26

Cite this article as: Stuehr et al.: sGC redox regulation and asthma. *BMC Pharmacology and Toxicology* 2015 **16**(Suppl 1):A26.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



* Correspondence: stuehrd@ccf.org

¹Department of Pathobiology, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio 44195, USA

Full list of author information is available at the end of the article