

XIV JCET LECTURE, 15.02.2013, 9.00:

Crosstalk between mitochondrial and NADPH oxidase derived reactive oxygen and nitrogen species - implications for vascular function

Andreas Daiber

The 2nd Medical Clinic, Molecular Cardiology

University Medical Center of the Johannes Gutenberg University, Mainz, Germany

Oxidative stress is a well established hallmark of cardiovascular disease and strong evidence for a causal role of reactive oxygen and nitrogen species (RONS) in these processes is based on improvement of cardiovascular complications by genetic deletion of enzymes involved in the synthesis of these reactive species as well as overexpression of antioxidant enzymes detoxifying these reactive species. Vice versa, overexpression of RONS producing enzymes as well as deletion of antioxidant enzymes results in aggravation of cardiovascular complications. With the present overview we present and discuss different pathways how mitochondrial RONS interact (crosstalk) with other sources of oxidative stress, namely NADPH oxidases, xanthine oxidase and an uncoupled nitric oxide synthase. The potential mechanisms of how this crosstalk proceeds are discussed in detail. Several examples from the literature are summarized (including hypoxia, angiotensin II mediated vascular dysfunction, cellular starvation, nitrate tolerance, aging, hyperglycemia, β -amyloid stress and others) and the underlying mechanisms are put together to a more general concept of redox-based activation of different sources of RONS via enzyme-specific "redox switches". Mitochondria play a key role in this concept providing redox triggers for oxidative damage in the cardiovascular system but also act as amplifiers to increase the burden of oxidative stress. Finally, we discuss the role of mitochondrial RONS formation in cardiac disease as well as inflammatory processes but also the role of mitochondria as potential therapeutic targets in these pathophysiological states.

CURRICULUM VITAE

Prof. Dr. rer. nat. et med. habil. Andreas Daiber

(Diploma in Chemistry)

Andreas Daiber was born in 1970 in Balingen, Germany. From 1990-1996 he studied Chemistry at the University of Konstanz. In October 1997 he completed his Master work (Diploma) in Chemistry and in May 2000 he finished his thesis work in Biochemistry with honors (summa cum laude) obtaining the PhD degree. After 1 year of postdoctoral work at the chair of Medical Chemistry (Prof. Dr. Volker Ullrich) at the University of Konstanz, he applied for a postdoctoral position at the University Medical School Hamburg-Eppendorf, Department of Experimental Cardiology (Prof. Dr. Thomas Münzel) and worked in Clinical Biology for almost 3 years until he accepted the offer for an assistant professor position in Molecular Medicine in October 2004 at the Johannes Gutenberg University Medical Center. In December 2008, Andreas Daiber was offered the position of a full professor in Molecular Cardiology. Since 1999 he was the principal investigator in 5 research projects either funded by the German Research Foundation, the German Ministry of Education and Research or the European Community. Since 2006 he is the Head of the laboratory of Molecular Cardiology. In 2011 he held a guest professorship at the Université Joseph Fourier at Grenoble, France. Besides numerous memberships in national and international scientific communities, reviewer activities for several scientific journals, he published 83 original research articles, 44 reviews, 21 book chapters and coauthored more than 80 published conference abstracts.