



March 2012

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.

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

This year's DIR Scientific Retreat in promises to be the best ever. We have nearly 100 scientific presentations by NHLBI staff and fellow, as well as three outstanding speakers. The location in Ocean City is very conducive to productive interactions, both during the formal sessions and informally. Registration closes today, March 9th. So go to the web site and sign up.

We are still looking for NHLBI postdoctoral fellows to be mentors for summer students. These students are hard-working and eager to learn. Being a mentor to a summer student is an outstanding way to learn supervisory skills. These students will not cost your lab anything, and will enrich your research program. So if you are interested, please contact us.

**10th Annual NHLBI DIR  
Scientific Retreat**

**March 28-30, 2012**

**The Princess Royale  
Ocean City, MD**

**Keynote Speaker:  
-Dr. Nancy Andrews, Duke**

**Scientific Speakers:  
-Dr. Alexandra Newton, UCSD  
-Dr. Zena Werb, UCSF**

***How Do I Increase My  
Chances of Success?***

By Herbert Geller, Ph.D.

**I**s getting your dream job like winning the lottery? We'd all like to believe that all the efforts that we're putting in to our training will lead to a research careers. However, in real life the situation is quite different: only a small percentage of our fellows actually go on to the jobs that they aspired to when they began their training. This situation has been dubbed the "lottery system" of employment, which is used by some, but not all fields, to select the lucky few who make it to the top.

An article in the "It's the Economy" column of the New York Times by Adam Davidson on Sunday Feb. 26th provides an analysis of this system, in which large numbers of people are hired at the bottom, into low paying positions, with only a few openings at the top. Perhaps the most stark example is in music or acting, where there

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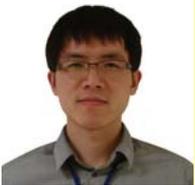
## New NHLBI Fellows



**Zhiyun Ge, Ph.D.**, is a new Visiting Fellow in the Laboratory of Ribonucleoprotein Biochemistry under Dr. Robert Hogg. Dr. Ge earned her Ph.D. in Biochemistry and Structural Biology from Stony Brook University, Stony Brook, NY. She was awarded the Departmental Retreat and Symposium Best Poster Award from the Department of Molecular Genetics and Microbiology, Stony Brook University. Dr. Ge's initial research project focuses on the mechanism of how the retroviral RSE antagonizes NMD.



**Amarjit Mishra, Ph.D.** is a new Visiting Fellow in the Asthma and Lung Inflammation Section under Dr. Stewart Levine. Dr. Mishra earned his Ph.D. in Veterinary Biomedical Sciences from Oklahoma State University, Stillwater, Oklahoma. He was the recipient of *The Joe Mack Mason Memorial Scholarship* which awards individuals for publication and scholarly activity by Office of Veterinary Research & Graduate Education. Dr. Mishra's initial research project focuses on the novel signaling pathways in Asthma pathogenesis and treatment.



**Xiangbo Ruan, Ph.D.** is a new Visiting Fellow in the Laboratory of Obesity and Metabolic Diseases under Dr. Haiming Cao. Dr. Ruan earned his Ph.D. from the Institute of Nutritional Sciences, SIBS, CAS. He was the recipient of the Merit Student Awards from Chinese Academy of Sciences and the Pfizer Scholarship. Dr. Ruan will be studying the function of lncRNA in metabolism using animal model.

## New Principal Investigator



**Susan Harbison, Ph.D.** is a new Principal Investigator heading the Laboratory of Systems Genetics in the Genetics and Developmental Biology Center. Dr. Harbison is an Earl Stadtman Tenure Track Investigator. She earned her Ph.D. in Genetics and Behavioral Biology from North Carolina State University. Dr. Harbison held postdoctoral positions in neuroscience and genetics at the University Of Pennsylvania Medical School, Philadelphia, PA and at North Carolina State University, respectively.

are many talented people try out for the few slots in orchestras or roles in movies that become available (and need to have other jobs while they do). However, the article also points out that this system has become endemic in almost all fields where talent and drive are required for success, such as law or consulting, in contrast to lower-paying jobs where showing up and following orders will keep you employed forever, even if it won't get you rich.

The unwholesome thing about our current economy is that there are relatively few positions in the middle – where you can be assured that your

training and experience will always be rewarded by a job. While we might declare medicine to be such a position, medicine is not run by the same rules – entry into the profession is carefully restricted to ensure that there will not be a glut of doctors. If we opened the doors to medical school as we have for graduate school, we will gradually evolve to see physicians in other, lower-paying, professions. In the past, one might get a decent paying job in industry that had a potential for advancement, but even these jobs have disappeared.

In the case of NHLBI Fellows, many start out with the hope or intent of being a Principal Investigator and running their own lab. So what happens to those who don't win the lottery, and not about to take jobs in retail sales or parking cars, what about them? They clearly need to have a plan for survival. While there is no definitive algorithm, the article does point out that you increase your chances of winning by buying more lottery tickets. For fellows, this means identifying alternate potential career paths, learning what it takes to be competitive, and then pursuing all these opportunities at once.

## **THE SCIENCE BEAT**

By Daniel Kraushaar, Ph.D.

**Pistolesi, S. & Tjandra, N. (2012).** Temperature Dependence of Molecular Interactions Involved in Defining Stability of Glutamine Binding Protein and Its Complex with L-Glutamine. *Biochem. 51*, 643-652.

The glutamine-binding protein (GlnBP) belongs to the class of periplasmic binding proteins (PBPs) that deliver substrates into the periplasm where they become available for further translocation by ABC transporters. GlnBP binds and delivers L-glutamine with high affinity and specificity, and meanwhile transitions from an open conformation into a closed conformation. Upon binding to L-glutamine, a flexible hinge region will bend and bring two globular domains of GlnBP into close contact. Conformational changes of PBPs into a closed state are functionally important and will facilitate downstream cellular events.

In a current NHLBI study, Pistolesi and Tjandra used nuclear magnetic resonance (NMR) to determine the thermodynamic differences between the ligand-bound and free forms of GlnBP. A NMR relaxation method was used to measure nano- and picosecond motions that can be used as a proxy for conformational disorder or entropy. Calculation and evaluation of changes in order parameters, which relate to changes in conformational entropy, across a range of temperatures, revealed insights into macromolecular stability and the thermodynamics of GlnBP ligand binding. Globally, both bound and free forms of the protein became more flexible with increasing temperature. Comparison of order parameters between bound and free GlnBP showed that binding of glutamine leads to a reduction in flexibility at all temperatures. Residue specific analysis further showed that motional

restriction is imparted primarily on the binding interface and hinge region of GlnBP. This conformational stabilization was presumed to occur as a consequence of favorable electrostatic interactions between the two domains that are in close contact in the closed conformation. Upon release of ligand, both hinge and globular domains will display higher degrees of freedom and flexibility in the absence of stabilizing forces.

Despite the global tendency of increasing residue flexibility with raising temperature, residue-specific analysis across a temperature range showed that certain residues would decrease or not change their flexibility upon increase in temperature. For instance hydrophobic residues capable of forming stacking interactions were found to decrease their flexibility with increasing temperature and overall stabilized the bound form at higher temperatures.

Interestingly, residues of the hinge region showed opposite temperature dependence in free versus bound state. When ligand is bound, hinge residues behave as 'negative', *i.e.* they become more flexible at increasing temperature, while in absence of ligand they behave as positive, *i.e.* less flexible. This finding supports the idea that the likelihood of GlnBP to adopt a ligand-free closed conformation diminishes at higher temperatures. Lastly, the authors show that backbone residues involved in salt bridges become more flexible with an increase in temperature and not necessarily more rigid as had been previously proposed by other studies.

Overall, the study's results correlate well with an induced fit model for GlnBP. As such it is assumed that ligand binding is accompanied by a general loss of conformational entropy.

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

**Recent Publications by NHLBI Fellows**

- Barbash, I. M., Saikus, C. E., Faranesh, A. Z., Ratnayaka, K., Kocaturk, O., Chen, M. Y., Bell, J. A., Virmani, R., Schenke, W. H., Hansen, M. S., Slack, M. C., & Lederman, R. J.** (2011). Direct Percutaneous Left Ventricular Access and Port Closure Pre-Clinical Feasibility. *Jacc-Cardiovascular Interventions* 4, 1318-1325.
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- Kim, M. K., Yang, S. T., Lee, K. H., Um, J. H., Liu, M. Y., Kang, H., Park, S. J., & Chung, J. H.** (2011). Promyelocytic leukemia inhibits adipogenesis, and loss of promyelocytic leukemia results in fat accumulation in mice. *Am. J. Physiol. Endocrinol. Metabol.* 301, E1130-E1142.
- Le, K., Li, R. F., Xu, S. W., Wu, X. Q., Huang, H. Q., Bao, Y. X., Cai, Y., Lan, T., Moss, J., Li, C. X., Zou, J., Shen, X. Y., & Liu, P. Q.** (2012). PPAR alpha activation inhibits endothelin-1-induced cardiomyocyte hypertrophy by prevention of NFATc4 binding to GATA-4. *Arch. Biochem. Biophys.* 518, 71-78.
- Pistolesi, S. & Tjandra, N.** (2012). Temperature Dependence of Molecular Interactions Involved in Defining Stability of Glutamine Binding Protein and Its Complex with L-Glutamine. *Biochem.* 51, 643-652.
- Ratnayaka, K., Saikus, C. E., Faranesh, A. Z., Bell, J. A., Barbash, I. M., Kocaturk, O., Reyes, C. A., Sonmez, M., Schenke, W. H., Wright, V. J., Hansen, M. S., Slack, M. C., & Lederman, R. J.** (2011). Closed-Chest Transthoracic Magnetic Resonance Imaging-Guided Ventricular Septal Defect Closure in Swine. *Jacc-Cardiovascular Interventions* 4, 1326-1334.
- Ryan, P. M., Bourdi, M., Korrapati, M. C., Proctor, W. R., Vasquez, R. A., Yee, S. B., Quinn, T. D., Chakraborty, M., & Pohl, L. R.** (2012). Endogenous Interleukin-4 Regulates Glutathione Synthesis Following Acetaminophen-Induced Liver Injury in Mice. *Chem. Res. Toxicol.* 25, 83-93.
- Yao, X. L., Dai, C. L., Fredriksson, K., Lam, J., Gao, M. X., Keeran, K. J., Nugent, G. Z., Qu, X., Yu, Z. X., Jeffries, N., Lin, J. P., Kaler, M., Shamburek, R., Costello, R., Csako, G., Dahl, M., Nordestgaard, B. G., Remaley, A. T., & Levine, S. J.** (2012). Human apolipoprotein E genotypes differentially modify house dust mite-induced airway disease in mice. *Am. J. Physiol. Lung Cell. Mol. Physiol.* 302, L206-L215.
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