



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.

Office of Education, DIR, NHLBI

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From the Director of the Office of Education

We hope you all had a great Holiday season and that your 2012 is off to a great start. At the time of our last newsletter, the NIH budget had still not been settled. Fortunately, congress and the President agreed on a budget just before the New Year, averting another government shutdown. While NIH overall received a modest increase, the actual NHLBI was cut by 0.5%. How this translates into budgets for DIR and the individual laboratories is still not clear, but it appears that we've dodged a major bullet this year. One area slated for a reduction is travel, but it is still the goal of DIR that Fellows should be able to attend the meetings that are necessary for their scientific and career progress.

Two NHLBI programs important for Fellows are preserved. First, we are still on track to have our NHLBI DIR retreat on March 28-30, although we still do not have an exact location. Registration will open in February, with a March 2nd deadline for Abstract Submissions. So get your abstract prepared and ready to submit when the site opens. Second, we are now recruiting for the NHLBI summer program, which will continue to sponsor one summer student per laboratory. The summer program is a great way for you to obtain valuable mentoring experience, and so I urge each NHLBI Fellow to speak with your advisor about how you can find and mentor a summer student.

Save the Date:

March 28-30, 2012
10th Annual NHLBI DIR Scientific Retreat
Location TBD



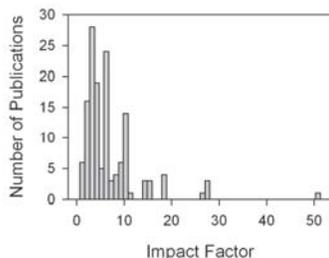
Where do we publish?

By Herbert Geller, Ph.D.

Scientific publications are the primary measure of achievement in our profession, and the work of NHLBI fellows is essential to the success of our research effort. So how did we do in 2011?

135 NHLBI Fellows (either current or former) were first author on 90 publications and co-author on 52, for a total of 142 publications in 2011. Of these, 8 Fellows had two first-author publications in 2011.

These publications appeared in 94 different journals. Table 1 (next column) presents the journals with the most publications from NHLBI Fellows, with J. B. C. leading the list with 10 publications, followed by Blood with 9 and PLoS One with 8. Figure 1 (right) presents a histogram of the impact factors of the journals in which fellows publish.



The average impact factor for the journals is 6.95, and the median impact factor is 5.03. Table 2 (below, right) presents a list of the highest impact journals. The highest impact journal was the New England Journal of Medicine (1 publication), followed by Nature Immunology (3 publications), Nature (1), and Nature Cell Biology (3).

Table 2

Journal	IF	# of articles
New England Journal of Medicine	51.296	1
Nature Immunology	27.596	3
Nature	26.681	1
Nature Cell Biology	18.485	3
Immunity	18.306	1
Journal of Clinical Investigation	15.754	2
Genes & Development	15.05	1
Journal of Experimental Medicine	14.484	1
Molecular Cell	14.033	1
Neuron	13.894	1
Nature Structural & Molecular Biology	11.502	1
Blood	10.558	9
Hepatology	10.446	1
Genome Research	10.256	1
Journal of Cell Biology	10.152	1
Circulation Research	9.854	1
Clinical Cancer Research	9.854	1
Proceedings of the National Academy of Sciences of the United States of America	9.771	5

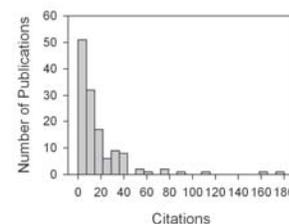
Table 1

Journal	# of articles
Journal of Biological Chemistry	10
Blood	9
Plos One	8
Proceedings of the National Academy of Sciences of the United States of America	5
Biochemistry	4
Biochemical Society Transactions	3
Molecular Biology of the Cell	3
Nature Cell Biology	3
Nature Immunology	3
American Journal of Physiology-Heart and Circulatory Physiology	2
Archives of Biochemistry and Biophysics	2
Cytometry Part B-Clinical Cytometry	2
Human Gene Therapy	2
Journal of Chemical Theory and Computation	2
Journal of Clinical Investigation	2
Journal of Magnetic Resonance Imaging	2
Molecular and Cellular Biology	2

nology (3 publications), Nature (1), and Nature Cell Biology (3).

These are aggregate statistics based on the impact factors of journals for 2010. As I mentioned last week, the impact factor of a journal for any year is calculated as the number of citations to articles in that journal that were published in the previous two years. Another way to look at the impact of our publications is to evaluate the citations in 2010 and 2011 to articles published in 2009. This approximates the IF in that we are using two years of citation data per article or journal.

The histogram of the citations to our papers is given in Figure 2 (right). The modal number of citations is 2-3/paper, with 12 papers each receiving that number of citations. The median number of citations per article is 11, while the mean is 18. This situation is due to a small number of articles that had a high number of citations, with two articles having 180 and 161 citations. At the other end, there were three papers published in 2009 that were not cited at all and another 3 cited once.



Overall, these numbers would suggest that about half of our fellows are publishing an article each year, that these articles are appearing in Journals with respectable impact factors, and that the overwhelming majority of our articles are being cited. Keep writing!

Recent Publications by NHLBI Fellows

- Case, L. B.** & Waterman, C. M. (2011). Adhesive F-actin Waves: A Novel Integrin-Mediated Adhesion Complex Coupled to Ventral Actin Polymerization. *Plos One* 6.
- Chen, K.** & Tjandra, N. (2011). Water proton spin saturation affects measured protein backbone (15)N spin relaxation rates. *J. Magn. Reson.* 213, 151-157.
- Enqvist, M., Nilsson, G., Hammarfjord, O., Wallin, R. P. A., Bjorkstrom, N. K., Bjornstedt, M., Hjerpe, A., Ljunggren, H. G., Dobra, K., Malmberg, K. J., & **Carlsten, M.** (2011). Selenite Induces Posttranscriptional Blockade of HLA-E Expression and Sensitizes Tumor Cells to CD94/NKG2A-Positive NK Cells. *J. Immunol.* 187, 3546-3554.
- Li, C. C., **Kuo, J. C.**, Waterman, C. M., Kiyama, R., Moss, J., & Vaughan, M. (2011). Effects of brefeldin A-inhibited guanine nucleotide-exchange (BIG) 1 and KANK1 proteins on cell polarity and directed migration during wound healing. *Proc. Natl. Acad. Sci. U. S. A* 108, 19228-19233.
- McGlinchey, R. P.**, **Yap, T. L.**, & Lee, J. C. (2011). The yin and yang of amyloid: insights from alpha-synuclein and repeat domain of Pmel17. *Physical Chemistry Chemical Physics* 13, 20066-20075.
- Nguyen, T. T.**, **Stevens, M. V.**, Kohr, M., Steenbergen, C., Sack, M. N., & Murphy, E. (2011). Cysteine 203 of Cyclophilin D Is Critical for Cyclophilin D Activation of the Mitochondrial Permeability Transition Pore. *J. Biol. Chem.* 286, 40184-40192.
- Pfeiffer, M., Kayzer, E. B., Yang, X. M., Abramson, E., Kenaston, M. A., **Lago, C. U.**, Lo, H. H., Sedensky, M. M., Lunceford, A., Clarke, C. F., Wu, S. J., McLeod, C., Finkel, T., Morgan, P. G., & Mills, E. M. (2011). Caenorhabditis elegans UCP4 Protein Controls Complex II-mediated Oxidative Phosphorylation through Succinate Transport. *J. Biol. Chem.* 286, 37712-37720.
- Saeed, F.**, Perez-Rathke, A., Gwarnicki, J., Berger-Wolf, T., & Khokhar, A. (2012). A high performance multiple sequence alignment system for pyrosequencing reads from multiple reference genomes. *Journal of Parallel and Distributed Computing* 72, 83-93.
- Sun, J. H., Kohr, M. J., **Nguyen, T.**, Aponte, A. M., Connelly, P. S., Esfahani, S. G., Gucek, M., Daniels, M. P., Steenbergen, C., & Murphy, E. (2012). Disruption of Caveolae Blocks Ischemic Preconditioning-Mediated S-Nitrosylation of Mitochondrial Proteins. *Antiox. Redox Sig.* 16, 45-56.
- Susarla, B. T. S., Laing, E. D., **Yu, P. P.**, Katagiri, Y., Geller, H. M., & Symes, A. J. (2011). Smad proteins differentially regulate transforming growth factor-beta-mediated induction of chondroitin sulfate proteoglycans. *Journal of Neurochemistry* 119, 868-878.
- Uchida, N.**, Hsieh, M. M., **Hayakawa, J.**, Madison, C., Washington, K. N., & Tisdale, J. F. (2011). Optimal conditions for lentiviral transduction of engrafting human CD34(+) cells. *Gene Ther.* 18, 1078-1086.
- Valdes, J. L.**, Tang, J. R., **McDermott, M. I.**, Kuo, J. C., **Zimmerman, S. P.**, Wincovitch, S. M., Waterman, C. M., Milgram, S. L., & Playford, M. P. (2011). Sorting Nexin 27 Protein Regulates Trafficking of a p21-activated Kinase (PAK) Interacting Exchange Factor (beta-Pix)-G Protein-coupled Receptor Kinase Interacting Protein (GIT) Complex via a PDZ Domain Interaction. *J. Biol. Chem.* 286, 39403-39416.

FelCom needs an additional representative for NHLBI.
Please contact the Office of Education if you are
interested in attending their monthly meeting.

THE SCIENCE BEAT

By Daniel Kraushaar, Ph.D.

Nguyen, T. T., Stevens, M. V., Kohr, M., Steenbergen, C., Sack, M. N., & Murphy, E. (2011). Cysteine 203 of Cyclophilin D Is Critical for Cyclophilin D Activation of the Mitochondrial Permeability Transition Pore. *J. Biol. Chem.* 286, 40184-40192.

Ischemia/reperfusion (I/R) injury can occur to many organs of the body when oxygen supply is absent due to restricted blood supply and is characterized by widespread cell death. Mitochondrial permeability transition pore or mPTP, a multiprotein complex, mediates cell death during I/R injury by rendering the mitochondrial membrane permeable to relatively small molecules. As such, mPTP opening results in loss of membrane potential and associated uncoupling of oxidative phosphorylation and ATP production that ultimately leads to production of reactive oxygen species and cell death. S-nitrosylation (SNO), represents a covalent attachment of a nitric oxide moiety to a protein thiol group, exerts protective effects on I/R injury through various mechanisms but whether and how it affects mPTP permeability has not been clearly established. In order to better define the role of mPTP in I/R injury and cytoprotection, Nguyen *et al.* focused their investigation on Cyclophilin D (CycD), a mitochondrial matrix protein and known regulator of mPTP. Mass spectrometry of resin-captured SNO proteins, revealed that CycD of ischemic preconditioned hearts becomes ni-

trosylated at Cys-203 and suggests that this residue may be critical for CycD function. Treatment of MEF cells with H₂O₂, which induces mPTP opening, was used in combination with AM-cobalt chloride quenching to measure mitochondrial permeability. H₂O₂ treatment of CycD^{-/-} MEFs lead to reduced quenching which is equivalent to reduced mPTP opening, demonstrating that CycD is required for efficient mPTP opening. Cys-203 of CycD was converted to serine by site-directed mutagenesis in order to establish whether Cys-203 is required for CycD-mediated opening of mPTP. To this end, CycD was replaced with either wild type or Cys-203 mutant CycD in CycD-deficient MEFs. Transfection with WT CycD efficiently restored mPTP opening whereas transfection with mutant Cys-203 CycD did not. Addition of the nitric oxide donor, GSNO, prior to H₂O₂ treatment, attenuated mPTP opening in WT MEFs but not Cys-203 or CycD^{-/-} mutants. This suggested that Cys-203 of CycD contributes predominantly to NO-mediated modulation of mPTP opening. Importantly, Cys-203 mutant MEFs that were subjected to oxidative stress exhibited reduced cell death suggesting that inhibition of CycD has cytoprotective effects. Expression of WT and Cys203 mutant CycD in CycD^{-/-} mice resulted in resistance to Ca²⁺ induced swelling of mitochondria isolated from liver tissue suggesting that CycD, and more specifically Cys203 regulate mitochondrial permeability *in vivo*. In summary Nguyen *et al.* have further defined the mechanistic basis for mPTP opening during I/R injury, highlighting the importance of the Cys-203 residue of CycD in modulating mPTP activity.

Bethesda/Chev Chase Restaurant Week January 23-29, 2012

Participating restaurants will offer two and three-course lunch for \$13 or \$16 and dinner for \$33. Enjoy great food at great prices! Please see restaurant website for complete menus and reservations.

Some participating restaurants:

- American Tap Room
- Assaggi Mozzarella Bar
- The Capital Grille
- Chef Tony's
- Jaleo
- Mon Ami Gabi
- Redwood Restaurant

For more information, visit:

<http://www.bethesda.org/bethesda/bethesda-chev-chase-restaurant-week-0>

2011 Year-end Roundup Publications by NHLBI Fellows

The Office of Education would like to apologize to those fellows whose papers below were not included in the monthly newsletter. If you find that we omit your paper, please let us know ASAP and we'll put it in the next newsletter.

- Andrade, M. V., Iwaki, S.,** Ropert, C., Gazzinelli, R. T., Cunha-Melo, J. R., & Beaven, M. A. (2011). Amplification of cytokine production through synergistic activation of NFAT and AP-1 following stimulation of mast cells with antigen and IL-33. *Eur. J. Immunol.* *41*, 760-772.
- Argraves, K. M., **Sethi, A. A.,** Gazzolo, P. J., Wilkerson, B. A., Remaley, A. T., Tybjaerg-Hansen, A., Nordestgaard, B. G., Yeatts, S. D., Nicholas, K. S., Barth, J. L., & Argraves, W. S. (2011). SIP, dihydro-SIP and C24:1-ceramide levels in the HDL-containing fraction of serum inversely correlate with occurrence of ischemic heart disease. *Lipids in Health and Disease* *10*.
- Aue, G.,** Lozier, J. N., Tian, X., Cullinane, A. M., **Soto, S.,** Samsel, L., Mccoy, P., & Wiestner, A. (2011). Inflammation, TNF alpha and endothelial dysfunction link lenalidomide to venous thrombosis in chronic lymphocytic leukemia. *Am. J. Hematol.* *86*, 835-840.
- Bulua, A. C., Simon, A., Maddipati, R., Pelletier, M., Park, H., **Kim, K. Y.,** Sack, M. N., Kastner, D. L., & Siegel, R. M. (2011). Mitochondrial reactive oxygen species promote production of proinflammatory cytokines and are elevated in TNFR1-associated periodic syndrome (TRAPS). *J. Exp. Med.* *208*, 519-533.
- Calado, R. T., Brudno, J., Mehta, P., **Kovacs, J. J.,** Wu, C., Zago, M. A., Chanock, S. J., Boyer, T. D., & Young, N. S. (2011). Constitutional Telomerase Mutations Are Genetic Risk Factors for Cirrhosis. *Hepatology* *53*, 1600-1607.
- Cunningham, K., **Uchida, Y.,** O'Donnell, E., Claudio, E., Li, W. L., Soneji, K., **Wang, H. S.,** Mukoyama, Y. S., & Siebenlist, U. (2011). Conditional deletion of Ccm2 causes hemorrhage in the adult brain: a mouse model of human cerebral cavernous malformations. *Hum. Mol. Gen.* *20*, 3198-3206.
- Gee, S. T.,** Milgram, S. L., Kramer, K. L., Conlon, F. L., & Moody, S. A. (2011). Yes-Associated Protein 65 (YAP) Expands Neural Progenitors and Regulates Pax3 Expression in the Neural Plate Border Zone. *Plos One* *6*.
- Haithcock, J., **Billington, N.,** Choi, K., Fordham, J., Sellers, J. R., Stafford, W. F., White, H., & Forgacs, E. (2011). The Kinetic Mechanism of Mouse Myosin VIIA. *J. Biol. Chem.* *286*, 8819-8828.
- Hardin, A. H., Sarkar, S. K.,** Seol, Y., Liou, G. F., Osheroff, N., & Neuman, K. C. (2011). Direct measurement of DNA bending by type IIA topoisomerases: implications for non-equilibrium topology simplification. *Nucl. Acid Res.* *39*, 5729-5743.
- Hsieh, M. M., **Fitzhugh, C. D.,** & Tisdale, J. F. (2011). Allogeneic hematopoietic stem cell transplantation for sickle cell disease: the time is now. *Blood* *118*, 1197-1207.
- Kashyap, M., Rochman, Y.,** Spolski, R., Samsel, L., & Leonard, W. J. (2011). Thymic Stromal Lymphopoietin Is Produced by Dendritic Cells. *J. Immunol.* *187*, 1207-1211.
- Lee, H. & Pastor, R. W.** (2011). Coarse-Grained Model for PEGylated Lipids: Effect of PEGylation on the Size and Shape of Self-Assembled Structures. *J. Phys. Chem. B* *115*, 7830-7837.
- Lelouvier, B. & Puertollano, R.** (2011). Mucolipin-3 Regulates Luminal Calcium, Acidification, and Membrane Fusion in the Endosomal Pathway. *J. Biol. Chem.* *286*, 9826-9832.
- Lu, Z. P., Bourdi, M., Li, J. H., Aponte, A. M., **Chen, Y.,** Lombard, D. B., Gucek, M., Pohl, L. R., & Sack, M. N. (2011). SIRT3-dependent deacetylation exacerbates acetaminophen hepatotoxicity. *Embo Reports* *12*, 840-846.
- Saeed, F.,** Perez-Rathke, A., Gwarnicki, J., Berger-Wolf, T., & Khokhar, A. (2012). A high performance multiple sequence alignment system for pyrosequencing reads from multiple reference genomes. *Journal of Parallel and Distributed Computing* *72*, 83-93.
- Sekine, Y., **Osei-Hwedieh, D.,** Matsuda, K., Raghavachari, N., Liu, D. L., Furuya, Y., Koike, H., Suzuki, K., & Remaley, A. T. (2011). High Fat Diet Reduces the Expression of Glutathione Peroxidase 3 in Mouse Prostate. *Prostate* *71*, 1499-1509.

NHLBI Holiday Dessert Potluck

Thanks to all who: baked desserts, bought desserts to contribute,
or just showed up to eat!

We hope you enjoyed your holiday!

New Principal Investigator



J. Robert Hogg, Ph.D. is a new PI in the Biochemistry & Biophysics Center. He was sought out during the Earl Stadtman Tenure Track Investigator search, which invited hundreds of hand-selected scientist to apply. Dr. Hogg earned his Ph.D. in Molecular and Cell Biology from the University of California at Berkeley. He previously worked under two Postdoctoral Research positions at University of California, Berkeley and Columbia University Medical Center. Dr. Hogg's current lab under BBC is Laboratory of Ribonucleoprotein Biochemistry.

2011 Year-end Roundup Publications by NHLBI Fellows Cont.

Siththanandan, V. B. & Sellers, J. R. (2011). Regulation of myosin 5a and myosin 7a. *Biochem. Soc. Trans.* *39*, 1136-1141.

Sun, J. H., Kohr, M. J., **Nguyen, T.**, Aponte, A. M., Connolly, P. S., **Esfahani, S. G.**, Gucek, M., Daniels, M. P., Steenbergen, C., & Murphy, E. (2012). Disruption of Caveolae Blocks Ischemic Preconditioning-Mediated S-Nitrosylation of Mitochondrial Proteins. *Antiox. Redox Sig.* *16*, 45-56.

Sung, H. J., Ma, W. Z., Starost, M. F., **Lago, C. U.,** Lim, P. K., Sack, M. N., Kang, J. G., Wang, P. Y., & Hwang, P. M. (2011). Ambient Oxygen Promotes Tumorigenesis. *Plos One* *6*.

Uchida, N., Bonifacino, A., Krouse, A. E., Metzger, M. E., Csako, G., Lee-Stroka, A., Fasano, R. M., Leitman, S. F., Mattapallil, J. J., Hsieh, M. M., Tisdale, J. F., & Donahue, R. E. (2011). Accelerated lymphocyte reconstitution and long-term recovery after transplantation of lentiviral-transduced rhesus CD34(+) cells mobilized by G-CSF and plerixafor. *Exp. Hematol.* *39*, 795-805.

Weniger, M. A. & Wiestner, A. (2011). Molecular Targeted Approaches in Mantle Cell Lymphoma. *Semin. Hematol.* *48*, 214-226.

Weniger, M. A., Rizzatti, E. G., **Perez-Galan, P.,** Liu, D. L., Wang, Q. Y., Munson, P. J., Raghavachari, N., White, T., Tweito, M. M., Dunleavy, K., Ye, Y. H., Wilson, W. H., & Wiestner, A. (2011). Treatment-Induced Oxidative Stress and Cellular Antioxidant Capacity Determine Response to Bortezomib in Mantle

Yao, X. L., **Dai, C. L.,** **Fredriksson, K.,** **Dagur, P. K.,** McCoy, J. P., Qu, X. A., Yu, Z. X., Keeran, K. J., Zywicke, G. J., Amar, M. J. A., Remaley, A. T., & Levine, S. J. (2011). 5A, an Apolipoprotein A-I Mimetic Peptide, Attenuates the Induction of House Dust Mite-Induced Asthma. *J. Immunol.* *186*, 576-583.

Yap, T. L., Gruschus, J. M., Velayati, A., Westbroek, W., Goldin, E., Moaven, N., Sidransky, E., & Lee, J. C. (2011). alpha-Synuclein Interacts with Glucocerebrosidase Providing a Molecular Link between Parkinson and Gaucher Diseases. *J. Biol. Chem.* *286*, 28080-28088.

Yong, A. S. M., Stephens, N., **Weber, G.,** Li, Y., Savani, B. N., Eniafe, R., Keyvanfar, K., Kurlander, R., Rezvani, K., & Barrett, A. J. (2011). Improved outcome following allogeneic stem cell transplantation in chronic myeloid leukemia is associated with higher expression of BMI-1 and immune responses to BMI-1 protein. *Leukemia* *25*, 629-637.