Plenary Session Proposal
SFRBM 2009 Meeting

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Chairs: *Xingen Lei, Cornell University*
Kathy K. Griendling, Emory University
Chang Chen, Chinese Academy of Sciences

Topic/Title: *Dual Roles of Antioxidant Enzymes in Oxidative Stress and Chronic Diseases*

Topic Background: It has been widely perceived by the scientific field and the general public that antioxidant enzymes are beneficial to health because these enzymes protect against oxidative stress. However, recent studies with genetically-manipulated animal models indicate that overexpression or knockout of selenium-dependent glutathione peroxidase-1 (GPX1), catalase, Cu,Zn-superoxide dismutase (Cu,Zn-SOD), Mn-SOD, and extracellular SOD alone or in combination produces mixed outcomes. Paradoxically, enhancing and decreasing their expression aggravates and attenuates oxidative and nitrative stress in certain cases, respectively. These and other similar findings suggest that our understanding of oxidative stress and antioxidant defenses is naïve. While evidences are accumulating to illustrate dual roles as a probably common feature of antioxidant enzymes, a large portion of scientists and the general public is very confused by the intriguing or discrepant publications in the field. Therefore, we propose to assemble leading experts from interdisciplinary fields and request them to provide an updated review and analysis on the physiological outcomes, molecular mechanisms, and pathological implications for the dual roles of antioxidant enzymes in coping with reactive oxygen species and reactive nitrogen species.

To our best knowledge, SFRBM Annual Meeting has never hosted a session on this topic. Because of the tremendous scientific interests in antioxidants and the recent public confusions on the potential hazardous effect of antioxidants such as the possible diabetes-promoting role of supplemental Se for cancer prevention in the human trial (SELECT), we propose to hold a session on this topic as follows:

Speakers: We propose a session on ***Dual Roles of Antioxidant Enzymes in Oxidative Stress and Chronic Disease*** and suggest six speakers that are world leading and/or rising scientists in this field.

1. **Joseph Beckman, Linus Pauling Institute, Corvallis, OR**
Title: ***Paradoxical Roles of SOD in Enhancing Nitration by Peroxynitrite***
Contact: *Dr. Joseph Beckman***,** Ava Helen Pauling Chair, Linus Pauling Institute, Director and Professor, Department of Biochemistry and Biophysics, Environmental Health Sciences Center, Oregon State University 1011 Agriculture & Life Sciences Building, Corvallis, OR 97331; E-mail: joe.beckman@ oregonstate.edu, Tel: (541)-737-8867, and Fax: (541)-737-4371.

Dr. Beckman is a world-known leading expert in the field of SOD and peroxynitrite, and has made

significant contributions to our current understanding of nitrative stress. He has published numerous important papers including the recent one in Nature Protocols. He is a Principal Investigator and Ava Helen Pauling Chair, Linus Pauling Institute, Director, Environmental Health Sciences Center, and Professor, Department of Biochemistry and Biophysics, Oregon State University. He is currently serving as the Principal Investigator of a NIH R01 and a P01 projects related to this proposal.

2. Paul Epstein and Lu Cai, University of Louisville, KY
Title: ***Protective Role of Reactive Oxygen Species in Pancreatic Beta Cells***
Contact: *Dr. Paul Epstein***,** Carol B. McFerran Chair, Professor of Pediatrics and Pharmacology and Toxicology, Director of Pediatrics' Diabetes Research and University of Louisville Transgenic Core, Louisville, KY 40292; E-mail: paul.epstein@louisville.edu, Tel: (502)852-2669, and Fax: (502)852-5634.

Dr. Epstein is a world leading expert in the field of causes and complications of diabetes, with a particular focus on the complications of diabetic cardiomyopathy and nephropathy. He has published a series of highly influential papers in Cell, PNAS, Diabetes, JBC, and Free Radical Biology and Medicine on oxidative stress as a primary cause of diabetic nephropathy and cardiomyopathy. Recently, his group has discovered a promoting role of catalase and metallothionein in sensitizing diabetes in nonobese diabetic mice. Their findings indicate a protective role of reactive oxygen species in pancreatic beta cells and underscore the importance of the dual roles of antioxidant enzymes or proteins in chronic diseases. Dr. Epstein does not often attend the SFRBM meeting, and his participation in the session will promote the interactions between scientists from SFRBM and diabetes fields. Dr. Lu Cai is an Associate Professor in the departments of Medicine and Radiation Oncology, the University of Louisville. As a close colleague of Dr. Paul Epstein, he is a leading and active researcher in the area of diabetes and free radical biology.

3. Chang Chen, Institute of Biophysics, Chinese Academy of Sciences, Beijing
Title: ***Novel Function of S-nitrosoglutathione Reductase in Nervous System***
Contact: Dr. Chang Chen, 15 Datun Road, Chaoyang District, Beijing 100101, China; E-mail: changchen@moon.ibp.ac.cn, Tel: +86-10-64888406, and Fax: +86-10- 64871293.

Dr. Chen is Professor and Deputy Director of Center for Computational and Systems Biology in Institute of Biophysics, Chinese Academy of Sciences. Her research focuses on elucidation of the relationship between protein function and cellular redox status (redox-based posttranslational modification of protein, including S-nitros(yl)ation and other form SH-modification). She heads the group that discovered the new functions of S-nitros(yl)ation in DNA repair system, nuclear transport, sumoylation regulation, and developed proteomic quantitative methods to detect *S*-nitros(yl)ation. She found out that the bioactivity of NO is not only controlled by its synthesis, but is also controlled by its metabolism: NOS-GSNOR double-gate control should be considered. Her work is published in PLoS ONE, Nucleic Acids Research, J. Neurochem. In addition, she is an active leader of the Chinese Free Radical Biology Society and played an important role in hosting the 14th SFRR conference in Beijing last year. She will be an excellent representative of both young woman scientists and rising international scholars for the conference.

4. Cindy D. Davis, National Cancer Institute, NIH, DHHS, Rockville, MD
Title: ***Pros and Cons of Antioxidant Nutrients in Human Cancer Prevention***
Contact*: Dr. Cindy D. Davis*, Program Director, Nutritional Science Research Group, Division of Cancer Prevention, National Cancer Institute, NIH, DHHS, 6130 Executive Boulevard Suite 3159, Rockville, MD 20892; E-mail: davisci@mail.nih.gov, Tel: (301)594-9692, and Fax: (301)480-3925.

Dr. Davis is currently a Program Director in the Nutritional Sciences Research Group at the National Cancer Institute. This group plans, develops, directs and coordinates extramural research programs in diet, nutrition and cancer as it relates to cancer prevention. She first joined the Grand Forks Human Nutrition Research Center, USDA, as a research nutritionist. Her research focuses on the effect of trace minerals,

particularly, selenium and copper, on cancer susceptibility. She has published more than 90 peer-reviewed journal articles and six invited book chapters. She is on the editorial boards of The Journal of Nutrition, Experimental Biology and Medicine, and Nutrition Reviews. Because of her research expertise and current administrative position, Dr. Davis will be an excellent speaker to report the most recent controversy on the negative outcome of SELECT (using supplemental selenium and vitamin E for human cancer prevention). Her talk will highlight the human health implications of dual roles of antioxidants.

5. Kathy K. Griendling, School of Medicine, Emory University, Atlanta, GA
Title: *Role of Nox Proteins in Vascular Disease*
Contact: *Dr. Kathy, K. Griendling*, Professor of Medicine and Cardiology, 1639 Pierce Dr., WMB-319, Emory University, Atlanta, GA 30322; E-mail: kgriend@emory.edu, Tel: (404)727-8386, and Fax: (404)727-3585.

Dr. Griendling is a world-leading expert in the area of oxidative stress and cardiovascular disease. Her research involves delineating the redox-sensitive molecular mechanisms responsible for regulation of vascular hypertrophy and migration. In particular, she investigates the signaling mechanisms and alterations in gene expression induced by angiotensin II and PDGF in vascular smooth muscle cells, with emphasis on the role of oxidative stress in modulating these events. Her group has identified the major oxidase in the vasculature--the NAD(P)H-dependent oxidase--and current work is directed towards cloning the multiple subunits of this enzyme, understanding the mechanisms regulating its activation and expression, and defining its role in a variety of mouse models of vascular disease. She has published over 100 papers in highly-regarded journals and has received numerous research grants, honors, and awards from NIH, the American Heart Association, and High Blood Pressure Council. As a member of seven professional societies and a role model of female scientist, her participation in this conference will help promote SFRBM**.**

6. Xingen Lei, Cornell University, Ithaca, NY
Title: *Antioxidant Enzymes and Diabetes: Foe or Friend*
Contact: Dr. Xingen Lei, Professor of Molecular Nutrition, Morrison Hall 252, Cornell University, Ithaca, NY 14853; E-mail: XL20@cornell.edu, Phone: (607) 254-4703, and Fax: (607) 255-9829.

Dr. Lei is an active researcher in the field of selenium biology and molecular nutrition. He has pioneered in using the transgenic and gene knockout mouse models to study *in vivo* dual roles and molecular mechanisms of GPX1 and Cu,Zn-SOD in coping with reactive oxygen species and reactive nitrogen species. His group has reported the intriguing metabolic syndrome-like phenotype in the GPX1 overexpressing mice and has made significant progress in elucidating the related mechanism. His research findings have been published in highly ranked journals such as PNAS and JBC and have given a number of prestigious awards and honors. He is an associate editor of Journal of Nutrition and the chair of the 14th Trace Elements in Man and Animals (TEMA) conference to be held in 2011 in China. He has been invited to write a review on dual functions of antioxidant enzymes by the Physiological Review (impact > 26). This proposed session will be a great accompany to that review. As he is not an official member of the SFRBM yet, this proposal serves as his application for the membership.