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UPCOMING EVENTS



16TH ANNUAL MEETING

November 18 - 22, 2009
Hyatt Regency
San Francisco, CA USA

17TH ANNUAL MEETING

November 17 - 21, 2010
Caribe Royale Hotel &
Conference Center
Orlando, FL USA

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THE RADICAL VIEW

Irwin Fridovich, Ph.D.



DOT: What was your most exciting discovery in research?

Fridovich: The most exciting moment was the time that Joe McCord and I first realized that xanthine oxidase was producing free superoxide and that the proteins that competitively inhibited the reduction of cytochrome c by xanthine oxidase must have contained an enzyme that catalytically scavenged that radical. We named that enzyme superoxide dismutase. At that moment we had consistent explanations for a decades worth of puzzling observations.

DOT: What do you see as "hot" areas of redox biology/oxidative stress?

Fridovich: You cannot foresee the future; by definition something unexpected is going to turn up. If that is not the case then it is not really research; it is more like manufacturing. When they were building the first cyclotron and were just at the point of dedicating it, a reporter came to the director and asked him if he could tell him what he expects to learn from the new and very expensive machine. He answered, "If I knew the answer to that question, we would not have built it".

DOT: What influenced you to pursue a scientific career?

Fridovich: In regards to professional development, Dr. Masur and Dr. Handler were very important. Dr. Masur first got me interested in Biochemistry, while Dr. Handler was the most impressive person I have ever met and a good role model. I attended City College of New York where I double-majored in Chemistry and Biology. During my Senior year I was taking courses in Analytical Organic Chemistry and Biochemistry. I took the Biochemistry course out of simple curiosity, as I did not know what it was, but it was one of the few biochemistry courses offered at the time to undergraduates in the entire U.S. The Organic Chemistry course was taught by Dr. Kuch, who in addition to teaching Analytical Organic Chemistry had another job in New Jersey with the Cyanamide Company where he offered me a job after graduation. At almost the same time, Dr. Masur offered me a job at Cornell Medical School, where he had a research lab. I accepted Dr. Masur's offer, and told Dr. Kuch that I was sorry. In the Mazur Laboratory, we were isolating the material from the kidneys that affected blood pressure. I loved the work in Biochemistry and admired and respected Dr. Masur, so when he suggested that I should go to Graduate School, I instantly agreed. He recommended Duke University and he told me that I did not need to apply as I had been already accepted! He had arranged my admission to the Biochemistry Department with Dr. Philip Handler, who was a friend of his. I did my PhD and postdoc studies at Duke University with Dr. Philip Handler, who was the Chairman of Biochemistry. After the postdoctoral fellowship I was offered a Faculty position at Duke University. I have spent my entire professional life at Duke University and I have loved every minute of it.



See pages 3 & 4 for more about SFRBM 2009.

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PRESIDENT'S MESSAGE

It's time for members to start planning to attend SFRBM's 16th Annual Meeting, to be held November 18-22, 2009 in San Francisco. The meeting, which has long been the premier venue for cutting-edge research in all aspects of redox biology, will also feature the latest technologies and applications in basic and translational research.



Our 2009 program offers a broader and more extensive range of topics with the inclusion of six more plenary lectures from the leaders in our field. SFRBM has always nurtured a collegial environment for the open exchange of the latest scientific advances, whether from a first-year graduate student, or from established investigators. Whether through poster symposia or our popular oral presentation sessions – where 50 abstracts will be selected through a rigorous peer review process – your most dynamic and exciting science will be on display. See pages 3-4 for more information about SFRBM 2009.

Since my last message, SFRBM's committees have been working diligently to develop valuable initiatives to benefit members in these challenging economic times. First, we have implemented the "SFRBM Cares" program, which provides members with an extra two (2) months to renew their membership in 2009. During this period, they continue to have access the latest scientific research via their on-line subscription to FRBM and receive other important society information. SFRBM has also extended the length of a postdoctoral fellow membership from three to five years from the date researchers received their doctorate.

For those members who might not have attended SFRBM 2008 in Indianapolis, please note that all presentations from our popular Free Radical School are posted at www.sfrbm.org so that you can download the slides as well as the speaker's accompanying audio file. SFRBM is working on several additional upgrades to the site, including re-instituting our Member Directory – useful for scientific collaborations – into a special member's only section.

SFRBM is in the midst of developing several Strategic Alliances that we hope will help our society grow as well as provide valuable educational opportunities to scientists outside of our primary field of expertise. Dr. Garry Buettner (Univ. of Iowa) represented SFRBM at the Society for Toxicology's Annual Meeting in March and delivered a well-received lecture on "The Basics of Free Radicals." As a result of SFRBM's direct support of the 4th International Workshop on Comparative Aspects of Oxidative Stress in Biological Systems in early April, 110 Mexican students and researchers are now SFRBM members for the next year and will receive an on-line subscription to our journal.

As always, this is your society so please let us know any suggestions or comments that you have.



**SFRBM's 16th Annual Meeting
November 18-22, 2009
Hyatt Regency Embarcadero
San Francisco, California**

SFRBM has secured a special room rate of \$150 per night.
On-line registration information will be available June 2009.

FEATURED PLENARY SESSIONS

- **Signaling at Membrane Microdomains: All Redox is Local**

Chairs: Michael Espey, Ph.D., NIH and Bulent Mutus, Ph.D., University of Windsor

Plasma membrane microdomains known as lipid rafts have emerged as an archetypical signaling scaffold. Cells utilize lipid rafts to sense and organize their responses to exogenous cues. A basic understanding of membrane lipid raft components and dynamics can translate into new drug design and better therapeutic strategies.

- **Oxidative Damage to DNA, Repair, Clinical Relevance**

Chairs: Henrik E. Poulsen, MD, University of Copenhagen, Denmark and Kevin Moore, MD, Ph.D., Royal Free & UCL Medical School, UK

Oxidative modification to DNA can have severe consequences for the cell and has been area of interest in the field for many years. The area has had methodological challenges, but these have recently been resolved to a high degree, and solid data with clinical relevance has emerged, as well as interesting insights into basic research. This session will focus on these aspects with a special emphasis on DNA modifications in human disease.

- **Paradoxical Roles of Oxidants and Antioxidant Enzymes in Metabolism and Diseases**

Chairs: Xingen Lei, Ph.D., Cornell University and Kathy K. Griendling, Ph.D., Emory University

Recent studies, in particular with genetically-manipulated animal models, demonstrate intriguing dual roles of oxidants and antioxidant enzymes in oxidative stress associated with metabolism and chronic diseases. Four leading experts from interdisciplinary fields will provide an updated, in-depth review on the physiological outcomes, molecular mechanisms, and pathological implications of altering cellular, tissue, and body status of oxidants and antioxidant enzymes.

- **ROS, Redox Regulation, and Redox Imaging in Cancer**

Chairs: B. Kalyanaraman, Ph.D., Medical College of Wisconsin and Daret St. Clair, Ph.D., University of Kentucky

Increasing evidence suggests that the redox balance between ROS/RNS generation and elimination helps maintain proper function of redox-sensitive signaling proteins in tumor cells. Whereas moderate levels of ROS/RNS (low levels of oxidative stress) are essential for cancer cell proliferation and survival, higher levels of oxidants (more severe oxidative stress) cause cancer cell death. Strategies to manipulate oxidant levels and oxidant-induced cell signaling may have significant implications in cancer therapy and will be highlighted in this symposium.

- **Ascorbic Acid: New Discoveries for an Old Vitamin**

Chairs: Balz Frei, Ph.D., Linus Pauling Institute and Maret G. Traber, Ph.D., Linus Pauling Institute

More than 70 years after its discovery, ascorbic acid remains a fascinating molecule that galvanizes scientists and the public alike. This session will cover ascorbate's redox chemistry that underlies a myriad of biological and physiological actions, from enzyme activities to antioxidant and pro-oxidant effects to possible roles in chronic disease prevention and cancer therapy.

- **Redox, Recipes and Food for Thought**

Chairs: Garry Buettner, Ph.D., University of Iowa and Lin Mantell, MD, Ph.D., North Shore University Hospital

What is the science behind the popular axiom of -- you are what you eat? There is ample evidence for harm due to nutritional deficiencies and ingestion of toxic agents. In contrast, the notion of benefit from diet has been difficult to characterize beyond the test tube. The session brings together several perspectives on the nutritional requirements for redox homeostasis.

SPECIAL SESSIONS & EVENTS

SFRBM will provide some great education and professional development opportunities for scientists at all levels.

Grantsmanship Workshop

Wednesday, November 18

3:30 – 6:00 pm

Ed Postlethwait (UAB) will lead this popular workshop aimed at younger investigators interested in learning the nuances of the NIH funding system and other funding bodies. This year, emphasis will be on training and entry level grants, plus updated information on NIH programs and the basics of crafting a proposal.

Negotiating for Success

Thursday, November 19

6:00 – 9:00 pm

The 7th Annual Opening Doors event, organized by SFRBM's Women in Science Committee is open to all. Attendees at this dinner workshop (price includes meal) will learn the basics of skillful negotiations, with experts from the society including senior professors and chairs sharing their negotiating secrets. Not to be missed by anyone up for promotion!

The Hitchhiker's Guide to Publishing a Highly Cited, High Impact Manuscript

Saturday, November 21

12:15 – 1:30 pm

Bruce Freeman (University of Pittsburgh Medical Center) and Anthony Newman (Elsevier) will speak about the changing face of publishing in the 21st century. This lunchtime workshop (price includes meal) will equip investigators of all ages with the skills to publish high impact papers in this challenging environment.

Registration for these workshops is often over-subscribed, so be sure to check out the full details on the SFRBM website, and register early.

Sunrise Free Radical School

Thursday, November 19 - Saturday, November 21

8:00 - 9:00 am

For the 15th consecutive year, the Sunrise Free Radical School will kick off each day of our Annual Meeting. Led by Balaraman Kalyanaraman (Medical College of Wisconsin), Alicia Kowaltowski (University of São Paulo, Brazil), and Aimee Landar (University of Alabama at Birmingham), the Free Radical School is designed to provide a detailed overview of the basic concepts of free radical chemistry and biology and is targeted towards students, fellows and those wishing to learn about new areas. This year we have selected a faculty of highly respected investigators in free radical research who will deliver lectures that complement both the workshop and plenary sessions.

ABSTRACTS

Abstracts are now being accepted through Tuesday, September 1 for SFRBM 2009. Please note that submitted abstracts must be previously unpublished work. Decisions on abstract acceptance for SFRBM 2009 will be posted on the SFRBM site during the week of October 5, 2009. Visit www.sfrbm.org to learn more about submitting an abstract.

2009 SFRBM Abstract/Poster Categories:

- Aging
- Antioxidants and Novel Therapeutics
- Cancer
- Cardiovascular Diseases
- Chemistry and Reaction Mechanisms
- Diabetes-Metabolic Syndrome
- Generation and Action of Reactive Species
- Inflammation and Immunity
- Neuroscience
- Nitric Oxide and its Interactions
- Nutrition and Health
- Oxidation of Macromolecules
- Proteomics and Genomics
- Pulmonary Diseases
- Signal Transduction and Gene Expression

LITERATURE REVIEW

Readers interested in nominating a paper or providing a short editorial review (less than 150 words), should contact Ashleigh Bates at abates@hp-assoc.com.

Role of Superoxide, Nitric Oxide and Peroxynitrite in Doxorubicin-Induced Cell Death in vivo and in vitro.

Mukhopadhyay, P. et al. Am J Physiol Heart Circ Physiol (March 13, 2009). doi:10.1152/ajpheart.00795.2008.

Doxorubicin (DOX) continues to be a widely used chemotherapeutic agent to treat a variety of cancers, despite its potential to elicit serious dose-dependent cardiotoxicity leading to degenerative cardiomyopathy/heart failure. DOX causes cell death, but the molecular mechanism involved remains elusive. This paper used a multitude of cool techniques to provide evidence that peroxynitrite is the major trigger of DOX induced cell death in cardiomyocytes both in vivo and in vitro. Generation of mitochondrial superoxide played a role in DOX-induced cardiotoxicity; however, nitric oxide was also required for cardiotoxicity; implicating peroxynitrite. DOX clearly increased nitrotyrosine formation that was independent of myeloperoxidase, and could be effectively blocked with peroxynitrite scavengers, or iNOS inhibitors, and SOD. These scavengers prevented toxicity in vivo and in vitro and elegant experiments clearly showed that DOX-mediated peroxynitrite generation lead to downstream activation of the mitochondrial and PARP dependent cell death pathways. Further work in evaluating peroxynitrite scavengers as possible therapeutic agents in preventing DOX-mediated cardiotoxicity appears to be warranted. *Review by Lee Ann MacMillan-Crow, Univ. of Arkansas for Medical Sciences.*

Dietary Nitrite Prevents Hypercholesterolemic Microvascular Inflammation and Reverses Endothelial Dysfunction. *Stokes, K.Y. et al. Am J Physiol Heart Circ Physiol (February 27, 2009). DOI:10.1152/ajpheart.01291.2008.*

Nitrite supplementation has proven beneficial in the treatment of various vascular inflammatory processes. The precise mechanism(s) underpinning these positive effects is currently under extensive debate however, there is a consensus that nitrite offsets endothelial dysfunction by serving as a reservoir of beneficial NO. In this paper, Stokes and colleagues reveal how dietary delivery of nitrite reverses several negative effects of hypercholesterolemia. Using C57Bl/J6 mice fed a high cholesterol diet; the authors demonstrate that supplementing the drinking water with nitrite normalizes plasma triglyceride levels and reverses endothelial dysfunction. In addition, nitrite served to abrogate the enhancement of adherent and emigrated leukocytes resulting from hypercholesterolemia. Nitrite supplementation was successful in normalizing high cholesterol diet-induced enhancement of C-reactive protein levels in the plasma and reversed hypercholesterolemia-mediated reduction of BH4. Combined, these carefully designed set of experiments clearly demonstrate the benefit of nitrite supplementation in reducing vascular inflammation and further stimulate the growing enthusiasm surrounding the nitrite field. *Review by Eric E. Kelley, University of Pittsburgh.*

Association of Reactive Oxygen Species Levels and Radioresistance in Cancer Stem Cells. *Diehn, M, Cho, R. W. et al. Nature. 2009 Apr 9;458(7239):780-3.*

Reactive oxygen species have been implicated in survival and self-renewal capacity of hematopoietic stem cells. This new study suggests that cancer stem cells (CSC) limit ROS production rendering them resistant to ionizing radiation. The investigators provide evidence that mammary epithelial stem cells with low DCF fluorescence have the ability to repopulate cleared mammary fat pads. Gene set enrichment analysis of breast CSC reveals that ROS metabolizing genes are elevated relative to non-tumorigenic

FREE RADICALS ABROAD

The DOT is beginning a series of articles spotlighting the research of SFRBM members outside the U.S. in order to increase awareness and foster collaborative efforts among all SFRBM members.

Our first stop is the laboratory of Dr. Laura Castro (right), Department of Biochemistry, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay. Dr. Castro's laboratory focuses on free radical-mediated damage/antioxidant intervention in biological systems by investigating the enzymatic production, chemistry and metabolism of both reactive oxygen and nitrogen species. This is exemplified by her studies demonstrating NO and ONOO⁻-dependent aconitase inactivation and her reports revealing cytochrome c serves as both a target for nitration as well as a H₂O₂-dependent catalyst of protein nitration. Anchored in the solid foundation of world-renowned free radical biochemistry in Montevideo, Dr. Castro's laboratory is pushing back the envelope to elucidate the complex interplay between ROS, RNS and biomolecules. Contact Dr. Castro at lcastro@fmed.edu.uy. *Article by Eric E. Kelley, School of Medicine, University of Pittsburgh.*



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Literature Reviews, *continued from page 5*

cells. CSC from human tumors or those isolated from spontaneous tumors of MMTV-WNT1 mice also display low ROS levels. These CSC populations are resistant to ionizing radiation induced DNA damage and resistance is attributed to increased antioxidant gene expression. These studies establish a tight connection between free radicals and cancer stem cell survival. It is also intriguing that the much maligned fluorophore, DCF, can be used to vitally select cells based on their intrinsic redox-state. *Review by J. Andres Melendez, Albany Medical College.*

Role of oxidative stress in the renal abnormalities induced by experimental hyperuricemia. Sánchez-Lozada, L., et al *Am J Physiol Renal Physiol* 295: F1134-F1141, 2008.

A 40-year-old controversy concerns the powerful reducing agent uric acid. Urate is a potent antioxidant associated with longevity, a neuroprotectant, and a cellular redox-messenger. However, the conditional pro-oxidant properties of urate may figure in (e.g.) gout, Lesch-Nyhan Syndrome, atherosclerosis, metabolic syndrome, and possibly in tissue-protective "preconditioning". Likewise, as "Orgotein", ectopic superoxide dismutase (SOD) ameliorates hyperuricemic syndrome in Dalmatian dogs, implying a pathogenic role for superoxide. Similarly, Sanchez-Lozada et al report that an SOD-mimetic, TEMPOL, reverses much kidney damage associated with relative-hyperuricemia in rats given the urate-oxidase-inhibitor oxonic acid. Significantly, plasma urate levels of their oxonate-treated rats measured about 3 mg/dl, well-within the human reference range. Long-term TEMPOL treatment protects glomeruli and reverses urate-associated hypertension as well as renal afferent arteriopathy and other anatomical and biochemical changes. The efficacy of SOD's and SOD-mimetics in ameliorating chronic urate "toxicity" has important etiologic and therapeutic implications. *Review by Peter H. Proctor, Proctor Clinic.*

SYMPOSIUM HONORS OBERLEY'S RESEARCH & LIFE

On April 3-4, 130 friends, family and colleagues of Dr. Larry W. Oberley gathered at the University of Iowa to honor his scientific achievements. The work of Dr. Oberley's group led to the hypothesis that manganese superoxide dismutase functions as a tumor suppressor and fueled an explosion of research into the role of oxidants in cancer. Presentations, talks and posters from former trainees, collaborators and contemporaries highlighted Dr. Oberley's achievements and seminal discoveries. Highlighting the meeting were key note lectures from Joe McCord on the history and future of SOD research and James Crapo on the use antioxidant mimetics in cancer research. Visit http://www.uiowa.edu/~frrbp/oberley_sym_events.html for a detailed meeting itinerary. *Submitted by J. Andres Melendez, Albany Medical College.*

Radical View, *continued from page 1*

DOT: What advice would you give to young researchers entering the field?

Fridovich: The most important thing is to be fascinated by the field you choose to work in, because if you really like what you are doing it would be very easy to work hard and to be productive. To really understand a field you should first work in it for a long time. Then you will be able to facilitate the work of others. Doing editorial work should come later, towards the end of a career in science.

DOT: What do you think about the direction that the Oxidative Stress field is going?

Fridovich: In early years of this endeavor we were finding out the basic facts about the enzymes and the reactions involved. Nowadays, the findings are more about protective effects of plant extracts, and more about practical applications; where you can not write down the chemistry that is going on. The former is more interesting to me.

DOT: What do you think about the political issues and business aspects of present science and research?

Fridovich: In the past you pursued the research in order to gain answers to questions that you had, without any thoughts about applications, or licensing, or patenting. It was just a quest for new knowledge. I see the opportunities presented by worked out patenting and licensing as a diversion from the real purpose of basic science.

DOT: How do you view your "Laboratory" vs "Office" years?

Fridovich: The part that I enjoyed most was the first 20 years of my career, when I did bench work. My hands were thinking during experiments- you have an intuitive feeling for what is going on. When you are cut off from the bench work it becomes less intuitive and less easy. For the past three decades I have tried to facilitate the work of other people who were doing the bench work. That is also rewarding, but the first two decades were more fun.

DOT: How do you achieve balance between your personal and professional life?

Fridovich: Everybody has some spare time and you choose how to spend it. When the children were small I spent my spare time with them. Now I spend it canoeing, wood working, gardening- doing something constructive rather than watching TV or golfing.

Interview by Ines Batinic-Haberle, Duke University Medical Center.