Society for Free Radical Biology and Medicine
Established 1987

SFRBM dot

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IN THIS ISSUE:

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Henry
FORMAN

President's Message

Henry Jay Forman, Ph.D.

I hope that you have all had an enjoyable summer and beginning of your fall activities. This is my eighth and final message as SFRBM President. It has been a pleasure to serve in that role, particularly as the Society has made some major strides towards greater recognition of the work that we do.

Here is a list of major goals SFRBM has achieved or begun in the past two years:

• Joined FASEB to increase advocacy efforts and develop stronger NIH relations. SFRBM Past President, Harry Ischiropoulos, will represent the Society on the FASEB Council.

• Hired public relations firm (Carney Communications) to develop and implement a PR plan focused on increasing the value and breadth of the SFRBM brand.

• Published the initial issues of *Redox Biology*, our Society's second journal, which we share with the Society for Free Radical Research – Europe. The journal is doing well as evidenced by a great number of downloads of articles, all of which are open access. The journal is currently looking for a new Associate Editor *(See page 8)*.

• Reformulated the *FRBM* Publications Committee so that it has greater authority in selection of Editors, society interactions with the publisher, and representation of our junior partner in the journal, SFRR-Europe.

• Formulated the *Redox Biology* Publications Committee to equally represent both SFRBM and SFRR-Europe in managing the journal and appointing editors.

• Created our Trainee Council, which has direct representation on SFRBM Council.

• Created a Mentoring Excellence Award.

• Produced a membership recruitment video.

• Provided $60K in support for career development for Young Investigators in the form of travel awards and mini-fellowship.

• Began a new contract with our publisher for *FRBM*, increasing the royalty revenue coming back to the society.

In the last DOT, I mentioned changes are taking place with the *FRBM* Associate Editors and the wonderful work Jack Roberts has done in that role. This year will also end the long service of Balaraman Kalyanaraman as an Associate Editor. Raman was one of the first three Associate Editors and has consistently handled the most manuscripts. Each year, his expertise in free radical chemistry and biology and electron spin resonance, in particular, has been of great importance to the journal becoming the premier forum for original research in the field. New Associate Editors will be appointed by the Publications Committee in the near future.

Having also been one of the first three Associate Editors with Raman and Matt Grisham, and then becoming the Reviews Editor, I also will be ending my service as an editor. The new Reviews Editor will be Giovanni Mann and he and I will be working together until the end of June 2015. We currently are working on a special issue on Nrf2 with some of the leading experts as guest co-editors.

The meeting in November will bring to a close my two years as President. Our next President, Neil Hogg, has already demonstrated to be a very active President-Elect, and I am confident that SFRBM will have excellent leadership for the next two years. I thank the Society's membership for giving me this wonderful opportunity to give back to our scientific community.

Radical View • Helmut Sies, MD, Ph.D.

by Alvaro Estevez, Ph.D., University of Central Florida

Helmut SIES

DOT: Tell us a bit about your background and how you got started in science.

Before I go into this, please let me clarify: mine is a "Non-Radical View", because my core interests were on hydrogen peroxide (H2O2) and singlet molecular oxygen (1O2), and peroxynitrite (ONOO-), all three being non-radicals.

I was born in 1942 in Goslar (Germany), which after the war was only a few miles to the West of the Iron Curtain, and I was raised in the nearby town of Seesen at the foothills of the Harz mountains. We could ski from our home, and at open spots on frozen ponds could watch the colorful kingfisher (Eisvogel) in the winter. Watching individual snowflakes through a simple microscope was an early impression. The elementary school teacher, Georg Henkel, supported our interest in nature, helping us make our own little 'discoveries'. The high school, Jacobson-Schule, offered Latin and physics by particularly gifted teachers, laying the foundation of what I would call (and hope for) 'coordinated thinking'.

The Michigan Council of Churches (Ann Arbor, Michigan) had a program for students to come to the United States for a high school year, and in 1959, I was one of the fortunate ones to sail on the Greek Liner "Arcadia" across the Atlantic ocean for a formative first half-year in the family of David P. Ward, M.D., at Pleasant Plain, Ohio, outside of Cincinnati. In his attic, he had a wonderful library of books, e.g. "The Theory of Resonance" by G.W. Wheland, and also Greek philosophers. Maybe these times further contributed to a genuine interest in science and its relationship to medicine.

Having returned to Germany and having tried to make up for a year of no Latin and almost no physics (I tried to take it as a sport), the University time started in 1961 at the University of Tübingen, with a studium generale at the Leibniz-Kolleg and as a medical student. Tübingen then was rich in excellent scientists, creating a bustling atmosphere particularly in biological sciences, and we as beginners were exposed to top-notch lectures, and biochemistry seemed to attract me most.

A top group in Physiological Chemistry at that time was that of Theodor Bücher, at Marburg University. Bücher had been a Ph.D. student with Otto Warburg in Berlin. He was about to move to the Ludwig-Maximilians-University at Munich, and I was fortunate to be accepted by him for my experimental M.D. thesis work in 1962. This is how it got started.

DOT: Can you trace a developmental line from then all the way to your current research interests?

Sure, although in hindsight things tend to look much more 'logical' than they were in reality. The little remembrances I mentioned from elementary school time, in one way or another, recur at later times and in different forms, but clearly the early excitement about learning something about nature and biology is a common thread. A main contributing factor is curiosity, together with a certain naïve way of looking at problems and, importantly, trying to employ new methods of addressing central questions.

DOT: What could be such a sequence, like in a chain of keywords?

Physiological chemistry—steady state enzyme kinetics (M.D. thesis 1967)—organ spectrophotometry—perfused liver—mitochondrial cytochromes—extramitochondrial cytochromes (cytochrome P-450)—catalase compound I in peroxisomes (Habilitation thesis 1972)—demonstration and quantitation of H2O2 in intact cells—glutathione peroxidase activity in situ—GSSG release—NADPH oxidation—GSH release—biliary release of glutathione S-conjugates—H2O2 metabolism—oxygen gradients, hypoxia—metabolic compartmentation (1982)--selenium biochemistry—ebselen as a GSH peroxidase mimic—single-photon counting (ultraweak photoemission)—lipid peroxidation—ethane release—antioxidants—oxidative stress

(1985)—tocopherols—carotenoids—nutritional biochemistry—photoprotection—peroxynitrite biology—polyphenols—cocoa polyphenols and vascular endothelium—selenoproteins.

Sorry, this list could be more detailed, and it is not truly a linear sequence, things come back around in circles, as methods evolve and new discoveries enlarge the field of redox biology. And it is amazing how this field currently is exploding towards a new level, with the modern imaging techniques reaching the molecular level!

DOT: Who has been your greatest teacher?

Theodor Bücher, chair of physiological chemistry at Munich, was an ingenious scientist and a most generous thesis advisor. He was able to propagate his genuine interest is biological research to his students and coworkers. Not only that, he gently led the way, making oneself think it was own decision-making, often by pointing out yet another ingenious way or method to make a problem testable experimentally in a more elegant or more direct way. Introducing novel methods allowing to monitor processes noninvasively was his motto.

Another major trait of his guidance was, early on, to let the student figure out him/herself about what's next and how and when to give up. What I say now to my students is what I learned from him: "Experimental work is to learn to live with a constant level of frustration!" Not everything works right-on, but either way there is an answer leading further. "Don't believe anything, even if published in textbooks!" Phrased differently: "Repeat the work that is the basis of your own future endeavors!" "Good controls!" "Make your own clean glassware", etc...!

Another trait I will come back to later, if you permit: early freedom, early 'own project'.

Britton Chance, head of the Johnson Research Foundation (JF) at the University of Pennsylvania, Philadelphia, was the icon of mitochondrial bioenergetics research in the 1960s. His institute was the mecca of redox biochemistry for a generation (actually, much more than that) of young and advanced scientists around the world. I had the great fortune to have caught his eye after telling him of the finding that in the normal intact perfused rat liver catalase was present as catalase Compound I, and that this depended on the infusion to the liver of substrate for H2O2 production or for peroxidatic reduction, such as ethanol or methanol. This work was made possible by Bolko Brauser's ingenious adaptation of the 'Rapidspektroskop' to a highly sensitive organ spectrophotometer in the Munich lab.

Brit, as we called him, and I jointly published a FEBS Letters on the H2O2 discovery in the liver, and we then embarked on further fruitful times at the JF, where I worked closely together with Nozomu Oshino from Osaka, and also with Alberto Boveris from Buenos Aires. The whole atmosphere at the JF, with the lunch seminars, and with lots of scientists working there, or passing through, was a great and unmatched stimulus in my career. Just to mention a few: Ron Estabrook, John Williamson, Ron Thurman, Toni Scarpa, Angelo Azzi.

DOT: What do you think are the most important factors that shaped your career? What influenced you to pursue a scientific career?

The joy of exploring the unknown, and even finding something novel and noteworthy; thanks to new methods and materials; but more importantly thanks to what you might call the research environment, the mentor, the doctoral students, the dedicated technicians. All of that I was fortunate to have access to at an early time. Although I finished the clinical studies and worked in clinical medicine for two years afterwards, the early exposure to experimental research in basic science fascinated me enough to embark on the postdoc pathway, with no regrets.

The exposure to bedside medicine reinforced the interest to explore the molecular basis of physiological and pathological processes, based on sound natural science.

DOT: When did you feel you were a "scientist"?

You mean when did I sense a certain level of achievement? Well, it probably relates to perceiving trust by others important in providing options: a mentor (Theodor Bücher) who permits work on an 'independent' project, a funding organization that early on provides grant support (Deutsche Forschungsgemeinschaft, National Foundation for Cancer Research), invitations to give seminars, inquiries from scientists to collaborate. All of this creates a core lab from which to build an international web of friends and colleagues. At that point one may find oneself as a peer among similarly oriented colleagues. It is highly motivating to be devoted to fascinating scientific questions across political or other borders.

In Munich, a dozen or so young scientists spontaneously met to discuss hot topics in redox research, and in 1977 we formed, maybe one of the first, an Oxygen Club ('Münchener Sauerstoffclub'), initially meeting bimonthly in a Bavarian beer garden.

DOT: Where do you think the Oxidative Stress field is going?

Subsequent to the early formulation of the concept of oxidative stress in

1985, several waves of research achievement ensued. I had the pleasure to be involved in the very early work on OxyR during my sabbatical with Bruce Ames at UC Berkeley, being amazed by the enormous increase in spontaneous mutagenesis in OxyR-deleted cells, and in blunting bacterial aerobic mutagenesis in OxyR-overexpressing cells. This was done together with Gigi Storz who later on elegantly elucidated the molecular basis of the mechanism by which H2O2 acts in this bacterial cellular redox switch. Major eukaryotic redox switches were discovered, NFkappaB, Nrf2/Keap1 and others, and redox control of signalling cascades is common knowledge these days. In 2007, Dean Jones and I updated the definition of oxidative stress to include the role in redox signalling.

The enormous current advances, not the least in the plant field, put redox biology on a new level, with highly useful genetically encoded molecular probes, Vsevolod Belousov's HyPer as a prototype. It is satisfying to see that the redox-sensitive component of HyPer and its congeners comes from OxyR!

In short: in terms of fundamental research, the oxidative stress field is going strong.

DOT: And in the other direction, translational research?

Thanks for this important question: A strong word of caution is warranted here! With some scientists together with highly motivated colleagues in industry, there has been a hype in overstressing oxidative stress in inappropriate ways. This led to translation into the public that anything 'antioxidant' is 'good for you', something like a fountain of youth, and then there developed all the marketing activities associated with the health food business. The idea that small-molecule compounds which exert antioxidant activity in the test tube could be used as wonder drugs has blemished the field. So much so, that in recent times among scientists the words 'oxidative stress' or 'antioxidants' generate adverse reactions, resulting in the the pendulum going the other way: 'Vitamin C is detrimental in sports medicine', or the like.

The negative trend is amplified by the inappropriate use of simple kits measuring 'total antioxidant capacity' (TAC) in plasma samples in vitro (which are neither 'total' nor do they involve the major cellular antioxidant enzymes). So, for a while we will still see publications of studies relying on these inconclusive assays.

I think finally the pendulum will return to a reasonable setting. To me there is no doubt that cellular and extracellular oxidants need to be matched by appropriate strategies for antioxidant defense. The issue is the fine-tuning and the biological redundancies for important processes.

DOT: What is your current interest as an emeritus professor?

In research, I am still interested in redox biology in general, notably H2O2 redox signaling. In nutritional biochemistry it is the field of cocoa polyphenols and vascular health, where together with Düsseldorf cardiologists Malte Kelm and Christian Heiss we were fortunate to show in 2002 that high-flavanol cocoa exerted astonishing positive vascular effects related to NO metabolism. Experimentally, in a small group with Holger Steinbrenner we are addressing fascinating topics in the field of selenoproteins, particularly in the area of gastrointestinal inflammation and the metabolic role of Se in adipocytes.

In the Oxygen Club of California (OCC), initiated by Lester Packer, together with Enrique Cadenas, I am gladly contributing to shaping meetings, helping young scientists to get a platform just as I got when I was in the beginning stages.

DOT: Final question: What do you think of SFRBM?

A great Society, whose developmental stages I have been following closely. The meetings and the journals are superb, and growing membership shows its continuing attractiveness. And happily for all of us, SFRBM is part of the global umbrella, the Society for Free Radical Research International (SFRRI), so we all are active in a truly international scientific network.

CONNECT **WITH US....**

We want to hear from you! Our Facebook and Twitter pages are a great way to let other SFRBM members, the media and industry influencers know what you are doing. So, if you're involved in some amazing research, if you see an article you think people should read or if your organization is doing something that will have an impact on our industry, send it our way.

Here are two ways to do that:

1. Via the web:
   carneycommunications.com/sfrbm
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Oxidative Stress

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Live-cell compatible	Yes	Yes	Yes
Can be added to complete media	Yes	Yes	Yes
Formaldehyde fixable	Yes	No	Yes
Multiplex ready	No	No	Yes
Signal to noise	+++++	+++++	+++++
Photostability	+++	++++	++
GFP compatible	No	Yes	Yes
RFP compatible	Yes	No	Yes
Cat. No.	C10422	C10443	C10444

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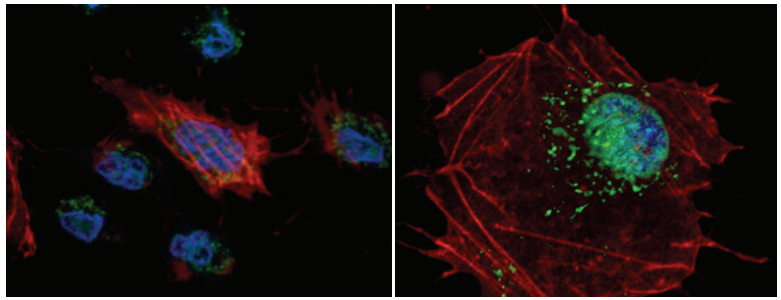

Imaging oxidative stress with CellROX® Green Reagent. Human osteosarcoma (U2-OS) cells expressing CellLight® Actin-RFP were treated with 100 µM menadione. Cells were stained with CellROX® Green Reagent (Cat. No. C10444) and NucBlue™ Live Cell Stain (Cat. No. R37605), washed, and imaged with Live Cell Imaging Solution (Cat. No. A14291DJ).

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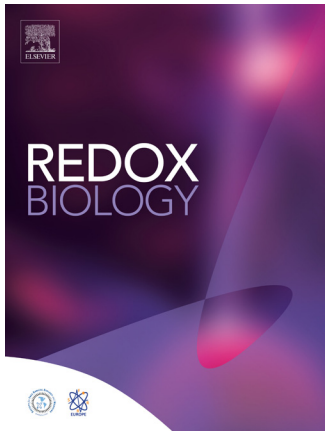
REDOX BIOLOGY - CALL FOR ASSOCIATE EDITOR

Starting January 2015, Application Deadline October 20, 2014



The Society for Free Radical Biology and Medicine (SFRBM) is seeking applications for an new Associate Editor based in "The Americas" (North, Central or South America), for the journal *Redox Biology* to start January 1, 2015. Details of the journal's aims and scope and editorial policy can be found at the journal's home page www.elsevier.com/locate/redox.

Preference will go to individuals with experience in the areas of aging, nutraceuticals, lifestyle interventions, neurobiology or cancer. Candidates with experience in other areas of redox biology are also encouraged to apply. Ideal applicants will be experienced, established investigators with an active research program in any of the above topic areas published by the journal. Prior experience on the editorial board of a journal would be an advantage, particularly in the redox biology field.

The duties of an Associate Editor are:

- To encourage submissions to the journal,
- Write editorials and collate virtual collections as requested by the Editors-in-Chief,
- Give oversight to themes or virtual collections, and
- Review all manuscripts they are assigned, select reviewers and prepare an integrated critique of the manuscript for the authors.

The Associate Editors will render decisions to maintain its rigorous scientific standards in a timely manner on manuscripts submitted to *Redox Biology* through a central office. The Associate Editors are expected to contribute at least one article to the journal per year, and participate in phone conferences as requested by the Editors-in-Chief and publisher. It is anticipated that Associate Editors will be members of SFRBM and the journal's publications committee and are encouraged to participate in these meetings.

Appointments are for an initial period of two years, renewable for a maximum of two further periods, as directed by the publications committee. Elsevier, the publisher, provides an honorarium and expenses.

To apply, provide a cover letter stating the reasons you would be an ideal person to be a new *Redox Biology* Associate Editor detailing previous editorial experience, along with a current CV. These must be in a single document in PDF format and sent as an attachment of under 5MB, in an email to both André Melendez, Publications Committee Chair at jmelendez@albany.edu and Kent Lindeman, SFRBM's Executive Director, at klindeman@hp-assoc.com.

Questions regarding editorial duties and journal philosophy may be directed to the Editors-in-Chief, Dr. Tilman Grune at tilman.grune@uni-jena.de or Dr. Victor Darley-Usmar at darley@uab.edu. For full consideration, send your application no later than October 20, 2014.

Plan to join us during SFRBM's Annual Meeting to be held NOVEMBER 19-23 in Seattle, WA, USA

FEATURED SESSIONS

- **Insights into Mechanisms of Neurodegenerative Diseases**
- **The Keap1-Nrf2 Signaling Pathway: Role in Disease and Pharmacological Approaches**
- **Oxygen in Development and Cancer**
- **Important Biological Functions of the Neglected Sources of Reactive Oxygen Species**
- **Translation of Redox Methodology from Bench to Bedside — Problems and Solutions**

SFRBM
NOVEMBER 19 - 23, 2014
SHERATON SEATTLE • SEATTLE, WA

ORAL PRESENTATIONS & POSTER SYMPOSIA CATEGORIES

- Adaptative Responses
- Biological Formation of Reactive Species
- Biological Regulation by Reactive Oxygen Species
- Cancer, Cell Proliferation and Death
- Cardiovascular Redox Biology and Pathology
- Chemotherapy
- DNA Damage and its Consequences
- Free Radical Chemistry and Biochemistry
- Hydrogen Sulfide Chemistry and Biology
- Inflammatory Oxidative Signaling and Injury
- Lipids In Redox Biology
- Macromolecule Modification
- Mitochondria and Cell Proliferation
- Nitric Oxide Chemistry, Biology and Physiology
- Novel Therapeutics
- Protective Enzymes
- Redox Imaging
- Redox Signaling
- Redox Reaction Mechanisms
- Signal Transduction and Gene Expression
- Superoxide and Superoxide Dismutases
- Targeted Antioxidants
- UV Effects and Atmospheric Pollutants

For further details regarding SFRBM 2014, please visit www.sfrbm.org and click on the SFRBM 2014 meeting logo. Questions about SFRBM 2014 can be directed to SFRBM via phone (317) 205-9482, fax (317)205-9481 or e-mail at info@sfrbm.org.

WORKSHOPS & SPECIAL PROGAMS

Will require additional fees and/or registration

PRE-MEETING WORKSHOP
Translation of Redox Methodology from Bench to Bedside - Problems and Solutions

Wednesday, November 19 | 8:15 am - 3:00 pm

Advances in redox biology depend on the availability of accurate and robust methods for detecting reactive oxygen species and identifying the products of their reactions. This is a challenging task and unfortunately, there are many otherwise excellent studies that have been let down by the misuse or misinterpretation of redox methodology. This workshop will critically assess how to study redox biology in cells, tissues and whole organisms. Speakers will give a critical overview of specific methodologies, focussing on their strengths and limitations and giving examples of where the methodologies have been appropriately applied.

12th ANNUAL OPENING DOORS EVENT
The Leadership in You

Thursday, November 20 | 6:45 pm - 9:00 pm

Speakers: Allan Butterfield, Ph.D., University of Kentucky and Phyllis Dennery, MD, Children's Hospital of Philadelphia Research Institute

Possessing a great idea, assembling a team to bring that conception to life is the first step in creating a successful project. While finding a new and exclusive idea is exceptional enough; the ability to successfully execute this idea is what separates the dreamers from the entrepreneurs. As soon as you make that exciting first hire, you have taken the first steps in becoming a prevailing leader. When finance is tight, stress levels are high, and the visions of instant success don't happen like you thought, it's easy to let those emotions get to you, and thereby your team. Take a deep breath, calm yourself down, and remind yourself of the leader you are and would like to become one. Join us to learn to explore some key qualities that every good leader should possess, and learn to emphasize.

PROFESSIONAL DEVELOPMENT WORKSHOPS

Thursday, November 20 | 1:00 pm - 2:15 pm

- Team Science: Overcoming the Challenges of Multidisciplinary Reasearch Teams
- First Impressions: Presenting Your Science & Yourself - the "Elevator Pitch"

Friday, November 21, 2014 | 1:00 pm - 2:15 pm

- NIH Mock Study Session
- Changing Roles: Moving from the Bench to Administrative Positions

MARK YOUR CALENDAR.....

Wed, Oct 15 | Early-bird Deadline, Save $50

Deadline for early-bird conference registration. Registrations received after this time will be charged an additional $50 late fee.

Fri, Oct 17 | Hotel Reservation Deadline

Reservation deadline for conference rate of $159 USD at the Sheraton Seattle. Reservations received after this date will be accepted on a space-available basis only and a higher hotel room rate may prevail.

SPECIAL SESSION
Goals and Priorities of the NIEHS

Saturday, November 22| 1:00 pm - 2:15 pm

Speaker: Leslie Reinlib, Ph.D., NIEHS, NIH

Dr. Reinlib was on the faculty of Tufts University and Johns Hopkins University before joining the NIH in 1990. He is currently a health scientist administrator in the Susceptibility and Population Health Branch, and director for the Breast Cancer and the Environment Research Program. He is also director for the Environmental Health Sciences Core Centers that support broad research on exposures, health, and disease at U.S. universities. Dr. Reinlib develops and administers programs in molecular and experimental carcinogenesis, genome integrity, environmental toxicology, and stem cell and developmental biology.

SUPPORTERS

SFRBM wishes to express its gratitude to the following institutions and companies that ensured the success of SFRBM 2014.

INNOVATIVE RESEARCH

(A minimum $5,000 contribution to support Annual Meeting Programming)

BAKER RUSKINN

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vmi Vascular Medicine Institute University of Pittsburgh

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(A minimum $2,500 contribution to support Annual Meeting Programming)

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Free Radical and Radiation Biology Program
IOWA
At the forefront of redox biology, free radical and cancer research

Redox Biology Center

Avanti® Polar Lipids, Inc.

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Lifetime Achievement AWARD

Jack Lancaster, Jr, Ph.D.

Jack Lancaster, Jr., Ph.D. of the University of Pittsburgh is SFRBM's 2014 Lifetime Achievement Award recipient.

Dr. Lancaster will give a featured lecture at our 21st Annual Meeting in Seattle, WA on Wednesday, November 19 at 6:35 pm titled, "A Radical Notion: Specialization is for Insects".

Dr. Lancaster was recognized for his key contributions in the area of biochemistry and molecular biology of nitric oxide, as well as related investigations in its cell biology and biomedical implications. Of particular merit has been the highly creative approach to these complex problems, characterized by a keen capacity to focus on important unforeseen questions, while contextualizing detailed fundamental mechanisms in vitro with in vivo disease pathways. Such a solid portfolio of research contributions not only left important marks in the field but has also been the basis for relevant formative activities at several levels. His scientific and teaching achievements have been directly or indirectly influencing many other important investigators in the field and are a worldwide reference.

Free Radical School Virtual Seminar Series

SFRBM offers virtual programming on a quarterly basis, providing valuable education on a wide range of topics. The sessions are open to SFRBM members only and are offered at no charge.

PLEIOTROPIC ANTI-INFLAMMATORY SIGNALING ACTIONS OF REDOX-DERIVED FATTY ACID ELECTROPHILES

Wednesday, October 29, 2014
1:00 pm Eastern (17:00 GMT/UTC)
Speaker: Bruce Freeman, Ph.D., University of Pittsburgh
Cost: FREE for SFRBM members

PROGRAM OVERVIEW

Bruce Freeman, Ph.D.

The modification of cell proteins by chemical reactions stemming from metabolic and environmental stimuli significantly expands the functional proteome. These post-translational protein modifications (PTPM) allow cells to dynamically regulate metabolism, growth, differentiation and immune responses. Notably, PTPMs continue to emerge as a critical component of nitric oxide (NO) and "redox" signaling. In addition to its initially-appreciated role in activating guanylate cyclase via heme-iron coordination, NO reacts with superoxide, lipid radicals and can be further oxidized by metalloproteins to yield some of the most reactive molecules in biology. These reactions yield products such as nitrogen dioxide that expands the breadth of reactions that transduce redox-dependent signaling.

One class of reactive species byproducts, electrophilic unsaturated fatty acids (oxo and nitroalkene derivatives), induce PTPM by reacting with protein thiols and other nucleophilic amino acids. Notably, multiple transcriptional regulatory mechanisms have protein constituents with functionally-significant electrophile-reactive amino acids. This highly conserved property provides cells with a capability to undergo stress-related adaptive signaling reactions. New clinical data will be presented regarding the mechanisms of formation of electrophilic fatty acid derivatives, how best to detect these reactive species and the PTPM they induce. The molecular targets, transcriptional changes, cell signaling reactions and physiological responses induced by low concentrations of electrophilic fatty acids are be non-toxic and anti-inflammatory in nature. In this regard, recent results from the clinical development of an exemplary electrophilic fatty acid as an anti-inflammatory drug will also be presented. In aggregate, this data supports the concept that lipid electrophile-mediated PTPM reactions link cell function with inflammatory and metabolic status.

ABOUT THE SPEAKER

Bruce Freeman, PhD is the Irwin Fridovich Professor and Chairman of the Department of Pharmacology and Chemical Biology at the University of Pittsburgh School of Medicine. His group studies the cell and tissue production and actions of reactive species (free radical and oxidant inflammatory/signal transduction mediators), with the goal of understanding fundamental mechanisms of redox signaling and tissue injury. Presently, new therapeutic strategies stemming from this work are being evaluated in FDA-approved human studies. Graduate and postdoctoral trainees from the Freeman lab have become leaders in their fields of investigation in both academia and the pharmaceutical industry.

LATEST ARCHIVED WEBINAR

NOS2 AND NITRIC OXIDE AS A DRIVER OF POOR PROGNOSIS IN ESTROGEN RECEPTOR NEGATIVE BREAST CANCER

Speaker: David Wink, Ph.D.,NIH, NCI
Originally presented July 30, 2014

TRAINEE CORNER: YIA SCORING CRITERIA

During the 2013 Annual Meeting in San Antonio, several trainees expressed interest in understanding the criteria by which their work is judged when competing for Young Investigator Awards (YIA). In order to address this concern, we believe it is important to highlight the criteria applied to the review process. Below, are the current judging criteria created by the SFRBM Junior Awards Committee after the 2011 Annual Meeting.

YIA scoring criteria and award eligibility: Each candidate receives individual scores from 3 judges at the Annual Meeting. Each judge's score is the sum of 3 items/areas:

ACCURACY (0-10)
Quality of data presentation and discussion (major criterion). It also considers the experimental design, use of adequate methodology and technical excellence.

IMPACT/INCREMENTAL CONTRIBUTION (0-10)
Originality and extent of conceptual novelty (major criterion). It also considers the background and degree of advance over previous knowledge, relevance, strength of mechanistic insights, and potential implications for other fields.

PRESENTER (0-10)
Critical thinking on results and related work (major criterion). It includes the knowledge level, quality, clarity and depth of presentation and ability to answer questions.

The final grade is the average score from the 3 assigned judges plus a 4th score from online double-blind abstract evaluations. Candidates receiving final grades of 22-24 or above are considered for the Young Investigator Award.

Qualification/expectation for YIA judges: In order to qualify as a judge for the YIA a SFRBM member must have at least two papers in the selected field as corresponding author within the last three years. In addition, the Junior Awards Committee encourages diversity among judges in regards to areas of interest, gender and geography. The Committee also advises judges to avoid potential bias or conflict of interest.

Helpful hints: All judges are different, and will grade using diverse methods. For example, a judge may falsely portray a lack of knowledge to give the presenter the opportunity to explain the research in a different manner. Additionally, sometimes judges may not ask questions but examine you as you present your research to others. Overall, remember you are not there only to compete, but to share your science, obtain new research ideas/questions, and to network with others in the field. Good luck to all of you at the annual meeting this year!

For more information contact the SFRBM Trainee Council at traineecouncil@sfrbm.org.

UPCOMING WEBINAR...

THE STATE OF THE PHD: EXPLORING CAREERS BEYOND THE PROFESSORIATE

Thursday, October 16, 2014
Speaker: Laurence Frabotta, Ph.D.,
University of Virginia
1:00 pm Eastern (12:00 pm Central, 11:00 am Mountain, 10:00 am Pacific; this is 17:00 GMT/UTC)

International attendees should convert the time accordingly.

REGISTER

Free Radicals Abroad

at the National University of Singapore

by Barry Halliwell, DSc, F-SFRBM

My research career in free radicals began in Oxford in the late 1960s and continued at Kings College London with spells at the University of California, Davis and Berkeley. Our early work was on how plants protect themselves against H2O2, the role of iron in free radical reactions, the development of 'biomarkers' of oxidative damage, and the role of antioxidants in human health and disease. In 1998 I came on sabbatical to the National University of Singapore (NUS) for a year but haven't left yet! It turned out to be a wise choice.

Dr. Barry Halliwell and his lab members

NUS has risen from being a staid teaching University to a highly-ranked research intensive University, already among the world leaders in some areas and advancing fast. As Singapore is a small country, the number of free radical researchers is correspondingly small, about five groups. There is a strong interdisciplinary element, especially working with clinicians to understand the role of free radicals in stroke, neurodegenerative diseases and ageing in humans, using modern biomarkers. We have continued our studies on the role of iron and other metals in atherosclerosis and neurodegeneration, in work together with Anatomists and Physicists; the latter provide advanced techniques to image metals in cells and tissues. In addition, NUS has developed a strong cross-disciplinary programme on Ageing, using at one end the nematode C. elegans to study fundamental mechanisms (e.g. the mechanism by which caloric restriction works, why knockouts of some antioxidant enzymes actually increase lifespan), and at the other to a local cohort of Singaporean elderly who are being tracked and studied, to elucidate the determinants of their health and disease.

Recently, an old interest of ours has been rekindled; in 1991 we published a paper characterising the antioxidant actions of ergothioneine: we are now revisiting its role in physiology and pathology, including human studies.

Many researchers in the world take cell culture for granted and do not realize that cells change rapidly in culture, one reason being that they are under fluctuating oxidative stress, as oxygen levels rise and fall. Several groups here study this, revealing how some tumour cells use free radicals to suppress apoptosis and how many studies of the effects of antioxidants on cells in culture have produced artefactual results.

So the Singapore free radical community is small but thriving and competitive for research funding, in a dynamic ecosystem. Come and visit us soon!

Foundation HONOR ROLL

We would like to thank the following members who made donations to the SFRBM Foundation in 2014.

GOLD ($250 - $499)

Stephen Black	Georgia Regents Univ.

SILVER ($100 - $249)

Tak Yee Aw	LSU Health Sciences Ctr
Paul Brookes	Univ. of Rochester
Eric E. Kelley	Univ. of Pittsburgh
Danny Manor	Case Western Reserve Univ.
Douglas Thomas	Univ. of Illinois at Chicago

BRONZE ($25 - $99)

Peter L. Gutierrez
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DID YOU KNOW?

Since 1995, SFRBM has provided over **$400,000** to support scientists in the early stages of their career. Join this great cause!

DONATE TODAY

My Mini-Fellowship Experience

Rebecca Parodi Rullán, University of Puerto Rico

SFRBM's mini-fellowship grant allowed me to travel to the University of Rochester School of Medicine, where I spent one month training under the supervision of Dr. Paul Brookes.

I met Dr. Brookes in February 2013 during the "Mitochondrial Dysfunction and Disease" meeting held by the Puerto Rican Physiological Society (PRPS) at the University of Puerto Rico School of Medicine. He was invited to be one of the guest speakers by my mentor, Dr. Sabzali Javadov.

Dr. Brookes is a prominent figure in the area of cardiac mitochondrial research, which is the same area of study I will use for my thesis project. Fortunately, I was able to meet Dr. Brookes, and I stated my interest in learning the ex vivo technique of heart ischemia/reperfusion in mice using the Langendorff setup – with the idea of having the possibility of including transgenic animal models to my thesis. Dr. Javadov's laboratory is known for its excellence in the heart Langendorff perfusion model using rats, which are easier to handle but lack the extensive availability of transgenic animals. At this point, Dr. Brookes offered to teach me the technique and suggested I apply for the SFRBM mini-fellowship.

This fellowship not only allowed me to learn a technique not available at my institution but the experience has given me much more than that. Firstly, Dr. Brookes and his laboratory members were always willing to explain and teach me not only the method I went to learn, but also additional methods that could help me develop a solid thesis project. Similarly, I was able to offer insights of some methods that were well-established in my laboratory that could be of any help to them. Secondly, I was given the opportunity to give a small talk to Dr. Brookes and colleagues on my current work and how the training they were providing would be of help in establishing my future work. This talk opened a small discussion in which suggestions were made to improve my project and, most importantly, I found a network of professionals in my area that are helping me become the scientist I strive to be.

I found that the SFRBM mini-fellowship gave me more than I could have ever imagined and I am extremely grateful. Without the support from SFRBM this experience would have been nearly impossible. I encourage any graduate student to apply for the mini-fellowship because the knowledge and experiences you can earn from it are endless.

In the end, I deeply thank SFRBM for the opportunity and Dr. Brookes for teaching me what is becoming the key piece to my thesis project. Our laboratories are in constant communication and I am very optimistic in establishing future collaborations with them. In addition to the great mentoring I currently receive from Dr. Javadov, I am confident I will look for Dr. Brookes as a guide towards a successful career in the field.

Deadline Coming Soon

SUBMIT BY OCTOBER 1

SFRBM is pleased to announce the 2014 Research Mini-Fellowship Grant which will provide additional research training opportunities for young investigators in the fields of free radical chemistry, redox biology and antioxidants that are not available at their home institution.

The program allows young investigators to cultivate collaborative relationships with established scientists, develop novel techniques or methodologies and expand their career development and research opportunities. A total of four fellowships will be funded each year. The deadline for the second cycle of 2014 is **October 1, 2014** and **two grants at a maximum of $5,000 USD** will be awarded for the stay in host Laboratory for the duration of **up to 2 months**.

Please visit http://www.sfrbm.org/sections/education/fellowships for application and program details.

2014 OFFICER & COUNCIL ELECTIONS

At the 21st Annual Meeting of the Society for Free Radical Biology and Medicine (SFRBM) in Seattle, Washington, several new officers and council members of the association will be installed. SFRBM is pleased to present the active membership with a slate of candidates for election.

A ballot email with the link to online voting was sent to all SFRBM members on September 22. All voting must be complete by October 17 at 5:00 pm US Pacific Time. Please make certain to exercise your right to choose the future leaders of our association. If you have any questions, please contact SFRBM at (317) 205-9482 or via email at info@sfrbm.org.

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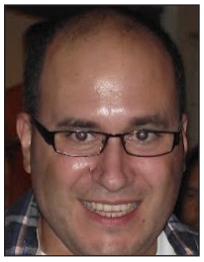

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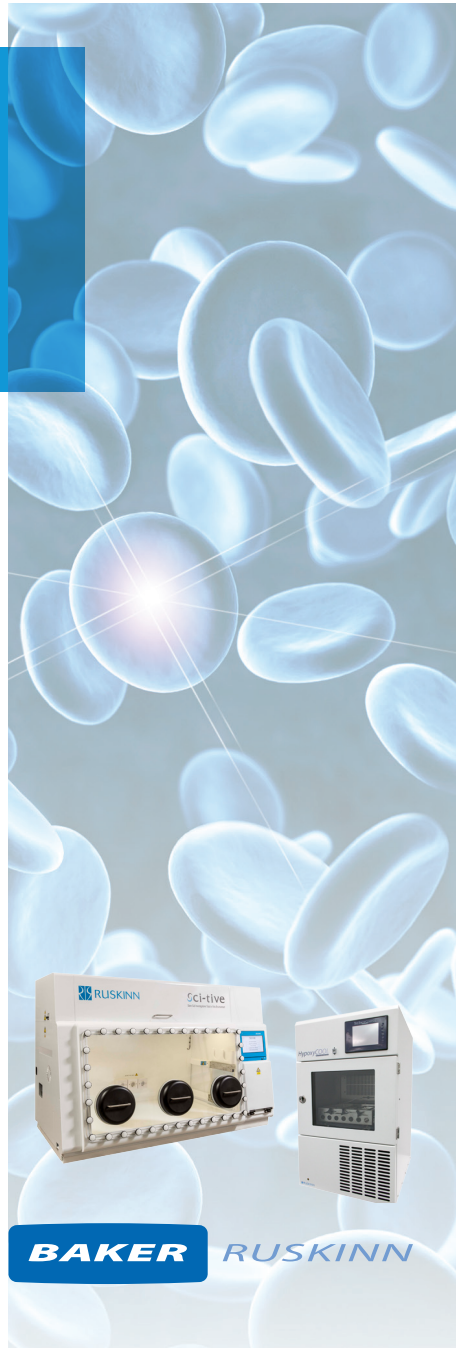

Literature Review

H_2S and •NO cooperatively regulate vascular tone by activating a neuroendocrine HNO–TRPA1–CGRP signalling pathway by Eberhardt, M., Dux, M., Namer, B., Miljkovic, J., Cordasic, N., Will, C., Kichko, T. I., de la Roche, J., Fischer, M., Suarez, S. A., Bikiel, D., Dorsch, K., Leffler, A., Babes, A., Lampert, A., Lennerz, J. K., Jacob, J., Martı, M. A., Doctorovich, F., Hogestatt, E. D., Zygmunt, P. M., Ivanovic-Burmazovic, I., Messlinger, K., Reeh, P., Filipovic1, M. R., *Nature Com* 5:4381 | DOI: 10.1038/ncomms5381

HNO is one-electron reduction product of •NO, with distinctive signaling pathways and has recently gained increased attention. H2S has already received considerable interest and was suggested as therapeutic though at low levels and thus with narrow therapeutic window. Its physiological effects are similar to that of •NO. Filipovic's group proposed that HNO is generated as a result of the direct reaction between H_2S and •NO. Both H_2S and •NO co-localize with transient receptor potential channel A1 (TRPA1). HNO activates TRPA1 through formation of N-terminal disulfide bonds which results in calcium flux followed by calcitonin gene-related peptide release which in turn causes local and systemic vasodilatation. •NO however acts on the level of guanylyl cyclase pathway. TRPA1 is expressed in sensory nerve fibers and activated by numerous metabolites and environmental irritants. This study indicates that HNO, formed in the reaction of NO and H_2S, is the endogenous activator of TRPA1 and that HNO donors are promising for the treatment of heart failure avoiding the problem of nitrate tolerance. The action is dependent upon •NO production and HNO-TRPA1-CGRP pathway. While the reactivity of Mn porphyrin-based redox-active therapeutics towards •NO has been reported *(Spasojevic et al, Nitric Oxide: Biology and Chemistry, 2000, 4, 526-533)*, recently the chemistry of Mn porphyrins with HNO has been described also *(Alvarez et al Inorg. Chem, 2014, 53(14):7351-60)*, implying a relevance of reactive nitrogen species in the mechanism of action of Mn porphyrin-based redox active therapeutics *(Reviewed by Ines Batinic-Haberle, Duke University School of Medicine)*.

Enigmatic Tylenol - It is not an opioid and it is not a non-steroid anti-inflammatory drug, NSAID, such as ibuprofen: What is its mode of action? Drahl C. *Chemical Engineering News* July 21, 2014, 31-32.

Alike ascorbate, Tylenol (acetaminophen) is just another example of how little we know about chemicals/drugs which we frequently use and which actions majority of population, who uses it, assumes to understand – in truth we do not know what it does. Moreover it causes liver toxicity; the toxic metabolite, N-acetyl-p-benzoquinone-imine, that leads to gluthatione depletion has been suspected to be the main effector of hepatocyte apoptosis during Tylenol-induced acute liver failure with N-acetylcysteine as the only drug of choice. 78,000 people report to emergency each year; while Tylenol overdose is suspected no good diagnostic marker exists. The alanine aminotransferase levels in blood peak too late, at 72 h after poisoning. Recently Ambros's team reported the possible use of microRNAs to identify earlier the Tylenol toxicity *(Ward et al, Proc Natl Acad Sci USA 2014, doi: 10.1073/pnas.1412608111)*. Mn porphyrin of unknown mechanism of action, $MnTBAP^{3-}$ *(Reboucas et al, J Biol Inorg Chem DOI 10.1007/s00775-007-0324-9)*, yet with frequently reported therapeutic efficacy in oxidative stress-based injuries, improved survival time, and dramatically reduced serum transaminase activity levels and parenchymal lesions in Tylenol-intoxicated mice *(Ferret et al, Hepathology, 2001, 33, 1173-1180)*. Interestingly the glutathione peroxidase and SOD activities were increased with $MnTBAP^{3-}$ alone and further on in Tylenol-treated mouse, suggesting $MnTBAP^{3-}$ has acted neither as SOD- nor catalase mimic (in agreement with what we know about it, *Batinic-Haberle et al, Antioxid Redox Signal, 2014)*; moreover adaptive response in upregulation of endogenous antioxidative defenses seemed likely. Tylenol has often been used for pain relief while data show that it does not even reduces pain in some tissues. The action, as inhibitor of prostaglandin H synthase (PGHS, commonly referred as cyclooxygenase, COX), requires certain conditions to happen, i.e. low levels of hydroperoxides. Levels of hydroperoxides though differ across tissues and organs *(Aronoff et al, Clin Pharmacol Ther 2006, doi: 10.1016/j.clpt.2005.09.009)*. While

all NSAIDs act on cyclooxygenase site of PGHS, Tylenol acts on its peroxidase site, presumably preventing formation of tyrosine radical. However if there is enough peroxide around, Tylenol may not be efficacious. Olivier Boutaud, whose discovery contributed to peroxidase idea, is convinced that inhibiting PGHS enzyme is not enough to reduce fever and relieve pain. Even if inhibiting PGHS is enough, it may be not the whole story. Peter Zygmunt and his colleague Edward Hogestatt believe that Tylenol metabolite AM404 acts on COX and endocannabinoid systems, both of which are involved in pain pathways. They further believe that Tylenol is an excellent tool to explore pain pathways even if its mechanism stays unresolved. The cross talk between COX enzymes and endocannabinoid signaling has been reported *(Hermanson et al, Nat Neurosci 2013, doi: 10.1038/nn.3480)*. The enrollment of serotonin neurotransmission has been implicated also *(Pickering et al, Clin Pharmacol Ther 2005, doi: 10.1016/j/.clpt.2005.12.307)*. Raffa's group suggests that Tylenol indirectly uses communications systems similar to opioids such as morphine *(Raffa et al, J Pharmacol Exp Ther, 2000, 295, 291)*. Replacing Tylenol as a drug, due to its liver toxicity, is hampered by not knowing what it exactly does. Its wide use justifies further (complicated) mechanistic studies *(Reviewed by Ines Batinic-Haberle and Artak Tovmasyan, Duke University School of Medicine)*.

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