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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.

Office of Education, DIR, NHLBI

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From the Director of the Office of Education

Most of us are concerned about what the future holds for us. While success often appears to depend upon chance events, these events occur within the context of your own experience and attitudes. My article this month is a synopsis of a recent report on scientific personnel needs for the future that emphasizes that the traditional career as a faculty member in a university will not be easy to achieve, and so future scientists will need to be prepared for a variety of careers. The achievements of our NHLBI fellows are consistent with this observation: while some do go onto faculty positions, many go to industry or public service. We know that NHLBI fellows are most concerned about their research progress, but the Office of Education is available to all fellows to talk about their career goals and aspirations and how to achieve them.

We hope you've recovered from the recent power outage, and are enjoying some of our hot summer. The Office of Education has several events planned in the coming weeks, and we hope to see you there!

Why Am I Here at NHLBI?

By Herbert M. Geller

This question is one that each fellow should periodically ask themselves. This question becomes particularly important in the current job market, where most fellows do not continue in careers that require laboratory research (a low percentage of Ph.D. scientists are obtaining PI positions while a somewhat greater percentage are obtaining permanent positions as bench scientists). A recent report by a Biomedical Work-

force Working Group of NIH (on the web at http://acd.od.nih.gov/bmw_report.pdf) highlighted the problem, noting that "commenters agreed that NIH is training more scientists than the workforce can support; exceptions included certain specialties such as veterinary research, biostatistics, and medical informatics. Supply of research funds is largely viewed to be inadequate and, in the current environment, creates a demand for cheap labor to perform the research." This same workforce report said [Cont'd on page 3](#)

Introduction to Grant Writing

Thursday, July 26th
2:00 PM - 5:00 PM

Required for all fellows who wish to write a
Lenfant fellowship or a K grant application
For more information, email direducation@nhlbi.nih.gov

THE SCIENCE BEAT

By Daniel Kraushaar, Ph.D.

Brzeska, H., Guag, J., Preston, G. M., Titus, M. A., & Korn, E. D. (2012). Molecular Basis of Dynamic Relocalization of Dictyostelium Myosin IB. *J. Biol. Chem.* 287, 14923-14936.

Class I myosins are composed of a single heavy chain that consists of a N-terminal globular motor domain which binds actin and has actin-activated ATPase activity. These myosins contribute to the proper formation of actin-rich protrusions such as pseudopodia of amoeboid cells. Dynamic events that orchestrate the localization of cytoskeletal components, including myosins, have to be tightly regulated but the molecular basis for this is not well understood. The current NHLBI study by Brzeska *et al.* was aimed at gaining a better understanding of the dynamic localization of *Dictyostelium* myosin IB (DMIB) with focus on its BH site. The BH site, originally discovered in *Acanthamoeba* myosin IC, binds to acidic phospholipids *via* a short sequence of basic and hydrophobic amino acids and is present in the tail region of DMIB. Live imaging of expressed fusion proteins was utilized to track DMIB and actin localization during various stages of the starvation cycle of *Dictyostelium*. Freshly plated cells display low motility and DMIB localizes uniformly to the plasma membrane. Subsequently cell movement increases and DMIB becomes enriched at newly formed pseudopodia and cell-to-cell contacts. Upon longer starvation, cells become elongated and highly polarized; at this stage DMIB is localized at the cell front where it co-localizes with PIP2/PIP3. In order to investigate the structural requirements of DMIB localization, several deletion mutants were expressed that either contained mutated residues within head and BH site or larger deletions of major regions such as head and tail. 'BH site' mutants exhibited loss of plasma membrane binding and were instead diffusely detected in the cytoplasm, demonstrating that the BH site is required for plasma membrane association. No other regions were found

to be required for the plasma membrane localization of DMIB. As cell movement commenced, 'tail-only' mutants failed to re-localize from plasma membrane to actin-rich protrusions and to the cell front during polarization. Instead 'tail-only' mutants retained a uniform distribution along the plasma membrane, which suggested that the head domain is required for dissociation from the plasma membrane and subsequent relocation of DMIB. Another interesting observation was made prior to re-localization of DMIB in the non-motile stage of cells; although both wildtype and 'tail-only' mutant mainly localize to the plasma membrane at this stage, a higher ratio of cytoplasmic to plasma membrane fluorescence was detected in cells expressing wildtype DMIB. This indicated that the head region reduces DMIB plasma membrane association presumably by binding to a cytoplasmic protein, which in further experiments was found to be actin. In line with this idea, a 'weak' actin-binding mutant exhibited reduced presence in the cytoplasm whereas 'strong' actin-binding mutants strongly co-localized with actin waves. Treatment with latrunculin A (LatA) causes rapid erasure of cortical F-actin before it slowly reappears along the plasma membrane. Twenty minutes after LatA treatment one-third of cells remained devoid of actin-patches and in these DMIB localized to the plasma membrane. In contrast, in cells with actin patches, DMIB strongly co-localized with F-actin. These data agree with a model whereby the binding of DMIB with F-actin *via* its head region competes with binding of its BH site with phospholipids and thereby ultimately determines the localization of DMIB. Such a model may help to explain an actin-coupled recruitment of DMIB from plasma membrane to pseudopodia as amoeboid cells initiate chemotactic cell movement. In summary, the authors of this study published in the *Journal of Biological Chemistry*, find that the BH site of DMIB is essential for plasma membrane association and that its re-localization requires an interaction between DMIB and F-actin. This finding likely will pertain to many other myosins and cytoskeletal proteins that contain similar BH sites.

THE SCIENCE BEAT needs a Postdoc to review and summarize fellows publications for the newsletter.

****Your article could be featured above!****

If interested, please email direducation@nhlbi.nih.gov

that “after a reasonable period of training – ideally three years – there is diminished value for the trainee in staying in a subordinate position. Also, the group feels that those postdoctoral researchers who do not go on to conduct research in an academic setting should receive training in the skills needed and information about other career options.”

In this climate, each person in training must assess whether the training they are getting is appropriate for their career and, if not, how they can get it. As a research institute, NIH has a primary mission of providing intensive research training for our graduate students and postdoctoral fellows. The lab experience is, and must be, the focus of postdoctoral training. However, the NHLBI DIR and the Office of Education firmly believes that fellows must receive training in all of the areas that are needed for success in many different jobs, and that the postdoctoral fellowship should not be extended beyond what is needed for training. Many skills, such as oral and written communication, supervisory skills and network-

ing are common ones that all trainees should receive. While grant writing skills might be considered necessary for those who wish to be academics, the same skills are required in writing a persuasive memo to sell your ideas in whatever context. Because of the nature of NIH, it is perhaps harder to learn budgetary management. Finally, teaching experience can be obtained through FAES.

One major recommendation by the working group was that career development and progress be monitored through the creation of an individual development plan (IDP). While our progress report form has many similarities with an IDP, the IDP is significantly more detailed in specific areas. More information about the IDP and how you might prepare on is on the FASEB web site: <http://www.faseb.org/Policy-and-Government-Affairs/Science-Policy-Issues/Training-and-Career-Opportunities-for-Scientists/Individual-Development-Plan.aspx>. I urge each of you to create one that fits your own career goals.

Another recommendation was that NIH facilitate training in non-academic areas by providing opportunities and information. Presently, there are many workshops and events organized by the NIH OITE. Moreover, the NHLBI encourages our fellows to take advantage of the rotation opportunities within NHLBI, at private foundations and certain cooperating businesses. An additional part of this recommendation is that businesses that receive NIH funding through the SBIR or STTR mechanisms be encouraged to provide experiences for postdoctoral fellows and graduate students. Implementation would clearly widen the rotation opportunities for NHLBI fellows.

The overall tenor of the report is that training should be for a purpose, that prospective trainees should have a clear idea of why they are in training, and that institutions should seek to provide training for a multiplicity of career opportunities. The NHLBI DIR is firmly committed to these principles and we welcome your feedback about ways in which we might be even more effective in the future.

Recent Publications by NHLBI Fellows

- Avila, C., **Huang, R. J.**, **Stevens, M. V.**, Aponte, A. M., Tripodi, D., **Kim, K. Y.**, & Sack, M. N. (2012). Platelet Mitochondrial Dysfunction is Evident in Type 2 Diabetes in Association with Modifications of Mitochondrial Anti-Oxidant Stress Proteins. *Experimental and Clinical Endocrinology & Diabetes* 120, 248-251.
- Brzeska, H., Guag, J., **Preston, G. M.**, Titus, M. A., & Korn, E. D. (2012). Molecular Basis of Dynamic Relocalization of Dictyostelium Myosin IB. *J. Biol. Chem.* 287, 14923-14936.
- Ugander, M.**, **Oki, A. J.**, Hsu, L. Y., Kellman, P., Greiser, A., Aletras, A. H., Sibley, C. T., Chen, M. Y., Bandettini, W. P., & Arai, A. E. (2012). Extracellular volume imaging by magnetic resonance imaging provides insights into overt and sub-clinical myocardial pathology. *Eur. Heart J.* 33, 1268-1278.
- Xue, H.**, Shah, S., Greiser, A., Guetter, C., Littmann, A., Jolly, M. P., Arai, A. E., Zuehlsdorff, S., Guehring, J., & Kellman, P. (2012). Motion correction for myocardial T1 mapping using image registration with synthetic image estimation. *Magn. Reson. Med.* 67, 1644-1655.
- Zhao, H.**, Kim, G., & Levine, R. L. (2012). Methionine sulfoxide reductase contributes to meeting dietary methionine requirements. *Arch. Biochem. Biophys.* 522, 37-43.