



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

I serve as a mentor for junior members of the Society for Neuroscience. During one chat with a person who was a junior faculty member, her major issue was "How can I publish in a high-impact journal?". While this question could be answered with factual information, I tried to refocus the discussion about why she felt this need, and to a discussion of what impact factor really means. This led to this month's column, which explains how the journal impact factor is calculated and also how journals can manipulate their contents to improve it. The major take-home messages are that not every paper in such a journal is high-impact, and high-impact paper will be recognized independently of the the journal in which it is published.

Save the date: the 2012 NHLBI DIR Scientific Retreat will be held on March 28-30 at a location to be announced. Our Keynote Speaker will be Dr. Nancy Andrews, vice chancellor for academic affairs and dean of the Duke University School of Medicine. Our Scientific Speaker will be Dr. Alexandra Newton, Professor of Pharmacology at UCSD and Dr. Zena Werb, Professor and Vice-Chair of Anatomy at the University of California, San Francisco. Click [here](#) for more information on this and previous retreats. See you all there!

Chasing the Impact Factor

By Herbert Geller, Ph.D.

We often hear the question "How can I publish in a high impact journal?" However, the question is often not really about publication practices; the real agenda likely is "if I publish in a high-impact journal, my research will be considered to be high impact" and "will get me a good job". So what's the evidence that this latter statement is true?

We'll begin by examining the meaning of the Journal Impact Factor (JIF) and how it is computed, and also whether it is being applied correctly. The JIF was originally

[Cont'd on page 2](#)

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Recent Publications by NHLBI Fellows

- Hu, G. Q., Schones, D. E., Cui, K. R., Ybarra, R., Northrup, D., Tang, Q. S., Gattinoni, L., Restifo, N. P., Huang, S. M., & Zhao, K. J.** (2011). Regulation of nucleosome landscape and transcription factor targeting at tissue-specific enhancers by BRG1. *Genome Res.* *21*, 1650-1658.
- Kidder, B. L., Hu, G. Q., & Zhao, K.** (2011). ChIP-Seq: technical considerations for obtaining high-quality data. *Nature Immunol.* *12*, 918-922.
- Kim, J. H. & Adelstein, R. S.** (2011). LPA(1)-Induced Migration Requires Nonmuscle Myosin II Light Chain Phosphorylation in Breast Cancer Cells. *J. Cell. Physiol.* *226*, 2881-2893.
- Maciejewski, M., Tjandra, N., & Barlow, P. N.** (2011). Estimation of Interdomain Flexibility of N-Terminus of Factor H Using Residual Dipolar Couplings. *Biochem.* *50*, 8138-8149.
- Park, Y. N., Masison, D., Eisenberg, E., & Greene, L. E.** (2011). Application of the FLP/FRT system for conditional gene deletion in yeast *Saccharomyces cerevisiae*. *Yeast* *28*, 673-681.
- Wagner, W., McCroskery, S., & Hammer, J. A.** (2011). An efficient method for the long-term and specific expression of exogenous cDNAs in cultured Purkinje neurons. *J. Neurosci. Methods* *200*, 95-105.
- Wu, W. W., Wang, G. H., Insel, P. A., Hsiao, C. T., Zou, S. G., Maudsley, S., Martin, B., & Shen, R. F.** (2011). Identification of Proteins and Phosphoproteins Using Pulsed Q Collision Induced Dissociation (PQD). *Journal of the American Society for Mass Spectrometry* *22*, 1753-1762.
- Yan, L., Wei, X., Tang, Q. Z., Feng, J. H., Zhang, Y., Liu, C., Bian, Z. Y., Zhang, L. F., Chen, M. Y., Bai, X., Wang, A. B., Fassett, J., Chen, Y. J., He, Y. W., Yang, Q. L., Liu, P. P., & Li, H. L.** (2011). Cardiac-specific mindin overexpression attenuates cardiac hypertrophy via blocking AKT/GSK3 beta and TGF-beta 1-Smad signalling. *Cardiovasc. Res.* *92*, 85-94.
- Zhao, H., Sun, J. H., Deschamps, A. M., Kim, G., Liu, C. Y., Murphy, E., & Levine, R. L.** (2011). Myristoylated methionine sulfoxide reductase A protects the heart from ischemia-reperfusion injury. *Am. J. Physiol. Heart Circ. Physiol.* *301*, H1513-H1518.

designed by Eugene Garfield, the founder of the Institute for Scientific Information (ISI), to compare the quality of published journals. The JIF was computed as the total number of citations to all the articles in a journal published during the previous two years divided by the number of "qualified" articles published by the journal during the same period of time. And what is the definition of the most important term ("qualified")? It includes research articles, letters, and review articles, but does not include non-research items such as news and views and commentaries, which still do get cited (sometimes as much as the original article). So if an letter in Science also has a commentary that expands the interpretation of the article, both will get cited, but only the letter will get

counted in the denominator, automatically doubling the contribution of the letter to the IF of the journal. Thus, since the ascendancy of the IF as a measure of quality, both Science and Nature have reduced the number of original research articles they publish, while at the same time increasing the number of News and Views and commentaries. Likewise, review articles get lots of citations, and so the more review articles a journal publishes, the higher their IF. If we control for these issues, this shrinks the difference in IF between the "high-impact" journals and the rest.

Now that we understand how IF can be manipulated, is true that the articles in a journal with a high average IF are themselves of high-impact? The distribution of citations to articles in journals is not Gaussian: it follows a

Bradford distribution, with an exponential decay of the number of citations vs. the number of articles. Thus, Nature finds that nearly 90% of their citations come from 25% of their articles. The converse is that 75% of their articles only contribute 10% of the citations. Moreover, retracted articles still contribute to the citation count. So the assertion that because an article is in a high-impact journal makes it high impact is clearly false. The distribution of citations is true for all journals, implying that there are many high-impact articles in journals that do not have a high average IF. There are no data that demonstrate that differences in the relative impact of articles specialty journals are significant. Since all articles are immediately available electronically, any article deemed significant

New NHLBI Fellows



Javier Traba Dominguez Ph.D., is a Visiting Fellow in the Laboratory of Mitochondrial Biology in Cardiometabolic Syndromes under Dr Michael Sack. Dr. Traba earned his Ph.D. in Molecular Biology from Universidad Autonoma de Madrid, Spain.

He was previously Visiting Researcher in the Department of Cell and Developmental Biology, University College London, UK. Dr. Traba's initial research project involves working on the protein Parkin, an E3 ubiquitin ligase that is mutated in juvenile Parkinson's disease patients.



Katarzyna Placek, Ph.D., is a Visiting Fellow in the Laboratory of Molecular Immunology under Dr. Keji Zhao. Dr. Placek earned her Ph.D. in Immunology from the Pasteur Institute in France. She was a short term postdoctoral fellow at Pasteur Institute in the Immunoregulation Unit in Paris, France. Dr. Placek's initial research project will be to examine conditional KO mice lacking different enzymes modifying histones in CD4+ T cells in order to find their role and target genes during the differentiation of CD4+ T helper cells.



Kem Sochacki, Ph.D., is an IRTA Fellow in the Laboratory of Molecular and Cellular Imaging under Dr. Justin Taraska. Dr. Sochacki earned her Ph.D. in Analytical Chemistry from the University of Wisconsin- Madison. She was the recipient of the

Robert H. Doremus Scholarship and the Gary Parr Memorial Award in 2005 and 2011 respectively. Dr. Sochacki is currently working on starting a project that images exocytosis proteins using fluorescence microscopy.



Majdi Halabi, M.D., is a Research Fellow in the Cardiovascular Intervention Program under Dr. Robert Lederman. Dr. Halabi earned his M.D. in Medicine from Sackler School of Medicine, Tel- Aviv University.

Dr. Halabi was previously a Senior Cardiologist in the Interventional Cardiology Unit at Rambam Medical Center, Haifa, Israel. His initial research project is working on accessing the LV from the chest wall through the RV.



Sara Menazza, Ph.D. is a Visiting Fellow in the Laboratory of Cardiac Physiology under Dr. Elizabeth Murphy. Dr Menazza earned her Ph.D. in Biochemistry and Biotechnology from the University o Padova, Italy. She is a member of the International Society for Heart Research, European Section. Dr. Menazza's initial research project involves protein ubiquitination in cardio-protection.

**NHLBI DIR Holiday Dessert Potluck
Thursday, December 15
1:00PM - 2:00PM
Building 10, Room 13S235A**



All are welcome to attend!

**** NHLBI Fellows, Staff Scientist & Clinicians, and Principal Investigators****

**Sponsored by the NHLBI Fellows' Advisory Committee
Bring a dish or drink to serve
Please contact the OE at direducation@nhlbi.nih.gov
with any questions.**



THE SCIENCE BEAT

By Daniel Kraushaar, Ph.D.

Kim, J. H. & Adelstein, R. S. (2011). LPA(1)-Induced Migration Requires Nonmuscle Myosin II Light Chain Phosphorylation in Breast Cancer Cells. *J. Cell. Physiol.* 226, 2881-2893.

The majority of breast cancer related deaths are caused by metastatic tumors and hence much research is currently being invested in understanding the molecular mechanisms that underlie breast cancer metastatic potential. Cancer metastasis fundamentally involves cell invasion and deregulated cell migration through the extracellular matrix. Lyosphosphatidic acid (LPA) is a phospholipid present in all mammalian cells and tissues including blood and serum. It is recognized as an important signaling molecule that alters a wide range of responses including cell migration among others. LPA signals via G protein coupled receptors and production of both LPA itself and its complementary receptors are elevated in many kinds of cancer including malignant breast cancer. LPA has been linked to numerous aspects of cancer progression yet the precise mechanisms of action are oftentimes not well understood.

In an NHLBI study, Kim & Adelstein elucidate the precise signaling cascade that emanates from LPA and ultimately controls the migration of breast cancer cells. In order to determine which of the three expressed isoforms of LPA receptors, LPA1-3, mediate LPA-induced migration, chemical receptor antagonists combined with siRNA knockdown of LPA receptors were utilized. *In vitro* wound healing assays, as well as transwell assays, that allow to measure cell migration and motility, showed that inhibition of LPA1 attenuated cell migration of 4T1 breast cancer cells most, compared to smaller effects seen after inhibition of LPA2 and LPA3. Nonmuscle myosin II (NM II) are hexameric complexes that consist of a pair of nonmuscle myosin heavy chains II (NMHC II), a pair of essential light chains and a pair

of regulatory light chains (RLCs). Phosphorylation of the RLC is critical for the generation of contractile force needed in cell migration and generally promotes cell movement. Immunoprecipitation of NMHC II isoforms A and B, and subsequent probing against phosphorylated RLC showed that LPA induced equal phosphorylation of both isoforms of NMHC II at Ser19, which became abolished when treated with the LPA1 receptor inhibitor. Knockdown of NMHC II A or B resulted in reduced LPA-induced cell migration and suggests that both isoforms are required for cell movement. Interestingly, rescue experiments with introduced NMHC II A into NMHC II B-depleted cells only achieved partial reversion of migration whereas almost complete reversion was seen with NMHC II A in NMHC II A-depleted cells, suggesting distinct and non-redundant functions for NMHC II isoforms. In order to decipher the upstream kinases responsible for NMHC II phosphorylation, two candidate kinases were examined, myosin light chain kinase (MLCK) and Rho kinase (ROCK). By using chemical inhibitors, as well as siRNAs against both kinases, the authors showed that inhibition of MLCK only partially inhibited LPA-induced migration whereas inhibition of ROCK caused a substantially greater decrease in cell migration, indicating that ROCK is the predominant kinase involved in breast cancer cell migration and NMHC II phosphorylation.

In line with this result, LPA stimulation of 4T1 cells, induced rapid activation of the GTPase protein, RhoA, as shown by its translocation from cytoplasm to membrane and increasing levels of GTP-bound RhoA. Most experiments were duplicated with similar results in another breast cancer cell line, MDA-MB-231, and indicate that LPA activation of the RhoA-ROCK pathway may be prevalent in regulating cell migration in breast cancer. In summary, Kim & Adelstein's study has helped to define the signaling pathways, triggered by LPA, which activates the RhoA-ROCK pathway and subsequently results in cytoskeletal reorganization through activation of NM II, which ultimately regulates cell migration of breast cancer cells.

will be known, no matter in what journal it is published. In fact, there are many who are suggesting that the number of downloads of a particular article is a more useful benchmark than the number of citations.

Is there a downside to aiming for a high-impact journal? You bet there is! One is obvious the criteria for publish-

ing in these journals is not just based on the scientific content, but is often based on the Editor's judgement of what articles will attract attention. Thus, research in fields which are considered "hot" have a higher probability of acceptance than those that are not. The other downside is that many of these journals will require an incredible

amount of supporting information, such that it would be impossible to achieve publication in a reasonable amount of time. Fellows are especially vulnerable: you are judged on your productivity, and it may be that, once you have a story, getting it published is likely to be more beneficial than waiting to embellish it in the hopes of hitting the jackpot.