

ORAL PRESENTATION

Open Access

Structural insights into sGC activation by different activators

Focco van den Akker^{1*}, Faye Martin¹, Vijay Kumar¹, Xiaolei Ma¹, Johannes-Peter Stasch², Martina Schaefer², Padmamalini Baskaran³, Annie Beuve³, Pete W van Dunten⁴

From 5th International Conference on cGMP: Generators, Effectors and Therapeutic Implications
Halle, Germany. 24-26 June 2011

Background

The soluble guanylyl cyclase (sGC) is a key enzyme involved in the production of the second messenger cGMP. Due its cardiovascular relevance, sGC has been the target of numerous drug discovery efforts leading to the development of many different activators and stimulators with pharmaceutical potential. One of such compounds is the sGC activator Cinaciguat (BAY 58-2667) which is in clinical trials for acute decompensated heart failure.

Results

We present here our latest structure-function studies related to sGC activation by different sGC activators. The activator complex structures reveal an intriguing mode of heme mimicry by these compounds. The observed activation conformational changes center around the αF helix that contains the H105 residue normally held in place by the heme moiety in the absence of the activators.

Conclusion

The structural insights gained from the complex structures could be used for further optimization and development of sGC activators.

Author details

¹Department of Biochemistry/RT500, Case Western Reserve University, Cleveland, OH 44106, USA. ²Cardiovascular Research, Bayer Schering Pharma AG, Wuppertal D-42096, Germany. ³Department of Pharmacology and Physiology, New Jersey Medical School, U. Of Medicine and Dentistry of New Jersey, Newark, NJ 07103, USA. ⁴Stanford Synchrotron Radiation Laboratory, Stanford University, Menlo Park, CA 94025, USA.

* Correspondence: focco.vandenakker@case.edu

¹Department of Biochemistry/RT500, Case Western Reserve University, Cleveland, OH 44106, USA

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

Published: 1 August 2011

doi:10.1186/1471-2210-11-S1-O11

Cite this article as: van den Akker *et al.*: Structural insights into sGC activation by different activators. *BMC Pharmacology* 2011 11(Suppl 1):O11.

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

BioMed Central