Society for Free Radical Biology and Medicine
Established 1987

SFRBM dot

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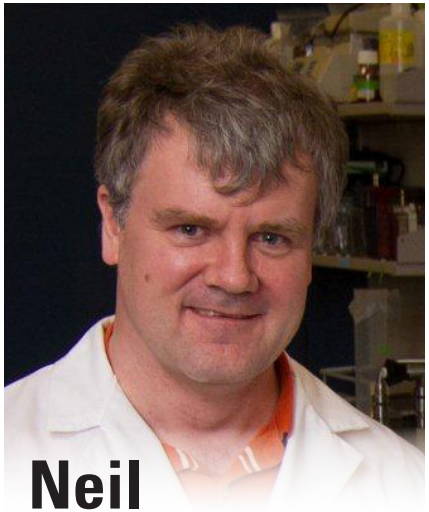
Dot Editor: Jianhua Zhang, Ph.D.
Issue Contributors: Ines Batinic-Haberle, Ph.D., Sumitra Miriyala, Ph.D., Clotilde Policar, Ph.D., Romulo Severo Sampaio, Allan Butterfield, Ph.D., Victor Darley-Usmar, Ph.D., Trent Tipple, Ph.D.



Neil
HOGG

President's Message

Neil Hogg, Ph.D., Medical College of Wisconsin

My first duty as SFRBM President during our recent conference was to present Henry Forman with the Distinguished Service Award. It is fitting therefore, in my first Dot message, to look back on what SFRBM has achieved under Henry's leadership. First, the two meetings in San Antonio and Seattle were very successful, and, in times of diminishing travel budgets, the meetings were well attended. Second, our membership of FASEB gives us a "seat at the table" of high level policy decisions, and I would like the thank past-president Harry Ischiropoulos for agreeing to serve as our representative on the FASEB Board and Margaret Briehl for serving on the Science Policy Committee. Third, the hiring of Carney Communications as our PR Company gives us an opportunity to spread our brand and our science into main-stream media and other public forums. I would like to thank Henry for his two years of service to the society and for his work as *FRBM* reviews editor. Henry will also leave this position to take over as editor-in-chief of *Archives of Biochemistry and Biophysics* next year.

On the subject of branding, the new SFRBM Council unanimously approved a motion that we should assess our own brand this year. I think most members would agree that the current name of our society is not a good representation of who we are or what we want to be. Carney Communications has advised us that our current brand does not play well in the outside world and that "Free Radicals" is to most people a rather scary term. Of course, it is vitally important to assess the wishes of the Society membership, and we will conduct a very short survey on this issue early in the New Year. I would strongly encourage everyone to participate in this survey and have your say.

Looking forward, planning for the 2015 meeting in Boston is already underway and I encourage everyone to submit session proposals. The 2016 meeting will be held jointly with the Society for Free Radical Research - International, and will be in San Francisco. With your assistance and participation we hope to continue presenting rigorous and vital science at our annual meetings.

I would like to thank past-president Garry Buettner for chairing the SFRBM Foundation Board since its inception. Chris Kevil will be taking over this position and I am sure he would chastise me if I did not remind you that the fiscal year is coming to a close and that now would be a great time to make that tax-exempt donation to the Society.

Finally, I would like to congratulate Rick Domann for being elected as President-Elect, and I look forward to working with Rick, the Vice-Presidents, Council and the membership over the next two years.

> "I think most members would agree that the current name of our society is not a good representation of who we are or what we want to be."

Radical View • Christopher Kevil, Ph.D.

by Sumitra Miriyala, Ph.D., LSU Health Sciences Center

Christopher KEVIL

DOT: Tell us about your background and when did you realize you were interested in science?

My initial realization of a love for science began in elementary school while performing a science fair project on different cellular functions of the brain. Soon after, I realized that I was fascinated with the idea of how tissues within organs work and how biochemical responses contribute to pathophysiology. This has guided my formal education and still contributes to my current research program.

DOT: Who has been your greatest teacher? What do you think the most important factors are that have shaped your career?

I have been lucky to have had input and advice from many outstanding teachers and mentors in the areas of free radical research, physiology and pathology over the years. However, I consider myself quite fortunate to have had two excellent free radical/redox biology leaders, Drs. Matthew Grisham and Victor Darley-Usmar, as outstanding teachers during my graduate and fellowship training. Their instruction helped me establish an important appreciation for free radical and redox biology research during disease that still impacts my research program today.

DOT: Briefly describe your research interest and what is the most notable research achievement from your lab?

My research interest centers on redox regulation of adaptive and pathophysiological vascular growth and remodeling. In my graduate work, I was keenly interested in how peroxides altered endothelial cell functions (e.g. solute barrier, growth, and inflammation properties). Over the years, it has become clear that several other redox molecules (e.g. GSH, NO, and H2S) also critically influence endothelial cell and vascular functions. From this collective interest, my research group has revealed that redox networks work together regulating numerous vascular functions. As for a notable research achievement, that's a difficult question. It's always challenging (if not impossible) to judge the impact of one's own work. However, if pressed, I would say that our group has made significant strides in revealing the importance of GSH and NO metabolites for ischemic vascular remodeling along with identification of therapeutic strategies that have been tested in clinical trials. But, this area of investigation is still 'young' (so am I—I think!) and I believe more exciting discoveries are yet to come.

DOT: What do you think is the direction the Oxidative Stress field is heading?

I believe oxidative stress or redox biology is heading in several directions with disease and clinical based studies being an important area. However, as the Society is a leading 'steward' of the area, it is important that we collectively work to educate and enlighten the broader research community with a sense of collegiality and collaboration. I also believe future areas of oxidative stress will be in large network studies coupled with genomics, metabolomics and proteomics. I believe we are merely scratching the surface of the biochemical complexity of our field and have such little clear insight into how it cooperatively functions with other molecular systems.

DOT: In the current climate in which investigators are faced with decreased NIH funding for research and low morale, what is the best advice?

Collaboration, cleverness and persistence. In this current climate, we are all challenged to be the absolute best that we can be. Often times, this alone will not win the day. It is important to remember that collaboration with

colleagues and experts beyond your area of expertise may provide new avenues and opportunities for funding. Persistence (a.k.a. 'grit') is also an overlooked attribute that is, of course, less glamorous but very important. Finally, I have also found that asking an important question regarding a poorly understood problem or topic is key in convincing a reviewer or study section that your project is meritorious and should be funded.

DOT: Being a mentor, you have shaped many students (graduate and postdoc) to enter academic and industry research, any tips how to shape individuals for these scientific fields?

I have found it important to help trainees identify what their true skills and strengths are so that they can begin to build a productive career from the beginning. I also encourage individuals to reflect on what it is they get enjoyment and pleasure from in science, as we all know that experiments fail and papers and grants may get rejected. Having a good sense of perspective and purpose are important over the course of one's career.

DOT: The Center for Cardiovascular Diseases and Sciences at LSU Health Science Center Shreveport has recently been approved by the Louisiana Board of Regents and you now serve as the Director for this program can you explain the benefits this center can contribute to the scientific field?

Our new Center for Cardiovascular Diseases and Sciences (CCDS) provides several unique opportunities for redox biology research. Investigators at LSU Health Shreveport have had a long-standing history in oxidative stress and free radical research related to cardiovascular disease and inflammation. The newly established CCDS builds from this foundation and is extending into new areas of redox biology of cardiovascular disease including mitochondrial function, hydrogen sulfide metabolism, nitric oxide metabolism along with applications in disease models and translational clinical studies. We also have strong infrastructure supporting animal, molecular and redox biology studies coupled with a highly collaborative environment between numerous investigators.

DOT: How has science/research changed during your life as a scientist?

The state of scientific research has changed considerably over the years. What I have noticed the most difference in is the scale and magnitude of research. Today, big data initiatives (omics and others), accurate disease modeling and cross discipline collaboration are critically important areas for research success.

DOT: How important is the SFRBM conference to you and your trainees?

The annual SFRBM meeting is very important for myself and members of my laboratory. It provides numerous opportunities to network with old and new friends, learn the latest scientific developments and provide valuable educational opportunities through the pre-meeting workshop and Sunrise Free Radical school.

DOT: What are your hobbies outside the laboratory?

I enjoy traveling, hiking and fishing with my family and friends.

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.

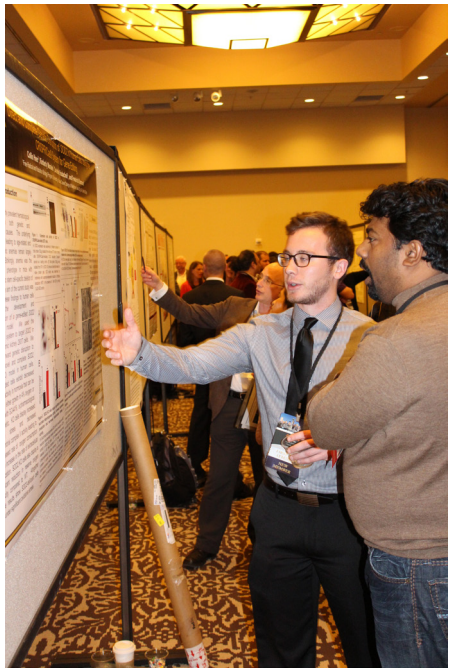
Here are two ways to do that:

1. Via the web:
   carneycommunications.com/sfrbm
   Password: SFRBMSocial
2. Through email:
   SFRBMSocial@carneycommunications.com

SFRBM 2014 RECAP: CANDIDS AND COMMENTS

"I especially liked the workshop this year. It was one of the best I have attended. It provided the pros and cons of different techniques, so that we can go back to the labs and use them correctly and in complementary ways.."

Margaret Tome, University of Arizona



"It was great to discuss excellent science with the colleagues in the field and to establish new collaborations.

Morana Jaganjac, Anti Doping Lab Qatar
First-Time Attendee

"My favorite thing about the meeting is the focus on student and post-doc presentations and development. I also thoroughly enjoyed the Sunrise Free Radical School.

Joshua Schoenfeld, The University of Iowa
First-Time Attendee

SFRBM 2014: PDS RECAPS

Could not be in two professional development sessions (PDS) at once OR could not make it to the Annual Meeting? Speakers Victor Darley-Usmar, Ph.D. and Trent Tipple, Ph.D., Univ. of Alabama at Birmingham have provided take-aways from two of the sessions.

FIRST IMPRESSIONS: PRESENTING YOUR SCIENCE AND YOURSELF - THE "ELEVATOR PITCH"

Elevator Pitch for Scientists

- Specific Aims Page, Short talks, Family gatherings all need a compelling and succinct story about your research
- Many Scientists focus on the " how and what" of their research not the "why"
- Diseases are a bad thing! Is not a compelling case for "why"
- Try all your talks with 60% why, 5% how and 35% what
- Take a look at the YouTube from Simon Sinek

Adminstrative Leadership

- These careers are a vocation not a back-up plan
- Many options and career paths beyond the bench
- Academic leaders lead by example

Jack Lancaster (L) receives Lifetime Achievement Award from SFRBM President Henry Forman

- You must be willing to serve the needs of the others
- A vision for your role is essential

TEAM SCIENCE: OVERCOMING THE CHALLENGES OF MULTIDISCIPLINARY RESEARCH TEAMS

- Team science augments progress and innovation due to interaction between networks of individuals with different backgrounds and perspectives
- Call the program officials at the NIH during the pre-submission process! They like to interact with investigators. They are open to discussing your project and giving feedback on your ideas and direction.
- For extramural funding, evidence of active collaboration is of great importance to review panels. This evidence is most easily provided through co-authored publications.
- Industry is excited to interact with academic investigators – understand that though priorities and confidentiality issues may differ, missions can align.

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

Complexa

ELSEVIER

LUOXIS

vmi Vascular Medicine Institute University of Pittsburgh

Seahorse Bioscience™

YOUNG INVESTIGATOR

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

Albany Medical College

BRUKER

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.

Cayman Chemical

FASEB CORNER

Harry Ischiropoulos, Ph.D.

I attended the FASEB Board of Directors meeting in Washington DC in early December as the SFRBM representative. Given SFRBM's new affiliation with FASEB, it was the first time we have had an in-person seat at the table with 26 other societies who are all interested in positively influencing law and policymakers about the importance of biomedical science research. It's important to recognize that SFRBM has something important to offer FASEB - we offer a consolidated representation of the redox biology, antioxidant and free radical chemistry research segment which is truly unique among their current member societies.

Strength can definitely be found in numbers - there are over 120,000 scientists (including 100+ Nobel laureates) that are part of FASEB's member societies. FASEB has developed a solid working relationship with the congressional appropriation committee members and they appreciate that FASEB provides data and presents fact-based, reasonable positions and proposals on various issues.

FASEB's highest priority at the moment is to circulate a consolidated research statement to key stakeholders in Congress, NIH/NSF and DOD. SFRBM has provided input to that statement. The FASEB website will be undergoing a "make over" since it is rather busy at present and hard to find important information. As an example, FASEB has developed nice advocacy tools all investigators can use but are currently difficult to locate. FASEB works with other advocate groups, since as the Coalition for Life Sciences and advocate patient groups, however it is not a priority.

SFRBM 2014 TRAVEL AWARD RECIPIENTS

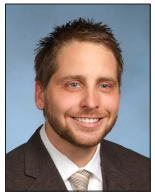
SFRBM's Junior Awards Committee wishes to congratulate the winners of the Society's annual Travel Awards. These awards were made available to students and postdocs who applied to attend SFRBM 2014 to present their research. Submitted abstracts were judged using a double blind review process. Ten (10) awards at $1,000 each were conferred to postdoc or student members of SFRBM outside of the United States. In addition, ten (10) Travel Awards at $500 each were presented to postdoc and student members in the US. Winners received special recognition and their awards at the SFRBM 2014 Awards Banquet in Seattle.

William Beavers, *Vanderbilt University*

Mitochondrial Proteins are Highly Adducted Targets of Endogenously Generated Lipid Electrophiles in LPS-Activated RAW264.7 Macrophages

Joshua Butcher, *University of Virginia*

Endothelial hemoglobin alpha by the HBA1 gene is crucial to release of NOderived metabolites into tissue and blood



John Cieslak III, *University of Iowa*

The Addition of Manganoporphyrins and Ascorbate to Standard of Care Chemotherapy Enhances Tumor-Specific Cytotoxicity in Pancreatic Cancer

Angela Davis, *University of Arizona*

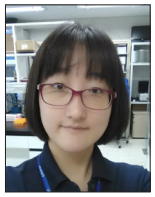
Redox-directed suppression of malignant cell invasion in a three-dimensional skin reconstruct model of metastatic melanoma

Carmine Gentile, *Heart Research Institute - Australia*

Post-transcriptional Regulation of eNOS and S-nitrosylation of Cell Cyclerelated Proteins in Human Endothelial Cells

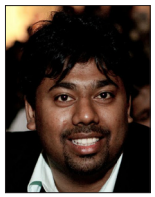
Ashwini Gore, *St. John's University*

NO Rescues Hyperoxia-Compromised Innate Immunity against Bacterial Infections via Enhancing Macrohage funtion



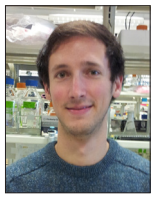
Kyeong-Ah Jung, *The Catholic University of Korea*

The c-MET/PI3K/BCRP signaling is involved in ovarian cancer cell resistance to photodynamic therapy and doxorubicin treatment



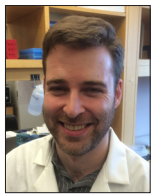
Nagarajan Kannan, *BC Cancer Agency - Canada*

Elevated ROS activates KIT, a lineage-specific signaling receptor in normal human mammary epithelial cells



Lucas Maddalena, *Brock University - Canada*

Inhibition of mitochondrial respiration by TPP-IOA, an anti-apoptotic inhibitor of cytochrome c peroxidase activity

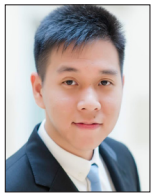


David McMillan, *University of Vermont*

Attenuation of GSTP1 decreases Fas S-glutathionylation-mediated lung epithelial cell apoptosis and fibrotic remodeling

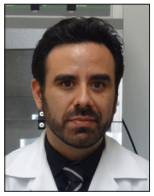
Thea Odgers, *Rutgers University*

Inducible Nitric Oxide Synthase Driven Macrophage Recruitment and Activation in Acute Lung Injury



Hong Yong Peh, *National University of Singapore*

Vitamin E isomer y-tocotrienol alleviates experimental house dust mite asthma



Andres Rodriguez, *Universidade de São Paulo*

Dynamic interaction between protein disulfide isomerase A1, Rac1 and its regulator RhoGDI during Nox1 NADPH oxidase-dependent vascular smooth muscle cell migration

Vikram Saini, *Univ. of Alabama at Birmingham*

Exposure to cigarette smoke causes DNA damage and contributes to drug resistance in Mycobacterium tuberculosis

Melissa Sammy, *Univ. of Alabama at Birmingham*

Mitochondrial DNA Contributes to the Development of Age Related Insulin Resistance in C57BL/6J and C3H/HeN mice

Angelica Bianchini Sanchez
Universidade de São Paulo

Quantification of 1,N2-propano-2'-deoxyguanosine in rat pulmonary DNA by micro chromatography - electrospray tandem mass spectrometry assay

Valquiria dos Santos, *Universidade de São Paulo*

Double strand break repair is required for maintenance of mitochondrial DNA integrity in human cells

David Schnell, *University of Kentucky*

MnSOD deficiency triggers pre-carcinogenesis metabolic switch

CALL FOR PROPOSALS

SFRBM2015
NOVEMBER 18-22
WESTIN BOSTON WATERFRONT — BOSTON, MA

SFRBM is now soliciting proposals from investigators for plenary session topics and speakers at SFRBM 2015, to be held November 18-22 in Boston, MA, USA.

PROGRAM FORMAT: SFRBM 2015 will feature four (4) morning plenary sessions (consisting of 4 lectures of 25 minutes each).

PROPOSAL DEADLINE: JANUARY 15, 2015: If you are interested in submitting a proposal, please send a Plenary Session Topic/Speaker Proposal to SFRBM by January 15, 2015. Proposals covering a broad range of topics are encouraged such as the role of dietary and cellular antioxidants in health and disease, redox cells signaling and the effects of reactive oxygen and nitrogen species in biological systems. Proposals, which have a clear theme and high profile speakers encompassing basic mechanisms through clinical applications, are of particular interest.

FOR MORE INFORMATION: Please visit http://www.sfrbm.org/sections/sfrbm15proposal

QUESTIONS: Please contact the SFRBM office at (317) 205.9482 or info@sfrbm.org

2014 YOUNG INVESTIGATOR AWARD RECIPIENTS

SFRBM recognized 15 outstanding student and postdoc members with Young Investigator Awards (YIAs) at the society's Closing Banquet in Seattle. Each winner received $500 cash and a free registration to the associations's 2015 or 2016 Annual Meeting.

Benjamin Rayner, *Heart Research Institute - Australia*

The myeloperoxidase-derived oxidant hypochlorous acid promotes extracellular trap formation and inflammatory cytokine expression in human monocyte-derived macrophages: a potential mechanism of atherosclerotic lesion development

Irwin Fridovich YIA Award - 1 of the top 2 scored abstracts/presentation at SFRBM 2014

Edward Bahnson, *Northwestern University*

Safety and Efficacy of a Systemically-Injected Targeted Therapy for the Injured Vasculature

Larry Oberley YIA Award - 1 of the top 2 scored abstracts/presentations at SFRBM2014

Brian Cunniff, *University of Utah*

Localized energy sensing targets mitochondria to the leading edge of migrating cells

Larry Oberley YIA Award in Cancer recognizing the highest scored abstract/presentation in the area of Cancer

Saurabh Aggarwal, *Univ. of Alabama at Birmingham*

Heme scavenging attenuates bromine induced lung injury

Urmi Basu, *University of Nebraska Medical Ctr*

Overexpression of redox-sensitive calcium/calmodulin-dependent protein kinase II (CaMKII) in central neurons augments angiotensin II (AngII)-induced hypertension

Janelle Bickta, *University of Pittsburgh*

Myoglobin Induces Mitochondrial Fusion to Decrease Cancer Cell Proliferation and Tumor Volume

Dustin Carroll, *University of Kentucky*

Simultaneous Quantitation of Oxidized and Reduced Glutathione via LC-MS/MS in Hematopoietic Tissues

James Galligan, *Univ. of Southern California*

Epigenetics and Oxidative Stress: Establishing a Link Through Histone Adduction

Thuy Nguyen, *Vanderbilt University*

Reactive -ketoaldehydes contribute to oxidative damage and aging in a SIR-2.1-dependent manner

Ashutosh Kumar, *NIEHS*

Immuno-spin trapping of alpha-synuclein radical formed in Maneb and paraquat-induced models of Parkinson's disease

Kranti Mapuskar *The University of Iowa*

Superoxide mediates alterations in Complex I activity seen in adult versus neonatal fibroblasts

Karla Maria Pires, *University of Utah*

Overexpression of human mitochondrial catalase preserves adipose tissue morphology but does not protect mice from high fat diet-induced metabolic impairment

Joshua Schoenfeld, *The University of Iowa*

Intracellular redox active metal ions mediate the differential susceptibility of lung and brain cancer cells to pharmacological ascorbate

Vlad Serbulea, *University of Virginia*

Oxidized phospholipids inhibit mitochondrial function of macrophages through a TLR2-ceramide dependent pathway

Thomas van't Erve, *NIEHS/NIH*

The ratio of 8-iso-prostaglandin F2α to prostaglandin F2α distinguishes enzymatic from nonenzymatic isoprostane formation

REDOX BIOLOGY ANNUAL REPORT

PAPERS INVITED IN 2015 FOR ALL TOPIC AREAS INCLUDING REDOX, BIOENERGETICS, AGING AND PATHOLOGY OF DISEASE.

Holly Van Remmen

The journal has now been online for 2 years and to date has over 230 accepted articles. The journal is now listed in *PubMed* and is averaging over 25,000 downloads per month and is being widely accessed across the world. We were sorry to see Tak Ye Aw, Ph.D. step down from her position as Associate Editor and thank her for her sterling contribution in helping get the journal of the ground. We welcome on board Holly Van Remmen, Ph.D. who will be spear heading our initiatives in the area of aging.

We have initiated several novel publishing features for the Redox Biology field including the graphical reviews, virtual collections, and educational reviews. The virtual collections allow easy and rapid access to papers on selected topics; to date we have collections covering bioenergetics, proteostasis, proteasome and autophagy, and our first collection on redox signaling. The graphical reviews are focused overviews with research oriented schemes, which are designed to be downloaded for seminars, with accompanying text elaborating the graphics. The educational reviews are designed for undergraduate and advanced graduate courses and are a teaching aid for those in our field as well as comprehensive basic reviews. If you would like to prepare one of these please contact us.

An article transfer service is in place for papers declined by *FRBM* which, when selected by the authors, transfers the paper and reviews across to *RB* automatically and will be used by the editors to render a decision after a rigorous rebuttal of the *FRBM* review. To reduce the burden on the peer review system we will consider any of your articles declined from other journals with a rebuttal to the reviewer's comments for *Redox Biology.* Our new fees for 2015 will be $350 for society members ($500 for non-members). The journal is now firmly established as the premier "gold" open access journal in our field, has a rapid decision and publication time so please send us your articles in 2015!

JOYS OF MENTORING

At SFRBM 2014 in Seattle, the Trainee Council presented its augural Mentoring Excellence Award to Allan Butterfield, Ph.D., University of Kentucky and Ines Batinic-Haberle, Ph.D., Duke University. Both the recipients had a fews words to say about the Joys of Mentoring...

ALLAN BUTTERFIELD

Since my research focuses on Alzheimer disease and chemotherapy induced cognitive impairment [see the SFRBM Discovery Award paper in FRBM 74:157-174 (2014) for details], students in the laboratory are highly motivated, knowing their research potentially will make a difference the large number of persons affected by these disorders.

My approach to mentoring is to require high standards of success in terms of research excellence. Students who join my lab understand from the beginning the high degree of effort and motivation required of them: 1) PhD students in my lab will publish twice the number of peer-reviewed papers in high impact journals as the national average for dissertation research in chemistry in the usual 4-5 year time period; 2) They will demonstrate focus and determination in their research tasks; 3) In addition, my students will demonstrate assertion and confidence in expounding and defending their ideas in a respectful, but determined, fashion. I provide an encouraging, supportive, and safe environment for these expectations for their success. In short, they know they can depend on me to

give them my best efforts in both direction of their research and as a trusted counselor to help them navigate their careers. This assurance, coupled to collaboration with other individuals in our group, helps them achieve these standards for success.

So, for me, the joy of mentoring is two-fold: primarily to see the success that persons in my lab attain in becoming highly capable scientists and individuals who contribute to advances in biomedical research; and, secondarily, their success leads to the lab's success in terms of reputation, papers published, and grants obtained. Commitment to excellence in mentoring is a win-win situation for both mentee and mentor.

INES BATINIC-HABERLE

I am thankful to all my students and postdocs for sharing the interwoven joys of science and life, and whose youthful spirit, energy and fresh and creative minds have kept me fit and optimistic.

The time spent with students often pays off in unexpected ways and at the end of the day is extremely rewarding.

Even the students who usually do not spend long hours in Lab, inspired by exciting results and passionate environment get immersed into work as never before.

Raising kids in parallel with career is not an easy task, and with a most considerate husband around, it still relies on a woman in first years of kid's life. Yet, the joy of raising kids enriches the careers of women and secure their happiness and thus help them understand all aspects of the life of their own female students

Foundation HONOR ROLL

PLATINUM ($500 - MORE)

Margaret Briehl	University of Arizona
Victor Darley-Usmar	University of Alabama at Birmingham
Henry Forman	University of Southern California
Terrance Kavanagh	University of Washington

GOLD ($250 - $499)

Stephen Black	Georgia Regents University
Robert Floyd	Oklahoma Medical Research Foundation
Albert Girotti	Medical College of Wisconsin
Neil Hogg	Medical College of Wisconsin
Peter Proctor	
Margaret Tarpey	University of Pittsburgh

SILVER ($100 - $249)

Tak Yee Aw	LSU Health Sciences Center
Marcelo Bonini	University of Illinois at Chicago
Paul Brookes	University of Rochester
Rick Domann	The University of Iowa
Luciana Hannibal	Universität Erlangen-Nürnberg
Nadine Hempel	University at Albany - SUNY
Eric Kelley	University of Pittsburgh
Rui-Ming Liu	University of Alabama at Birmingham
Danny Manor	Case Western Reserve University
Lin Mantell	North Shore University Hospital
Jayasree Nath	Walter Reed Army Inst. of Research
Sruti Shiva	University of Pittsburgh
Doug Spitz	The University of Iowa
Doug Thomas	University of Illinois at Chicago
Jianhua Zhang	University of Alabama at Birmingham

BRONZE ($25 - $99)

Phyllis Dennery	Children's Hospital of Philadelphia
Peter Gutierrez	
Lawrence Myers, Jr.	
Joanna Rybka	Nicolaus Copernicus University

Oxidative Stress

Using CellROX® reagents to monitor reactive oxygen species

Oxidative damage is a fact of life associated with aging and disease. To measure oxidative stress in live cells, CellROX® reagents generate a fluorescent green, orange, or deep red signal. You can use flow cytometry, fluorescence imaging, or microplate fluorometry to monitor the signal and easily multiplex with immunostaining or with other fluorescent reporters.

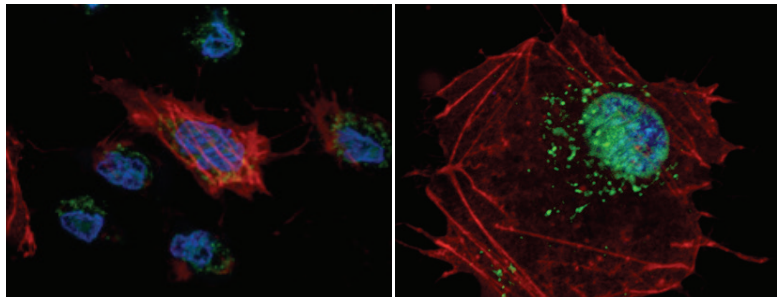
Advantages of using CellROX® reagents include:

- A choice of measuring reactive oxygen species with deep red, orange, or green fluorescence
- Flexible workflow for imaging, flow cytometry, or microplate assays
- Choice of colors for multiplexing with other fluorescent reporters

CellROX® reagent selection guide

	Deep red	Orange	Green
Ex/Em max	640/665 nm	545/565 nm	485/520 nm
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

To see more products for ROS detection, see our Oxidative Stress selection guide at **lifetechnologies.com/cellrox**



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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Free Radical School Virtual Seminar Series

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PEROXIREDOXIN: PEROXIDASE, REGULATOR AND SENSOR OF LOCAL PEROXIDES, AND PROTEIN CHAPERONE

Thursday, January 22, 2015
10:00 am Eastern (15:00 GMT/UTC)
Speaker: Sue-Goo Rhee, Ph.D.,
Yonsei University College of Medicine
Cost: FREE for SFRBM members

REGISTER

PROGRAM OVERVIEW

Sue Goo Rhee, Ph.D.

Peroxiredoxins are a ubiquitous family of peroxidases that are found from bacteria to humans and contain an active site cysteine that is sensitive to oxidation by peroxides. Peroxiredoxin not only function as peroxide-eliminating enzymes but also as sensors and regulators of local peroxides and as protein chaperones. These functions are regulated through various posttranslational modifications such as tyrosine and threonine phosphorylation, lysine acetylation, or active site cysteine hyperoxidation. The peroxiredoxin regulatory mechanisms will be discussed in the context of the control of growth factor signaling, steroidogenesis, metabolism, and circadian rhythm.

ABOUT THE SPEAKER

Sue Goo Rhee, Ph.D. is a Distinguished Professor at Yonsei University College of Medicine, Yonsei Biomedical Research Institute. His group discovered a family of peroxiredoxin (Prx) that catalyzes reduction of H2O2 and established that mammalian cells express six distinct Prx enzymes that not only protect against oxidative damage but also mediate cell signaling by modulating intracellular H2O2 levels. We showed that growth factors (EGF) induce a transient increase in intracellular H2O2 levels and that the essential cysteine of protein tyrosine phosphatases is the target of specific, reversible oxidation by H2O2 produced in cells stimulated with growth factors. These observations led to a new paradigm in receptor signaling wherein protein tyrosine phosphorylation is achieved not via activation of receptor protein tyrosine kinases alone, but through concurrent inhibition of protein tyrosine phosphatases by H2O2. Our studies revealed that Prx isozymes are extensively regulated via phosphorylation as well as hyperoxidation of the active site cysteine to cysteine sulfinic acid, with the reverse reaction catalyzed by sulfiredoxin. The reversible Prx cysteine hyperoxidation discovered by us proved critical for feedback regulation of steroidogenesis and constitutes a universal marker for circadian rhythms in all domains of life.

LATEST ARCHIVED WEBINAR

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

Speaker: Bruce Freeman, Ph.D.
Originally presented October 29, 2014

TRAINEE CORNER: CALL FOR NOMINATIONS

The Society for Free Radical Biology and Medicine (SFRBM) is searching for 5 new members for the Trainee Council. Two members of the Trainee Council (i.e. Chair and Vice-Chair) will have seats on the SFRBM Council.

The SFRBM Trainee Council will represent undergraduates, graduate and medical students, and residents as well as clinical and post-doctoral fellows. SFRBM encourages trainee level members of any age, ethnicity and nationality; from industry, government and academia; and from any country, to consider this leadership opportunity.

DUTIES OF THE TRAINEE COUNCIL

Trainee Council members are expected to organize and promote the following:

- Support the development of SFRBM programming and initiatives for early-career scientists
- Organize and oversee the SFRBM Mentoring Excellence Award
- Represent the interests of early-career scientists as a liaison to the SFRBM Council leadership

ELIGIBILITY

Candidates must be active members of SFRBM at the trainee level and young investigators who have great ideas for how the SFRBM can support early-career scientists. Self-nominations are encouraged.

TERM OF SERVICE

The Trainee Council consisting of 6 total members will be elected to two-year terms, and the Chair and Vice Chair will have seats on the SFRBM Council. The first two-year term will commence in April 2015 and will expire in April 2017.

APPLICATION MATERIALS

- Name, affiliation and contact information (i.e., physical mailing address, email and phone).
- A brief description of the candidate's research interests (limit of 100 words), a statement outlining ideas on how SFRBM could better serve its current trainee members (limit of 200 words), and career goals (limit of 200 words).
- The candidate's brief curriculum vitae.
- A letter of recommendation from the candidate's mentor.
- If the candidate's mentor is not a SFRBM member, an additional letter of recommendation from an active member in good standing with SFRBM is required.

Please submit a single PDF file containing all application materials to the attention of Kent Lindeman, SFRBM Executive Director, at klindeman@hp-assoc.com no later than February 1, 2015.

ELECTION

The Young Investigator/Trainee Committee, chaired by Anne Diers, Ph.D., will screen all nominations, and the top 10 nominees will be presented for election by all SFRBM student and postdoc members. The election will take place in March 2015.

Please contact Kent Lindeman at klindeman@hp-assoc.com or (317) 205-9482 if you have any questions.

Free Radicals Abroad

at the Ecole Normale Supérieure — Paris
Bio-inorganic chemistry and SOD mimics at ENS-Paris

by Clotilde Policar, Ph.D.

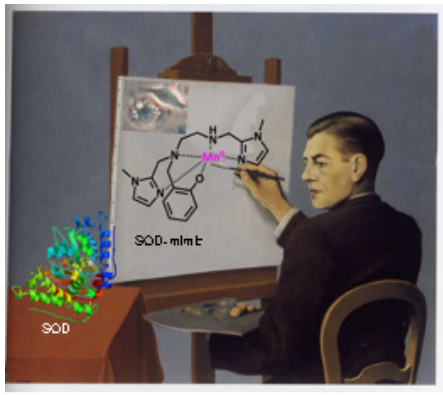
At the Ecole Normale Supérieure in Paris, the research group Metals in Biology—Inorganic Cellular Chemistry, studies metal complexes in a cellular context. Part of the work is dedicated to the design and study of low molecular weight complexes that are able to dismutate the superoxide radical. The group is led by Clotilde Policar and gathers a large range of expertise in chemistry, with Hélène Bertrand, specialized in organometallic chemistry, Nicolas Delsuc in peptide chemistry and sub-cellular imaging, François Lambert in ligands synthesis, and inorganic chemistry. They work in close collaboration with bio-physicists and cell-biologists.

The Metals in Biology—Inorganic Cellular Chemistry group at ENS in Septembre 2013
Second row: J.P. Monserrat, G. Gazzah, S. Clède, V. Ching, P. Demay-Drouhard, N. Delsuc, A.-S. Bernard
First row: F. Lambert, J. Zhu, C. Policar, M.-L. Low, H. Bertrand, S. Hostachy, E. Mathieu

The group Metals in Biology—Inorganic Cellular Chemistry settled at ENS in 2009, and before, the two senior members, François Lambert and Clotilde Policar, were based at Institut de Chimie Moléculaire et des Matériaux d'Orsay (Univ. Paris-Sud 11). They were interested in the design of Mn-complexes to characterize intermediates in the catalytic cycle of manganese superoxide dismutase (MnSOD). For that purpose, they designed a series of low-molecular weight manganese complexes inspired from the active site of SOD, or SOD mimics. In SOD, Mn is in a trigonal bipyramidal environment with one carboxylato and two histidine moieties in a triangle, and a farther histidine with a water molecule (H2O or HO—) in the two apical positions. Starting from complexes with Mn(II) coordinated by a tripodal amine functionalized with two imidazole and one carboxylato, they introduced modifications to increase bulkiness around the metal ion or to tune the redox potential of the Mn(III)/Mn(II) couple to that of SOD. In the course of this research, they isolated original coordination polymers with MnII-OCO-MnII along the chain. Adducts MnOO were characterized by low-T spectroscopies, including UV-visible and electron paramagnetic resonance, showing unambiguously an Mn(III) redox state, with a coordinated peroxo: the reaction of Mn(II) with superoxide in these complexes is an oxidative addition onto the Mn(II) ion.

Bearing in hand a series of complexes reacting efficiently with superoxide, the next step was to assay their bio-activity in a cellular context. At that time, the research group had just settled at ENS. For the record, French bio-inorganic chemistry was born in the 80's at ENS, with the group of Daniel Mansuy, a leading figure in CYP450 and one of C. Policar's thesis supervisors. Marc Fontecave, now professor at College de France, the most famous French academic institution, Marius Réglier, now research director in Marseille, Jean-Pierre Mahy, now professor at Paris-Sud 11 University, or Isabelle Artaud, now research director in Paris V University, were doctoral students or worked at ENS and from this initial spot, they swarmed all over France, creating a strong national network in bio-inorganic chemistry —http://www.groupe-francais-de-chimie-bioinorganique.u-psud.fr or FrenchBIC, network of about 25 laboratories distributed all around France. Daniel Mansuy moved to Paris 5 at the end of the 80's and bioinorganic was, in a way, re-born at ENS in 2009.

The chemistry department of ENS gathers chemists from different areas, from molecular synthetic chemistry to physical-chemistry, all focusing on systems at the interface with biology. Understanding and controlling inorganic compounds inside cells require a wide range of techniques including imaging, and new approaches to translating our knowledge in inorganic chemistry from the round-bottom flask into biological media



From Magritte, La clairvoyance
Allegory of Bio-inorganic chemistry

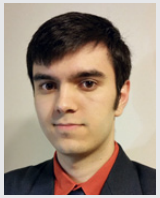
and cells. In particular, a group of bio-electrochemists, led by Christian Amatore (ENS, Laboratoire PASTEUR), works on the quantification of reactive oxygen species using ultramicroelectrode at the single cell level. In collaboration with Frederic Lemaître and Manon Guille, macrophages were used to show that one of the complexes of the SODm series, chosen as a leading complex, efficiently reduces the flow in reactive oxygen species (ROS) with a major reactivity on the superoxide radical, evidenced through an assay using ferricytochrome c (McCord-Fridovich assay, developed at Duke University). This was a strong evidence that these derivatives remain active in a cellular context.

In addition to that work on SOD-mimics, the group Metals in Biology shows a strong interest in sub-cellular imaging using innovative techniques. Indeed, the bio-activity of a molecule is strongly related to its location inside cell-compartments. The group has recently pioneered the development of M-CO probes for sub-cellular IR-imaging. These probes absorb IR-light in the 2000 cm—1 energy-range, which is the window of transparency in IR-range for biological samples. Vibrational imaging is an emerging technique and shows some advantages: weak energies, no electronic excited state involved, no photobleaching, easy implementation from cells to tissues imaging, reliable quantification. Recently, M-CO probes that are also fluorescent, emissive in the visible (530 nm) after an absorption close to the visible range (350 nm), have been used in a correlative imaging approach, in the IR and fluorescence. For these valuable Single Core Multimodal Probes for Imaging, we have coined the term SCoMPIs.

Nature can be a rich source of inspiration for chemists providing insights to develop systems with a tuned reactivity and also opening up many challenges. Both the development of IR-probes and their application in sub-cellular imaging and the design of SOD mimics and their study inside cells are part of this bio-inspired and bio-challenged chemistry.

Research Mini-Fellowship **GRANT RECIPIENTS**

SFRBM is pleased to announce the 2014 second cycle Research Mini-Fellowship Grants have been awarded to Vlad Serbula, University of Virginia; Venkata Vaka, University of Mississippi Medical Center; and Iva Vukelic, University of Rijeka.



Vlad Serbulea
University of Virginia
Research: Liquid Chromatography/Mass Spectrometryl
Training Site: Vanderbilt University
Mentor: Sean Davies, Ph.D.

Venkata Vaka
University of Mississippi Medical Center
Research: Mitochondrial Complex_I and ROS
Training Site: Virginia Commonwealth University/
McGuire Veterans Affairs Medical Center
Mentor: Edward J. Lesnefsky, MD, FAHA, FACC

Iva Vukelic
University of Rijeka
Research: Nuclear fractionation and quantification of nuclear NF-kB with ELISA method
Training Site: University of Nebraska Medical Center
Mentor: Rebecca Oberley-Deegan, Ph.D.

The deadline for the first cycle of 2015 Research Mini-Fellowhship Grant is May 1, 2015. A total of four fellowships will be funded each year. For more information, please visit http://www.sfrbm.org/sections/education/fellowships.

Literature Review

Sulforaphane treatment of autism spectrum disorder (ASD), by Singh K, Connors S, Macklin E, Smith K, Fahey J, Talalay P, Zimmerman A**,** *Proc. Natl. Acad. Sci. USA 2014***,** DOI: 10.1073/pnas.1416940111**).**

Autism spectral disorder affects 1-2% of predominantly male individuals and with no treatment available presents huge medical and economic problem. Sulforaphane is an isothiocyanate isolated from broccoli. It has been chosen for this study as oxidative stress, low antioxidant capacity, depressed glutathione synthesis, reduced mitochondrial function and oxidative phosphorylation, increased lipid peroxidation and neuro-inflammation have been involved in autism (James SJ et al, Am J Clin Nutr 2004, Giulivi c et al JAMA 2010). Kensler TW et al (Top Curr Chem 2013) reported the effects of sulforaphane on activation of Nrf2-Keap1 pathway which are presently of growing interest and seem to be involved in the actions of natural and synthetic redox-active drugs commonly viewed as antioxidants It seems that isothiocyanates do not act (directly) as antioxidants, but activate gene products such as NAD(P)H:quinone oxidoreductase 1, glutathione transferase, glutamate cysteine ligase, heme oxygenase and thioredoxin reductase via activation of Nrf2 pathway (Zhang Y et al Free Radic Biol Med 2005). Sulforaphane is now in extensive clinical evaluation. Dietary sulforaphane is of low toxicity. Recent study by Singh et al involved 44 young male adults age 13-30 with moderate to severe ASD in a placebo-controlled, randomized, double-blind Clinical Trial. The sulforaphane group was treated daily for 18 weeks with capsules of sulforaphane-rich broccoli sprout extracts with either 9 mg or 18 mg or 27 mg of sulforaphane (Mr=177.29) for patients weighting either <100 lb or 100-199 or >200 lb, respectively. The symptoms were followed with 3 widely accepted behavioral measures which were completed at 18 weeks by parents/caregivers and physicians: Aberrant Behavior Checklist, Social Responsiveness Scale, and Clinical Global Impression Improvement Scale. Those patients receiving sulforaphane showed substantial improvement in behavior. Significantly greater number of patients treated with sulforaphane had improvement in social interactions and verbal communications than patients from placebo-treated group. Upon discontinuation, the scores returned to pretreatment levels (*Reviewed by Ines Batinic-Haberle, Duke University*).

Sulforaphane

The HMGB1-RAGE axis mediates traumatic brain injury-induced pulmonary dysfunction in lung transplantation, by Weber D, Gracon A, Ripsch M, Fisher A, Cheon B, Pandya P, Vittal R, Capitano M, Kim Y, Allete Y, Riley A, McCarthy B, Territo P, Hutchins G, Broxmeyer H, Sandusky G, White F and Wilkes S, *Sci. Transl. Med. 6*, 252ra124 (2014). DOI: 10.1126/scitranslmed.3009443.

Those people who die from traumatic brain injury (TBI) are potential sources of lung transplants. It is very disappointing that currently only 20% of lungs are functionally transplantable due to the damage caused by TBI. The same is likely true for other organs also. TBI can result in secondary damaging events that take place in hours or days since injury and impair lungs which are to be transplanted. Among others, those are acute respiratory distress syndrome and acute lung injury. Recent research aiming to identify the pathophysiological mechanisms of acute lung injury has focused on non-traditional pro-inflammatory mediators and their receptors. Of particular interest is the class of danger-associated molecular patterns, such as high-mobility group box-1 (HMGB1) that could be quickly released into the cytoplasm after stress, injury or disease. Depending upon the status of affected cell, the cytoplasmic HMGB1 could be passively released into the extracellular space. So far, the mechanism by which the TBI causes pulmonary dysfunction remains unclear but may involve the interaction of HMGB1 protein with the receptor for advanced glycation end products (RAGE). Daniel J. Weber and co-workers demonstrated that the HMGB1-RAGE axis plays a role in the mechanism by which TBI induces lung dysfunction. That could comprise the primary pathway of lung injury through impacting the major transcription factor, NF- B activation in airway epithelial cells, which in turn leads to excessive local and systemic inflammation. Therefore, targeting this pathway prior

to lung transplantation may improve the post-surgery outcome of a recipient, preventing his/hers pulmonary complications; practical aspects - when and how that could be achieved in people dying from TBI - need to be addressed (*Reviewed by Romulo Severo Sampaio and Ines Batinic-Haberle, Duke University*).

Ditching of chemistry can really bite you - Structural misassignment stems from long-standing use of incorrect recipe to prepare anticancer drug, TIC10, by Stu Borma, *C&EN*, 92(23) 32, 2014.

The recent problems related to the structure of an anticancer drug may be at least in part due to the fact that many pharmaceutical companies have laid off their chemists and disbanded their medicinal chemistry divisions. The anticancer drug, TIC10 or ONC201, originated from the German patent (now-expired), owned by C. H. Boehringer Sohn, in Ingelheim, which covers a family of 43 compounds as antiseizure drugs along with synthetic procedures. The National Cancer Institute (NCI) picked up TIC10 for its publicly accessible Diversity Set II database along with structure indicating three rings fused in a linear fashion. Wafik S El-Deiry of Pennsylvania State University discovered its anticancer activity (*Sci Trans Med 2013, DOI: 10.1125/scitranslmed.3004828*). The mass spectrometry was used in efforts to confirm the listed structure with NCI database. Penn State was granted a patent to use the drug to treat cancer and licensed it to Oncoceutics who is sponsoring Phase I/II Clinical Trials. However, Kim D Janda and co-workers at Scripps Research Institute California recently discovered that the structure has ben misassigned (*Angew Chem Int Ed 2014, DOI: 10.1002/anie.201402133*). The new corrected angular structure has been applied for a patent and has been licensed exclusively to Sorrento Therapeutics (*C&EN, May 26, 7*). Eight companies were selling TIC¬10 (*CAS registry #41276-02-2*) (with misassigned structure) for research purposes. Oncoceutics Chief Business Officer, Lee Schalop, notes that all their studies required for the drug approval were carried out with bioactive drug. The patenting/licensing issues (and thus the ownership) of the misassigned drug waits to be solved (*Reviewed by Ines Batinic-Haberle, Duke University*).

Artificial sweeteners induce glucose intolerance by altering the gut microbiota, by Suez J, Korem T, Zeevi D, Zilberman-Schapira G, Thaiss CA, Maza O, Israeli D, Zmora N, Gilad S, Weinberger A, Kuperman Y, Harmelin A, Kolodkin-Gal I, Shapiro H, Halpern Z, Segal E and Elinav E, Nuture, 181-186, 514, 2014. DOI: 10.1038/nature/13793.

The excessive preoccupation with weight has driven even lean people to consume non-caloric artificial sweeteners (NAS). A simple habit has the potential to induce deleterious metabolic alterations. NAS is commonly regarded to provide sweet taste to foods without the associated high energy content of caloric sugar. Furthermore, they are considered safe and beneficial and recommended for weight loss and type 2 diabetes mellitus. So far, supporting scientific data remain controversial: some studies showed benefits for NAS consumption and a little induction of a glycaemic response, while others have demonstrated weight gain and an increase in type 2 diabetes risk. The increased use of NAS coincides with the dramatic increase in the obesity and diabetes epidemics; the data from Suez et al study suggest that artificial sweeteners may enhance the epidemics which they were intended to fight. A comprehensive study performed on mice fed either sugar or saccharin clearly indicates that NAS drives development of glucose intolerance via compositional and functional alterations to intestinal microbiota. The effects are also transferable to germ-free mice upon faecal transplantation of microbiota configuration of NAS-fed mice and were further substantiated on 7 adult individuals. Multiple additional pathways were found in saccharin-consuming mice associated with diabetes mellitus and obesity including sphingolipid metabolism and lipopolysaccharide biosynthesis. In a study on 381 non-diabetic individuals a positive correlation was found between NAS consumption and clinical parameters including increased weight and waist-to-hip ratio (obesity tendency), higher fasting blood glucose and elevated serum alanine aminotransferase (secondary hepatic damage linked to non-alcoholic fatty liver disease). Several bacterial taxa that changed during NAS consumption were previously associated with type 2 diabetes in humans such as over-representation of Bacteroides and under-representation of Clostridiales. Additionally, the results from short- and long-term human NAS consumer cohorts suggest that human individuals feature a personalized response to NAS, probably due to the differences in their microbiota function and composition (*Reviewed by Romulo Severo Sampaio and Ines Batinic-Haberle, Duke University*).

Society for Free Radical Biology and Medicine (SFRBM)
8365 Keystone Crossing
Suite 107
Indianapolis, IN 46240
(317) 205-9481
(317) 205-9481 Fax
info@sfrbm.org
www.sfrbm.org