



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

The Holiday Season is fast approaching, with many different groups celebrating according to their own tradition. It is especially important that those of us who are fortunate enough to be paid for our efforts think of those in need. This year many non-profit organizations are struggling to fulfill their mission. Each of us can help by contributing something to the charity of your choice. The Combined Federal Campaign makes this process very easy. If you have not received a CFC donation card, ask your administrator for one. Even if you donate just a small amount to one charity, it makes a difference.

Get your abstracts ready for the DIR Scientific Retreat! Look for the opening of the Retreat Web Site in mid-January, with an abstract deadline at the end of February. We have three outstanding speakers for the retreat, as well as the usual activities of posters and oral presentations by NHLBI fellows. Not to mention the scientific trivia contest! I look forward to seeing all of you there.

I wish you all the best for the New Year!

What are Employers Looking For?

By Herbert Geller, Ph.D.

What are employers looking for? In the academic world, the criteria to obtain a job are that the applicant has the knowledge, skills and ability to do outstanding creative science. Ostensibly, these are the same criteria by which all of us senior folk met when we were hired. In reality, though the written criteria are the same, the levels of achievement required to get a tenure-track position have increased significantly over the years, such that many of the senior investigators admit that they would not be hired in the current climate. The main reason, as you might have guessed, is the economy: there are far fewer job openings now than in past years, and so the process of elimination is taking a much higher toll than it might have. Here is a typical job ad statement "*Applicants must have a doctorate degree and should have developed, or demonstrate the potential to de-*

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Save the Date:

March 28-30, 2012

10th Annual NHLBI DIR Scientific Retreat

Location TBD

Recent Publications by NHLBI Fellows

Aue, G., Du, Y., Cleveland, S. M., Smith, S. B., Dave, U. P., Liu, D. L., **Weniger, M. A., Metais, J. Y.**, Jenkins, N. A., Copeland, N. G., & Dunbar, C. E. (2011). Sox4 cooperates with PU.1 haploinsufficiency in murine myeloid leukemia. *Blood* 118, 4674-4681.

Barbash, I. M., Schenke, W. H., **Halabi, M.**, Ratnayaka, K., Faranesh, A. Z., Kocaturk, O., & Lederman, R. J. (2011). Experimental Model of Large Pulmonary Embolism Employing Controlled Release of Subacute Caval Thrombus in Swine. *J. Vasc. Interv. Radiol.* 22, 1471-1477.

Bond, L. M., Brandstaetter, H., Sellers, J. R., Kendrick-Jones, J., & Buss, F. (2011). Myosin motor proteins are involved in the final stages of the secretory pathways. *Biochem. Soc. Trans.* 39, 1115-1119.

Francis, R., Xu, X., **Park, H.**, **Wei, C. J.**, **Chang, S.**, Chatterjee, B., & Lo, C. (2011). Connexin43 Modulates Cell Polarity and Directional Cell Migration by Regulating Microtubule Dynamics. *Plos One* 6.

Ghanima, W., Junker, P., Hasselbalch, H. C., Boiocchi, L., Geyer, J. T., **Feng, X. M.**, Gudbrandsdottir, S., Orazi, A., & Bussel, J. B. (2011). Fibroproliferative activity in patients with immune thrombocytopenia (ITP) treated with thrombopoietic agents. *Brit. J. Haematol.* 155, 248-255.

Gore, A. V., Swift, M. R., Cha, Y. R., Lo, B., McKinney, M. C., **Li, W. L.**, Castranova, D., Davis, A., Mukoyama, Y. S., & Weinstein, B. M. (2011). Rspo1/Wnt signaling promotes angiogenesis via Vegf/Vegfr3. *Development* 138, 4875-4886.

velop, an outstanding research program and a record of extramural funding. Applicants must also exhibit a commitment to excellence in teaching."

Here they require hard evidence of "outstanding" research (such as significant published papers) and not only are they asking that you be able to obtain funding, they are actually screening for those candidates that have obtained it. They are not taking any chances at all.

This same phenomenon is taking place in industry: because there are fewer jobs and the relatively larger number of job candidates, employers can be more picky. Formerly, employers would look for a person that can do the job, and not care too much about what specific skills they had, because they would undergo a significant amount of on-the-job training. Not anymore. Today, employers are looking for those with a specific skill set to enable immediate productivity. For example, a current job ad is looking for "Two years experience conducting research and analysis in the field of geriatrics, behavioral health and/or child

health and at least one publication in peer reviewed literature and/or teaching/speaking experience."

What does it take to get a job?

Given this climate, what can you do as a potential candidate to make sure that you meet the requirements for the job you want? First, I would read job ads. You will find that most ads for a particular type of position require a common set of skills. You then can engage in activities that provide you with that set of skills. A quick search of indeed.com for the term "scientist" found these common themes: "*Contributes as a team member*", "*Demonstrated ability to critically evaluate and interpret data*", "*Excellent written and oral communication skills*" and "Supervise research associate level scientist". Knowing this, you can engage in activities that will demonstrate these skills on your resume. Many members of the Fellows Advisory Committee find that this demonstrates team work, while next two attributes are normally acquired in the lab. You can also gain supervisory experience by

taking on a post-bac or a summer student.

In the academic environment, in addition to outstanding publications, the two most often mentioned features are the ability to teach and the ability to obtain peer-reviewed funding. Experience in both can be acquired here: Fellows can teach through FAES, or they can find part-time teaching opportunities at local community colleges. NHLBI Fellows can compete for a Lennant Fellowship, apply for Postdoctoral fellowships from private foundations, and apply for a career transition award, either the NHLBI K22 for US Citizens or Permanent Residents or the NIH K99/R00 for visa holders.

In summary, knowing the requirements to get a job will certainly help you focus your efforts on fulfilling them. For more specific advice, please contact the Office of Education.

THE SCIENCE BEAT

By Nisha Narayan, Ph.D.

Kim JH, Adelstein RS. LPA(1) -induced migration requires nonmuscle myosin II light chain phosphorylation in breast cancer cells. (2011) Cell Physiol. 226(11):2881-93.

Cell migration is an essential developmental process that guides the directional movement of cells to specific locations. It has important roles in several cellular processes such as wound healing and embryonic development and errors in it may lead to aberrations such as tumor formation and metastasis. External stimuli, including cytoskeleton-related signaling molecules, play a big role in the enhanced migration seen in neoplastic cells. This study describes the molecular interplay between the lysophosphatidic acid (LPA) receptor and nonmuscle Myosin II (NM II) in the context of LPA-induced migration in breast cancer cells.

The initial experiments in the study establish through transwell migration assays with the breast cancer cell line 4TI, that the migration of these cells indeed depends on LPA. They also established which LPA receptor type is involved in this process by using chemical antagonists as well as an siRNA approach on the major receptor types LPA₁, LPA₂ and LPA₃ and found that LPA₁ is required for LPA-induced migration of these cells. Based on previous studies that have indicated a role for LPA as one of the stimuli for several of the small G protein families, they then investigated the status of the activation of these families by LPA. Upon a 10-minute activation by LPA, only RhoA was translocated from the cytosol to the membrane in 4TI cells, while other small G proteins including Rac1 and Cdc42 were not. Having found RhoA to be a target for LPA stimulation, they then tackled

the identification of downstream goals for RhoA signaling in migration. Rho Kinase (ROCK) is widely recognized as a downstream effector of RhoA in various cell types, while other reports allude towards the role of NM II in migration. Therefore inhibitors against NM II (blebbistatin) and ROCK (Y27632) were both tested in the context of LPA-induced migration in wound-healing assays as well as in transwell migration assays. The ROCK inhibitor and blebbistatin both potently blocked migration induced by LPA, so they sought to examine the phosphorylation of the regulatory light chain (RLC) of NM II by ROCK after LPA treatment. Using immunoblotting techniques, each of the two NM II isoforms, NM II-A and NM II-B were found to be phosphorylated in the RLC. This phosphorylation was significantly enhanced by LPA, but was diminished in the presence of ROCK inhibitors or RhoA inhibitors, suggesting that ROCK is involved in LPA-induced RLC phosphorylation of NM II. To rule out the involvement of Myosin light chain kinase (MLCK) in the phosphorylation event, an inhibitor, ML-7, and MLCK siRNA were used. Both showed a very slight decrease in LPA-induced migration compared to the ROCK inhibitor, implying that MLCK is not significantly involved in LPA-induced migration.

Finally, to confirm the roles of NM II-A and NM II-B in LPA-induced migration, their levels were completely ablated in 4TI cells by lentiviral shRNA knockdowns and migration assessed in these cells by wound-healing assays. LPA-induced migration and invasion were both marginally reduced in the knockdown cells suggesting that both NM II-A and NM II-B played important roles in the LPA-induced migration of breast cancer cells. This study therefore proposes a novel molecular mechanism for the signaling mechanism and pathways involved in triggering the cellular migration process in breast cancer cells.

**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**

New NHLBI Fellows

Zhe Chen, Ph.D. is a new Visiting Fellow in the Laboratory of Molecular Genetics under Dr. Hong Xu. Dr. Chen completed her Ph.D. in Biochemistry and Molecular Biology from Tsinghua University, Beijing,

China. Before coming to NIH, she worked in the Laboratory of Molecular Enzymology, School of Life Sciences at Tsinghua University. Dr. Chen's initial research project is working with molecular genetics in drosophilas.



Kim-Lien Nguyen, M.D. is a new Clinical Fellow in the Laboratory of Cardiac Energetics under Dr. Andrew Arai. Dr. Nguyen earned her medical degree from David Geffen School of Medicine at the University of California, Los Angeles, CA. She completed her residency in Internal Medicine from Johns Hopkins, Osler Medical Service and had a clinical fellowship in general cardiology at UCLA Medical Center. Dr. Nguyen's currently working to develop a quantitative method to analyzing myocardial perfusion using cardiac magnetic resonance imaging.

Recent Publications by NHLBI Fellows Continued

Hirasaka, K., **Lago, C. U.**, Kenaston, M. A., Fathe, K., Nowinski, S. M., Nikawa, T., & Mills, E. M. (2011). Identification of a Redox-Modulatory Interaction Between Uncoupling Protein 3 and Thioredoxin 2 in the Mitochondrial Intermembrane Space. *Antiox. Redox Sig.* 15, 2645-2661.

Kang, H., Suh, J. Y., Jung, Y. S., **Jung, J. W.**, Kim, M. K., & Chung, J. H. (2011). Peptide Switch Is Essential for Sirt1 Deacetylase Activity. *Mol. Cell* 44, 203-213.

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.

Martina, J. A., Wu, X. F. S., Catalfamo, M., Sakamoto, T., **Yi, C.**, & Hammer, J. A. (2011). Imaging of lytic granule exocytosis in CD8(+) cytotoxic T lymphocytes reveals a modified form of full fusion. *Cellular Immunology* 271, 267-279.

Saikus, C. E., Ratnayaka, K., **Barbash, I. M.**, Colyer, J. H., Kocaturk, O., Faranesh, A. Z., & Lederman, R. J. (2011). MRI-Guided Vascular Access With an Active Visualization Needle. *J. Magn. Reson. Imaging* 34, 1159-1166.

Schroeder, J. L., Bakalar, M., Pohida, T. J., & Balaban, R. S. (2011). Rapid overlapping-volume acquisition and reconstruction (ROVAR): automated 3D tiling for high-resolution, large field-of-view optical microscopy. *J. Microsc.* 243, 103-110.

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

Vire, B., David, A., & Wiestner, A. (2011). TOSO, the Fc mu Receptor, Is Highly Expressed on Chronic Lymphocytic Leukemia B Cells, Internalizes upon IgM Binding, Shuttles to the Lysosome, and Is Downregulated in Response to TLR Activation. *J. Immunol.* 187, 4040-4050.

Wang, A. B., Ma, X. F., Conti, M. A., & Adelstein, R. S. (2011). Distinct and redundant roles of the non-muscle myosin II isoforms and functional domains. *Biochem. Soc. Trans.* 39, 1131-1135.

Wohlfert, E. A., Grainger, J. R., Bouladoux, N., Konkell, J. E., Oldenhove, G., Ribeiro, C. H., Hall, J. A., Yagi, R., Naik, S., Bhairavabhotla, R., Paul, W. E., Bosselut, R., **Wei, G.**, Zhao, K. J., Oukka, M., Zhu, J. F., & Belkaid, Y. (2011). GATA3 controls Foxp3(+) regulatory T cell fate during inflammation in mice. *J. Clin. Invest.* 121, 4503-4515.