



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

Herbert M. Geller, Ph.D., Director  
Angela N. Theofilos, Program Coord.  
Aurora J. Taylor, Program Coord.

### DIREducation@nhlbi.nih.gov

Building 10, Room 6N248  
Tel: 301-451-9440

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### ***From the Director of the Office of Education***

As I walked through the Vendors Tent show, I was very gratified to be greeted by former NHLBI fellows who are now employed as technical service representatives. These fellows, like other NHLBI fellows, are finding satisfaction in a scientific career that does not involve full-time bench work. NHLBI is committed to supporting our fellows as they search for a job outside NIH, whether this in academia, industry, government or public service. Towards that end, we offer our fellows an opportunity to sample what life is like outside the DIR through short-term rotation opportunities. Many of our fellows have obtained their jobs after doing such a rotation, with at least two fellows this month alone. A complete list of rotation opportunities is provided on Page 2 of this newsletter. Please contact the Office of Education if you are interested.

One major aspect of the scientific job interview is the "job talk". Your talk can often make or break your chances of getting the job. This year, we have several ways for you to prepare for your own job talk: 1) Attend the talks given by job candidates for Tenure Track positions at NIH. We are beginning the season of Stadtman recruiting, and each Stadtman candidate was selected based on their achievements. Thus, just seeing what kind of talk they give and how it is received by the attendees can provide lots of useful information. 2) Help your colleagues at NHLBI who are preparing their own job talks by attending their practice sessions. 3) Practice your own job talk in front of NHLBI investigators and fellows, and receive valuable feedback.

### ***How I Landed My First Job in Industry***

By Zheng You, Ph.D.

As of Oct. 1<sup>st</sup>. I am no longer a Postdoctoral Fellow, but instead I am embarking on a new career. I am now a Research Investigator at the Experimental Station of DuPont Company. I would like to share my experience that led to this appointment.

Ever since graduate school, my primary career goal has always been to obtain a research position

(cont'd on p.4)

**Save the Date:  
April 27-29, 2011**

**9th Annual NHLBI DIR  
Scientific Retreat**

**Cambridge, MD  
Hyatt Regency**

## ***Science Rotations for NHLBI Fellows***

Have you thought about leaving the bench? Are you interested in a career which takes advantage of your scientific and analytical skills? If so, you may be interested in participating in NHLBI DIR Rotations with any of the organizations listed below. Rotations typically last 3 – 6 months, most often full-time, and are scheduled at the end of your NHLBI fellowship. Rotations or details can also be arranged for displaced Staff Scientists. Contact the Office of Education if you are interested.

### **Fellows Rotation in Extramural Research –**

<http://dir-intranet.nhlbi.nih.gov/oe/document.aspx?frer.htm>

- With the NHLBI or NIGMS Extramural Program to focus on Research Administration or Review

### **Battelle National Laboratories – <http://dir-intranet.nhlbi.nih.gov/oe/documents/battelle.htm>**

- With any of several National Labs administered by Battelle

### **Technology Transfer Rotations — <http://www.nhlbi.nih.gov/resources/tt/index.htm>**

- With the NHBI Office of Technology Transfer

### **The FASEB Public Policy Research Fellows Program – [www.faseb.org](http://www.faseb.org)**

- With the FASEB in Bethesda to focus on Science Policy

### **Center for Innovative Technology — [www.cit.org](http://www.cit.org)**

- To focus on Business Development with Virginia's Center for Innovative Technology in Herndon, Virginia

### **Adjuvant Global Partners – [www.adjuvant.com](http://www.adjuvant.com)**

- To focus on Venture Capital and Business Development in their Bethesda, MD office.

### **Research!America— [www.researchamerica.org/](http://www.researchamerica.org/)**

- To gain experience in science policy

## ***THE SCIENCE BEAT***

*By Nisha Narayan, Ph.D.*

*Wang A, Ma X, Conti MA, Liu C, Kawamoto S, Adelstein RS. (2010). Nonmuscle myosin II isoform and domain specificity during early mouse development. Proc Natl Acad Sci U S A. Aug 17;107(33):14645-50.*

The cell derives its shape, integrity and protection from the cytoplasmic framework of proteins called the cytoskeleton. It is composed of cytoskeletal filaments that include microtubules, intermediate filaments, actin and myosin. Of these, actin and myosin together are responsible for the processes of cell migration, adhesion and cytokinesis. The essentiality of nonmuscle myosins in mouse embryonic development has already been established, but the differential functions of the two isoforms II-A and II-B have not been defined. In this study, the authors investigate the functions of the domain specificity of the isoforms in mouse development.

Three separate genes (*Myh9*, *Myh10*, *Myh14*) encode the nonmuscle myosin heavy chains (NMHCs), which together with the light chains are referred to as NM II-A, II-B, and II-C and not only show considerable homology in primary and molecular structure. The in vivo functions of two of the isoforms, NM II-A and NM II-B, have been studied following germline ablation, and show dramatically different phenotypes: death by embryonic day (E)6.5 because of a failure in cell-cell adhesion and visceral endoderm formation in the case of NM II-A and lethality by E14.5, resulting from cardiac and brain defects following II-B. These results suggest that both isoforms are essential for mouse development, but their individual jobs in embryogenesis are ambiguous. To characterize the exact function of the two isoforms, the study generated cell lines using a genetic replacement technique whereby GFP-tagged human NM II-B and GFP-tagged human NM II-B and II-A chimera cDNAs were used to replace the mouse NM II-A isoforms under an NM II-A promoter, so that the mutant mice or cells lacked endogenous NM II-A but instead expressed the knock-in proteins.

(cont'd on p.6)

**Featured CORE:  
The Electron Microscopy  
Core Facility  
Mathew P. Daniels, Ph.D.,  
Director**

The Electron Microscopy (EM) Core Facility, located in building 14E, provides advice, technical support, training and collaboration to NHLBI scientists who need to examine the structure of biological or material samples at a higher resolution (in the range of 0.4 - 200 nanometers) than light microscopes provide. We have supported a wide range of projects for more than half of the Investigators and Principle Investigators in the NHLBI/DIR since the Core started in 2006. We especially enjoy interacting with so many of the NHLBI Staff Scientists, postdoctoral fellows, and students. I am fortunate to have two highly experienced EM technicians working in the Core, Patricia S. Connelly, the lead technician/lab manager, and Myoung-Soon Sarah Hong of the Laboratory of Cell Biology as well as Shervin G. Esfahani, a Technical IRTA. The Core is equipped for preparation and imaging of samples by a range of EM technical approaches, such as: 1) In standard EM

histology, cells or tissues are chemically fixed, embedded in epoxy resin, sectioned and viewed in the transmission EM (TEM). This is analogous to conventional histology, but provides better preservation of the tissues or cells and higher resolution of structural detail. We will soon adapt a variation on this approach in which samples are rapidly frozen, followed by chemical fixation and embedding at very low temperatures, so the structure of tissues and cells is preserved in a more life-like state. These techniques may be combined with immuno-gold labeling of intra- and extracellular antigens. 2) Negative staining is especially useful and convenient for the examination of large molecules, polymers, membrane or lipid vesicles and virus particles. Particles or large molecules are adsorbed to a support film and quickly embedded in a thin film of a heavy metal salt, so the structure is revealed in negative contrast with the TEM. 3) Scanning electron microscopy (SEM) provides a global view of the surface structure of cells, small organisms, surfaces within fractured tissues and various materials with easier preparation methods than for TEM. You may view images obtained by these 3 approaches on the EM Core Facility Intranet web

site and learn more about our technical capabilities and equipment.

In late October, a new, state-of-the-art TEM will be installed. This TEM, a second TEM and an SEM are all equipped with high-resolution digital cameras. We encourage Core users who anticipate an extended project or imaging many samples to be trained by Core staff in the use of the EMs so they can obtain images independently. As imposing as the EMs look, the training of novices takes only a few hours!

If you wish to incorporate EM into a project, contact me to set up a meeting. We will discuss your goals and the appropriate EM approach to use then schedule the experiments. Chemical fixation of tissues or cells is done in your lab by protocols we provide and the rest of the preparation is done in the Core. Technical support is generally provided on a first-come, first-served basis, but we can adjust our schedule to accommodate the timing of experiments. We help Core users with interpretation and analysis of their images and with preparation of EM figures and text for manuscripts as needed.

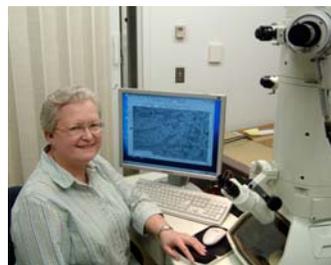
## Staff of the Electron Microscopy Core



Matt Daniels, Director



Sarah Hong, Lab Tech



Pat Connelly, Lab Tech



Shervin Esfahani, IRTA

EM Core location: Building 14E, Room 104 • [choms@nhlbi.nih.gov](mailto:choms@nhlbi.nih.gov) • 301-496-4711

**Recent Publications by NHLBI Fellows**

- Bao, J. J., Scott, I., Lu, Z. P., Pang, L. Y., Dimond, C. C., Gius, D., & Sack, M. N.** (2010). SIRT3 is regulated by nutrient excess and modulates hepatic susceptibility to lipotoxicity. *Free Radic. Biol. Med.* *49*, 1230-1237.
- Daly, M. J., Gaidamakova, E. K., Matrosova, V. Y., Kiang, J. G., Fukumoto, R., **Lee, D. Y., Wehr, N. B., Viteri, G. A., Berlett, B. S., & Levine, R. L.** (2010). Small-Molecule Antioxidant Proteome-Shields in *Deinococcus radiodurans*. *Plos One* *5*.
- Gunaratne, R., Braucht, D. W. W., Rinschen, M. M., Chou, C. L., Hoffert, J. D., Pisitkun, T., & Knepper, M. A.** (2010). Quantitative phosphoproteomic analysis reveals cAMP/vasopressin-dependent signaling pathways in native renal thick ascending limb cells. *Proc. Natl. Acad. Sci. U.S.A.* *107*, 15653-15658.
- Hernando, D., Liang, Z. P., & Kellman, P.** (2010). Chemical Shift-Based Water/Fat Separation: A Comparison of Signal Models. *Magn Reson Med Sci* *64*, 811-822.
- Hwang, S., **Gunaratne, R., Rinschen, M. M., Yu, M. J., Pisitkun, T., Hoffert, J. D., Fenton, R. A., Knepper, M. A., & Chou, C. L.** (2010). Vasopressin increases phosphorylation of Ser84 and Ser486 in Slc14a2 collecting duct urea transporters. *Am. J. Physiol. Renal Physiol.* *299*, F559-F567.
- Le, Y., Stein, A., Berry, C., Kellman, P., Bennett, E. E., Taylor, J., Lucas, K., Kopace, R., Ched'Hotel, C., Lorenz, C. H., Croisille, P., & Wen, H.** (2010). Simultaneous Myocardial Strain and Dark-Blood Perfusion Imaging Using a Displacement-Encoded MRI Pulse Sequence. *Magn Reson Med* *64*, 787-798.
- Sellers, S., **Gomes, T. J., Larochele, A., Lopez, R., Adler, R., Krouse, A., Donahue, R. E., Childs, R. W., & Dunbar, C. E.** (2010). Ex Vivo Expansion of Retrovirally Transduced Primate CD34+ Cells Results in Overrepresentation of Clones With MDS1/EVI1 Insertion Sites in the Myeloid Lineage After Transplantation. *Mol Ther* *18*, 1633-1639.
- Terasaki, Y., **Yahiro, K., Pacheco-Rodriguez, G., Steagall, W. K., Stylianou, M. P., Evans, J. F., Walker, A. M., & Moss, J.** (2010). Effects of Prolactin on TSC2-Null Rat Cells and in Pulmonary Lymphangiomyomatosis. *Am. J. Respir. Crit. Care Med.* *182*, 531-539.
- Wang, A. B., Ma, X. F., Conti, M. A., Liu, C. Y., Kawamoto, S., & Adelstein, R. S.** (2010). Nonmuscle myosin II isoform and domain specificity during early mouse development. *Proc. Natl. Acad. Sci. U.S.A.* *107*, 14645-14650.
- Zwolak, A., Uruno, T., Piszczek, G., Hammer, J. A., & Tjandra, N.** (2010). Molecular Basis for Barbed End Uncapping by CARMIL Homology Domain 3 of Mouse CARMIL-1. *J. Biol. Chem.* *285*, 29014-29026.

in the biotech or pharmaceutical industry. During the three years' training here at NIH, I became aware of many other career options, thanks to all the career fairs and seminars organized by NHLBI and the Office of Education at the NIH. After considering these options such as consulting, patent law and even teaching in college, I still felt that doing research in industry fit my interest and personality best.

I started preparing my resume in my second year as a postdoc. The career and resume service at the Office of Education was of great help to me, where I got valuable advice on the format, the vocabulary and grammar of

my resume. I also sought help from a couple of former and current colleagues who had worked in industry and they gave me a lot of candid comments about my resume and suggested what I should do to improve it. I think it's really worthwhile to get as much feedback as possible from people with different perspectives.

I don't remember how many resumes I have sent out, but I remember the sense of desperation that I felt for a very long period of time. Every resume I sent went silent. I tried to go to every career seminar on campus and dreamed that there would be some magic wand that could make

things happen, but it seemed to me that every single one of these talks boiled down to one word, networking. To me, and probably to most new graduates and postdocs, networking is a daunting task and is easier said than done, because we just don't know that many people who could help with our careers. Nevertheless, I joined LinkedIn, loaded my resume to many job websites such as Monster.com, jobfox.com, careerbuilder.com, etc., hoping that my "talent" would be found by recruiters. It turned out that this passive way of waiting to be found didn't work out.

Later on, I focused more on job openings (cont'd on p.5)

***New NHLBI Fellows***

**William Proctor, Ph.D.**, is a Research Fellow in the Laboratory of Molecular Immunology under Dr. Lance Pohl. He earned his degree in Pharmaceutical Sciences from Eshelman School of Pharmacy, University of North Carolina, Chapel Hill. Dr. Proctor received the Top Presentation Award at the GPEN Conference for giving the top student podium presentation. His initial research project is focused on the role of glucocorticoid signaling and drug induced liver injury.



**Alejandra Negro, Ph.D.**, is a Research Fellow in the Translational Medicine Branch under Dr. Manfred Boehm. She earned her degree in Molecular Pathology from the University of California, San Diego. Dr. Negro was previously a Post Doctoral Fellow at the University of Miami, School of Medicine. Her current research project involves working to identify the genetic mutations and investigating the molecular mechanisms underlying the phenotype in patients with rare inherited vascular disorders.



**Mattias Carlsten, M.D., Ph.D.**, is a Visiting Fellow in the Hematology Branch under Dr. Richard Childs. Dr. Carlsten earned his M.D. Ph.D. in a dual program from Karolinska Institute in Stockholm, Sweden. His Ph.D. is in Experimental Medicine from the Center for Infectious Medicine, Department of Medicine. Dr. Carlsten received the Martin Rind Foundation award for project funding. At NIH he will be working on the modulation of receptor-ligand interactions to improve NK cell-based immunotherapy against cancer.



**Jinguo Chen, M.D.**, is a Senior Research Fellow in the Hematology Branch under Dr. Neal Young. Dr. Chen received his M.D. from Second Military Medical University in Shanghai. Before coming to NIH, he served as the Vice Director of the Department of Radiation Medicine at the Naval Medical Research Institute in Shanghai. Dr. Chens research project deals with genomic analysis for subjects protected with H1N1 virus vaccine.

posted on biospace.com and indeed.com, and applied for anything that fit my background, even only remotely so. I received a lot of e-mails to thank me for applying for their positions, or to inform me that even though I had "a lot of talents", they had found better candidates. However, a month after I sent my application to DuPont, when I almost forgot that I even applied for such position, an e-mail with a positive tone came from the hiring manager, asking me to select a time and date from a list of 10 time slots for a panel telephone interview. I was excited and nervous. My mentor was very supportive and gave me lots of suggestions on where to find resources that I needed. A colleague of mine also shared her own experience on interviews and lent me several books on how to prepare. It was really helpful to

go through every question and get the answers ready, not by memorizing, but by gathering the key points to the questions, because you want to sound natural and spontaneous on the phone. There were four scientists on the panel for my phone interview, and it was a little awkward in the beginning but it went pretty well. They were mostly concerned about my scientific background and asked a lot questions regarding my research. A couple of weeks later, I was invited to the on-site interview, where I was asked to give a 1-hour presentation and meet individually with 12 people in the lab including lab managers, scientists with different expertise and HR manager. It was a long and stressful day, but it was so fast paced that I had no time to feel tired and I felt comfortable meeting with everyone there.

At the end of the interview, the hiring manager told me that they were going to interview 2 or 3 more people and the decision would be made at least 3 weeks later. For some reason, it took them more than a month to finalize the hiring, and obviously, I heard the good news.

I think I just want to say that when you decide to go on to the job market, make every effort to polish your application package, and network when you can, but don't feel hopeless if you know nobody in the field, because your resume does speak for you. Good luck to all!

Note: You can connect with Dr. You and other NHLBI alumni by joining the NHLBI Fellows and Alumni Group on LinkedIn.

Using immunofluorescence staining with antibodies to NMHC II-A or II-B together with E-cadherin of the embryos, it was found that all the mutant embryos (designated  $A^{b^*}/A^{b^*}$ ,  $A^{ab}/A^{ab}$ ,  $A^{ba}/A^{ba}$ ) were comparable to the normal  $A^+/A^+$  embryo, and showed normal gastrulation, normal visceral endoderm, size and morphology at E6.5, in contrast to  $A^-/A^-$  embryos, which have unidentifiable cell layers and a disorganized visceral endoderm. This finding proves that the E6.5 lethality of the  $A^-/A^-$  mice is due to the absence of both the NM II-B and II-C from the visceral endoderm. Substitution of NM II-A by NM II-B or the chimeras is however, lethal as the mice are arrested between E9.5 and E10.5 with the

$A^{b^*}/A^{b^*}$  and  $A^{ba}/A^{ba}$  embryos, and between E11.5 and E12.5 with the  $A^{ab}/A^{ab}$  embryos due to defects in angiogenesis. On the other hand, NM II-A is required in placenta development and to prevent placental defects that were observed in the  $A^{b^*}/A^{b^*}$  mice. Though they form proper allantoic structures, the mutant placentas are thinner and more compact making the different layers of the placenta difficult to distinguish.

The authors also show that the mutant Mouse Embryonic Fibroblast (MEF) cells show defects in cell migration, including decreased phospho-paxillin staining, indicative of fewer focal adhesions as well as abnormal stress fibers and thinner actin filaments which

fail to align according to the direction of the migration. Taken together, the authors find that when the cross-linking function of NM II is required, the isoforms are interchangeable in vivo, such as during the process of cell-cell adhesion. However, during cell migration and focal adhesion formation, processes in which the actomyosin complex interacts with cell matrix adhesion proteins and which require not only motor activity but also the right localization, substitution in vivo is ineffective. The most crucial finding however is that the essential role of NM II in visceral endoderm formation and function is isoform-independent, whereas placenta development depends specifically on the NM II-A isoform.

## Job Talk

**"Exploring the T cell epigenome:  
poised genes and T cell memory"**  
Artem Barski, Ph.D.

**October 14, 2010  
3:30pm  
Building 10/7S235**

Your job talk is perhaps one of the most important that you can give. Rehearsing in front of an audience will provide you with feedback that will help you improve your talk, and listening to other fellows is a way to improve your own presentation. Our office will arrange for you to do both.

[direducation@nhlbi.nih.gov](mailto:direducation@nhlbi.nih.gov)

## Looking for leadership opportunities?

**Join the Fellows Advisory  
Committee (FAC)**

**The FAC meets at 4pm on the second  
Monday of every month**

**If you're interested in attending,  
please email  
[direducation@nhlbi.nih.gov](mailto:direducation@nhlbi.nih.gov)**