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Office of Education, Division of Intramural Research
National Heart, Lung, and Blood Institute

FELLOWS NEWSLETTER

The Fellows Newsletter is published monthly by the Office of Education, Division of Intramural Research, National Heart, Lung, and Blood Institute and distributed to NHLBI DIR members to promote the interest of DIR Fellows.

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From the Director of the Office of Education

This note is to call your attention to the work of the Fellows Advisory Committee, an essential group working with the DIR Office of Education. This committee is comprised of NHLBI fellows who volunteer their time and efforts to participate in designing and implementing programs that benefit all NHLBI Fellows, and to be the "eyes and ears" for the Office of Education. The list of current members of the committee is presented on the sidebar at the left. Our goal is to have at least one representative from each Lab and Branch.

The Committee has major input into each of the activities that are run by the Office of Education. The major one, of course, is the Fellows Retreat, an annual event that brings together many of our fellows at an off-campus location. The next retreat in Spring 2013 is in the early stages of planning, so your help would be valuable. The committee selects speakers, arranges the program, and provides essential help to make sure the retreat works for you. The members of the committee have been instrumental in suggesting and planning the Holiday Parties. Regular meetings of the committee are held once a month, at 4:00 PM on the second Monday of the month. If you would like to participate in these meetings, please contact the office for information.

NHLBI DIR Seminar Series

Gregg Fields, Ph.D.
Vice President of Scientific Affairs
Torrey Pines Institute for Molecular Studies

"Unraveling the Mechanism of Collagenolysis"
Tuesday, November 13
11:00 AM - 12:00 PM
Building 50, Room 1227/1233

New NHLBI Fellows

Michel De Messieres, Ph.D., is a new Visiting Fellow in the Biochemistry and Biophysics Center under Dr. Jennifer Lee. Dr. De Messieres earned his Ph.D. is physics from the University of Maryland, College Park. He holds a MS in Elementary education and previously taught at both the grade school and high school level. Dr. De Messieres initial research project is an ApoCIII study – determine amyloid formation and test for tubulation when interacting with lipid vesicles as well as setting up fluorescence microscopy.

Gregory Alushin, Ph.D. is a new Visiting Fellow in the Cell Biology and Physiology Center under Dr. Clare Waterman. Dr. Alushin earned his Ph.D. in Biophysics from University of California, Berkeley. He was the 2012 recipient of both the ASCP Norton B. Gilula Award and the Alan Bearden Award in Biophyics. Dr. Alushin's initial research project is to investigate the role of domain-repeat proteins in the formation and regulation of focal adhesions.

Elizabeth Mushaben, Ph.D., is a new Research Fellow in the Cardiovascular- Pulmonary Branch under Dr. Stewart Levine. Dr. Mushaben earned her Ph.D. in Molecular and Developmental Biology from the University of Cincinnati. She was the recipient of the 2011 Outstanding 5th Year Platform Presentation, University of Cincinnati Molecular and Developmental Biology Annual Graduate Student Symposium. Dr. Mushaben's initial research project will involve looking at the role of hemoglobin and haptoglobin complexes in asthma using both *in vitro* and *in vivo* model systems, namely bone marrow derived macrophages and OVA models of allergic asthma in mice.

The Office of Education wishes you a Happy Thanksgiving!

Recent Publications by NHLBI Fellows

Dutta, D., Williamson, C. D., Cole, N. B., & Donaldson, J. G. (2012). Pitstop 2 Is a Potent Inhibitor of Clathrin-Independent Endocytosis. *Plos One 7*

Ghysels, A., Miller, B. T., **Pickard, F. C.,** & Brooks, B. R. (2012). Comparing normal modes across different models and scales: Hessian reduction versus coarse-graining. *J. Comput. Chem. 33*, 2250-2275

Kellman, P., **Wilson, J. R., Xue, H.**, **Ugander, M.**, & Arai, A. E. (2012). Extracellular volume fraction mapping in the myocardium, part 1: evaluation of an automated method. *J. Cardiovasc. Magn. Res. 14*

Kellman, P., **Wilson, J. R., Xue, H.**, Bandettini, W. P., Shanbhag, S. M., Druey, K. M., **Ugander, M.,** & Arai, A. E. (2012). Extracellular volume fraction mapping in the myocardium, part 2: initial clinical experience. *J. Cardiovasc. Magn. Res. 14*

Smyth, J. T., **Beg, A. M.**, Wu, S. L., Putney, J. W., & Rusan, N. M. (2012). Phosphoregulation of STIM1 Leads to Exclusion of the Endoplasmic Reticulum from the Mitotic Spindle. *Curr. Biol. 22*, 1487-1493

Tanaka, M., Jaruga, P., Kupfer, P. A., Leumann, C. J., Dizdaroglu, M., Sonntag, W. E., & Chock, P. B. (2012). RNA oxidation catalyzed by cytochrome c leads to its depurination and cross-linking, which may facilitate cytochrome c release from mitochondria. *Free Radic. Biol. Med. 53*, 854-862

Yi, J. H., Katagiri, Y., Susarla, B., **Figge, D.**, Symes, A. J., & Geller, H. M. (2012). Alterations in sulfated chondroitin glycosaminoglycans following controlled cortical impact injury in mice. *J. Comp. Neurol. 520*, 3295-3313

THE SCIENCE BEAT

By Zhiyun Ge, Ph.D.

Tanaka, M., Jaruga, P., Kupfer, P. A., Leumann, C. J., Dizdaroglu, M., Sonntag, W. E., & Chock, P. B. (2012). RNA oxidation catalyzed by cytochrome c leads to its depurination and cross-linking, which may facilitate cytochrome c release from mitochondria. *Free Radic. Biol. Med.53*, 854-862

Reactive oxygen species (ROS) refer to chemically reactive molecules containing oxygen, such as oxygen ions and peroxides.ROS are produced as a normal product of cellular metabolism and contribute significantly in biological functions. Environmental stress (e.g., UV or heat exposure) can result in the over-production of ROS and excessive amount of ROS can cause extensive damages to cells, including damage of DNA/RNA, lipid peroxidation, oxidations of amino acids in proteins, and inactivation of specific enzymes. Therefore, oxidative damage initiated by ROShas been implicated in the functional decline that is characteristic of aging or neurodegenerative diseases. Although the majority of previous research efforts were dedicated to studying DNA damage caused by ROS, emerging evidence in recent years suggests that elevated levels of oxidized RNA are involved in the pathogenesis of various diseases, including Parkinson's disease and Alzheimer's disease.When DNA/RNA is oxidized, depurination and depyrimidination usually accompany the oxidation of bases. Theabasicdeoxyribose moiety after depurination/ depyrimidination can be detected via the reaction between the aldehyde moiety in the abasic sugar derivatives and an aldehyde-reactive probe (ARP). Previously, Tanaka et al. developed a method to isolate and quantify levels of oxidized RNA generated by ROS, using ARP as a sensitive probe. Cytochrome c (cyt c) possesses peroxidase activity and nucleic acids are preferentially oxidized by cyt c-mediated pathway in the presence of H_2O_2 through electrostatic interaction. It has been shown that ROS can promote the dissociation of cyt c from the inner mitochondrial membrane, resulting in its release to the cytoplasm and subsequent apoptosis.

In this study, Tanaka et al. investigated the molecular mechanism and the physiological effects of cyt c-mediated RNA oxidation. First, the authors analyzed the oxidation products of synthetic RNAs and determined that guanosine in the RNA was the predominant ribonucleoside oxidized in cyt c-mediated oxidation, while the Fe(II)/ascorbate-mediated oxidation oxidized all ribonucleosides with no obvious preference. Next, the authors quantified the major oxidized derivative in oxidized RNA, the 8-OH-Guo, with the stable isotope dilution method and Gc/MS. Results showed that the amount of 8-OH-Guo generated from Fe(II)/ascorbate-catalyzed oxidation is dependent on the H_2O_2 concentration. In contrast, the 8-OH-Guo obtained from cyt c-catalyzed oxidation is not sensitive to H_2O_2 concentration or cyc c concentrations. In addition, the low quantity of 8-OH-Guo detected in the RNA oxidized by cyt c promoted the authors to further examine and confirm the depurination of the oxidized RNA and the generation of abasicsites. The authors then further showed that the aldehyde moieties on the abasic sites resulted from cyt c-catalyzed oxidation reaction can easily form Schiff base with the amino groups in proteins, leading to the cross-linking of the oxidized RNA to cyt c in the presence ofH_2O_2. Finally, the authors investigated the physiological function of the cross-linked cyt c-RNA by examining the oxidative interaction between the RNA and the liposome (containing 25% CL and 75% PC) bound cyt c. Results showed that the oxidation of the RNA by cyt c/H_2O_2 and the subsequent cross-linking of the RNA and cyt c led to the release of cyt c from CL-containing liposomes, which may represent the release of cyt c from the mitochondria to the cytosol. Thus, the authors propose that the cyt c-catalyzed oxidation of RNA peroxidation plays a role in oxidative stress-induced, mitochondria-mediated apoptosis. This is the first time RNA oxidation has been shown to regulate a protective signaling pathway and facilitate apoptosis in response to oxidative stress.

Would you like to contribute to the Fellows Newsletter?

We are seeking writers on topics of interest to NHLBI fellows.

Please email direducation@nhlbi.nih.gov for more information