



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 beginning of the new year is often a time to evaluate where we are in our lives as compared to where we would like to be. For NHLBI fellows, this translates into assessing your progress towards your chosen career, and determining what you need to get there. While working hard in the laboratory is often the focus of a postdoctoral fellowship, fellows need to be mindful that publications are not sufficient. My column this month on Page 3 illustrates this issue from the perspective of our ongoing Stadtman searches for tenure-track investigators.

Each year, about 20% of postdoctoral fellows leave NHLBI. We have used the beginning of the year to determine how our fellows did in 2010, and the results (presented on Page 5) are quite interesting: of the 34 departing fellows, 16 obtained faculty positions (4 in US institutions, and 12 abroad). The major career paths for others were in industry (4), staying at NIH (5), or continuing their training elsewhere (4). Overall, these statistics would suggest that NHLBI fellows are achieving their goals.

Registration will open soon for the 2011 NHLBI scientific retreat. This year will be an outstanding scientific experience, with speakers who are each leaders in their fields. Our Keynote, Dr. Pollard, is not only a former NHLBI fellow, but has served in several important administrative positions, such as President of the Salk Institute and is now Graduate Dean at Yale.

9th Annual NHLBI DIR Scientific Retreat

April 27-29, 2011

Cambridge, MD • Hyatt Regency

Keynote Speaker:

Thomas Pollard, M.D.

***Sterling Professor of Molecular, Cellular,
and Developmental Biology
Yale University***

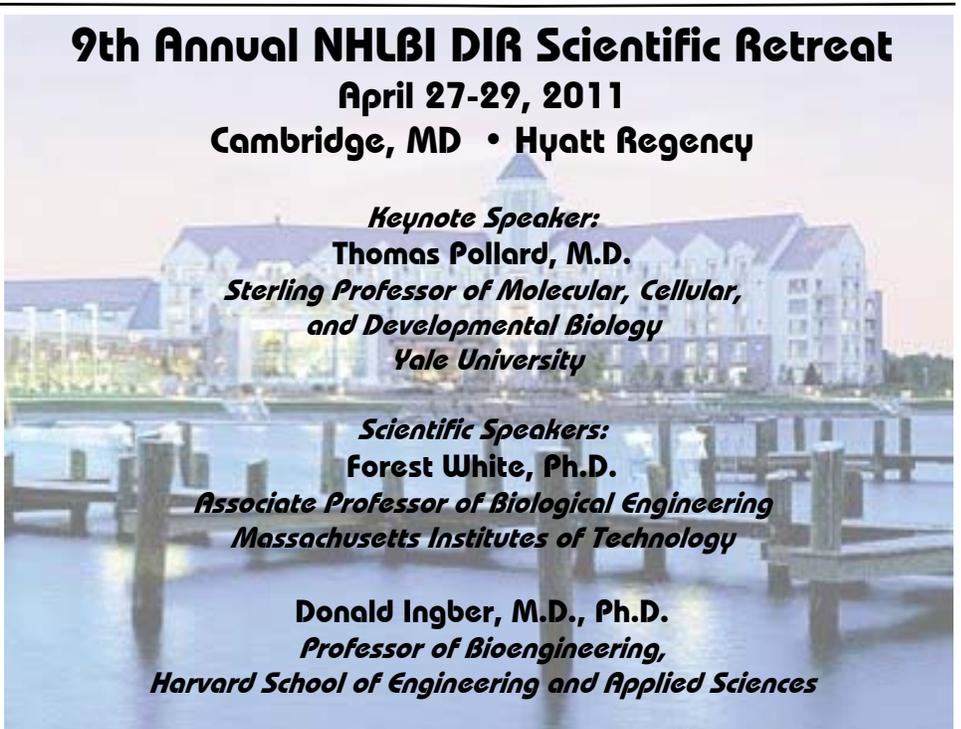
Scientific Speakers:

Forest White, Ph.D.

***Associate Professor of Biological Engineering
Massachusetts Institutes of Technology***

Donald Ingber, M.D., Ph.D.

***Professor of Bioengineering,
Harvard School of Engineering and Applied Sciences***



Recent Publications by NHLBI Fellows

- Bartee, E., **Eyster, C. A.**, Viswanathan, K., Mansouri, M., Donaldson, J. G., & Fruh, K. (2010). Membrane-Associated RING-CH Proteins Associate with Bap31 and Target CD81 and CD44 to Lysosomes. *PLoS ONE* 5.
- Cai, X. O.**, Pacheco-Rodriguez, G., **Fan, Q. Y.**, Haughey, M., Samsel, L., **El-Chemaly, S.**, Wu, H. P., McCoy, J. P., Steagall, W. K., Lin, J. P., Darling, T. N., & Moss, J. (2010). Phenotypic Characterization of Disseminated Cells with TSC2 Loss of Heterozygosity in Patients with Lymphangioliomyomatosis. *Am. J. Resp. Crit. Care Med.* 182, 1410-1418.
- de Latour, R. P., **Visconte, V.**, **Takaku, T.**, **Wu, C.**, Erie, A. J., Sarcon, A. K., Desierto, M. J., Scheinberg, P., Keyvanfar, K., Nunez, O., Chen, J. C., & Young, N. S. (2010). Th17 immune responses contribute to the pathophysiology of aplastic anemia. *Blood* 116, 4175-4184.
- Heimann, E., **Jones, H. A.**, Resjo, S., Manganiello, V. C., Stenson, L., & Degerman, E. (2010). Expression and Regulation of Cyclic Nucleotide Phosphodiesterases in Human and Rat Pancreatic Islets. *PLoS ONE* 5.
- Kanchanawong, P.**, Shtengel, G., **Pasapera, A. M.**, Ramko, E. B., Davidson, M. W., Hess, H. F., & Waterman, C. M. (2010). Nanoscale architecture of integrin-based cell adhesions. *Nature* 468, 580-U262.
- Larkin, J. D.**, Fossey, J. S., James, T. D., Brooks, B. R., & Bock, C. W. (2010). A Computational Investigation of the Nitrogen-Boron Interaction in o-(N,N-Dialkylaminomethyl)arylboronate Systems. *J. Phys. Chem. A* 114, 12531-12539.
- Larkin, J. D.**, Frimat, K. A., Fyles, T. M., Flower, S. E., & James, T. D. (2010). Boronic acid based photoinduced electron transfer (PET) fluorescence sensors for saccharides. *New J. Chem.* 34, 2922-2931.
- Liu, W. L., Lee, H. W., Liu, Y. Q., **Wang, R. H.**, & Rodgers, G. P. (2010). Olfactomedin 4 is a novel target gene of retinoic acids and 5-aza-2'-deoxycytidine involved in human myeloid leukemia cell growth, differentiation, and apoptosis. *Blood* 116, 4938-4947.
- Ma, X. F., **Jana, S. S.**, Conti, M. A., Kawamoto, S., Claycomb, W. C., & Adelstein, R. S. (2010). Ablation of Non-muscle Myosin II-B and II-C Reveals a Role for Nonmuscle Myosin II in Cardiac Myocyte Karyokinesis. *Mol. Biol. Cell* 21, 3952-3962.
- O'Seaghda, C. M.** & Fox, C. S. (2011). Genetics of Chronic Kidney Disease. *Nephron Clin. Pract.* 118, C55-C63.
- Rochman, Y.**, Kashyap, M., Robinson, G. W., Sakamoto, K., Gomez-Rodriguez, J., Wagner, K. U., & Leonard, W. J. (2010). Thymic stromal lymphopoietin-mediated STAT5 phosphorylation via kinases JAK1 and JAK2 reveals a key difference from IL-7-induced signaling. *Proc. Natl. Acad. Sci. U. S. A* 107, 19455-19460.
- Rousset, X.**, Vaisman, B., Amar, M., **Sethi, A. A.**, & Remaley, A. T. (2009). Lecithin: cholesterol acyltransferase - from biochemistry to role in cardiovascular disease. *Current Opinion in Endocrinology Diabetes and Obesity* 16, 163-171.
- Shen, W. X.**, Ahmad, F., Hockman, S., Ma, J., **Omi, H.**, Raghavachari, N., & Manganiello, V. (2010). Female infertility in PDE3A(-/-) mice Polo-like kinase 1 (Plk1) may be a target of protein kinase A (PKA) and involved in meiotic arrest of oocytes from PDE3A(-/-) mice. *Cell Cycle* 9, 4720-4734.

New NHLBI Fellows



Stephen Swatkoski, Ph.D., is a Research Fellow in the Proteomics Core under Dr. Marjan Gucsek. Dr. Swatkoski earned his Ph.D. in Chemistry from the University of Maryland, College park. In graduate school, he developed new sample preparation techniques for bottom-up proteomic analyses. Dr. Swatkoski's will be involved in mass spectrometry-based proteomic analyses of tissue samples.



Zhengyuan Wang, Ph.D., is a Visiting Fellow in the Cardiovascular Pulmonary Branch under Dr. James Taylor. Dr. Wang earned his Ph.D. in Computational and Systems Biology from the National University of Singapore, Alliance with Massachusetts Institute of Technology. Dr. Wang will be focusing on Sickle Cell disease while here at NIH.

Skills for Success: Publication is Not Enough

By Herbert M. Geller, Ph.D.

The beginning of a new year is always a good time to take stock of where we are and where we would like to be. This is especially important for postdoctoral fellows – your time as a Fellow at NHLBI is limited, and, consequently, your goal is to make the best use of this time to get you to the next step. While this seems obvious, many fellows have the belief that they simply need to work hard in the lab to get publications, and then everything else will fall into place. While this does work in some situations, for most jobs, having a strong publication record is not sufficient.

Many of you attended the first round of interviews for Stadtman tenure-track candidates. All those invited had great publication records and strong letters from their graduate and postdoctoral advisors, yet most will not get further consideration. So what are the issues that stopped them?

According to Dr. Alan Michelson, the major one was a failure to articulate and defend an outstanding plan for their future research – search committees are looking beyond what an individual did in a mentor's laboratory in order to evaluate how successful they might be when they establish and direct their own research group. Is the research that they propose likely to be important and original? Candidates were favorably considered if their work involved innovative experimental and/or computational approaches. Another criterion was the deeper implications of the work – is their area very narrow, or will their observations have broad impact? How well they responded to questions was important, especially during the “chalk talk” part of the interview – were their answers superficial, or did they come across as being deeply immersed in their subject? Finally, did they seem like they would interact well with others on campus and take advantage of the unique environment of NIH.

When I've interviewed fellows departing for industry jobs, they stressed

that it was their mastery of their research area and its wider implications, as well as specific technical skills, that got them the job. In addition, because industrial science is mostly a team enterprise, they were also evaluated on how well they interacted with their future colleagues.

The take-home message from these experiences is that staying in the lab and writing papers in your mentor's area are never, by themselves, adequate to get you to your first job. Take the time to hone the other skills you need. A good place to start is by creating an individual development plan which can serve as a protocol for skills development. There are many different ones available, but two in particular may be of interest: one developed by FASEB and one specifically for NHLBI fellows.

Links to both can be found on the Office of Education web site: <http://dir-intranet.nhlbi.nih.gov/oe/document.aspx?new-fellows.htm#Individual>

Recent Publications by NHLBI Fellows Continued

- Sloand, E. M., Pfannes, L., Ling, C., **Feng, X. M.**, Jasek, M., Calado, R., Tucker, Z. C. G., **Hematti, P.**, Maciejewski, J., Dunbar, C., Barrett, J., & Young, N. (2010). Graft-versus-Host Disease: Role of Inflammation in the Development of Chromosomal Abnormalities of Keratinocytes. *Biol. Blood Marrow Transpl.* *16*, 1665-1673.
- Wong, S. S., Keyvanfar, K., **Wan, Z. H.**, Kajigaya, S., Young, N. S., & Zhi, N. (2010). Establishment of an erythroid cell line from primary CD36(+) erythroid progenitor cells. *Exp. Hematol.* *38*, 994-1005.
- Yang, Y.**, Gu, D. Y., Aisa, H. A., & Ito, Y. (2010). Evaluation on the performance of four different column models mounted on the compact type-I coil planet centrifuge. *J. Chromatog. A* *1217*, 7612-7615.
- Yao, X. L., **Fredriksson, K.**, Yu, Z. X., Xu, X. L., Raghavachari, N., Keeran, K. J., Zywicke, G. J., Kwak, M., Amar, M. J. A., Remaley, A. T., & Levine, S. J. (2010). Apolipoprotein E Negatively Regulates House Dust Mite-induced Asthma via a Low-Density Lipoprotein Receptor-mediated Pathway. *Am. J. Resp. Crit. Care Med.* *182*, 1228-1238.
- Zhi, N.**, **Wan, Z. H.**, Liu, X. H., Wong, S., **Kim, D. J.**, Young, N. S., & Kajigaya, S. (2010). Codon Optimization of Human Parvovirus B19 Capsid Genes Greatly Increases Their Expression in Nonpermissive Cells. *J. Virol.* *84*, 13059-13062.

Need practice giving a Chalk Talk?
The OE can arrange a practice session with valuable feedback.
Email us at direducation@nhlbi.nih.gov

THE SCIENCE BEAT

By Daniel Kraushaar, Ph.D.

Rochman, Y., Kashyap, M., Robinson, G. W., Sakamoto, K., Gomez-Rodriguez, J., Wagner, K. U., & Leonard, W. J. (2010). Thymic stromal lymphopoietin-mediated STAT5 phosphorylation via kinases JAK1 and JAK2 reveals a key difference from IL-7-induced signaling. Proceedings of the National Academy of Sciences of the United States of America 107, 19455-19460.

Jak/STAT signaling pathways regulate cytokine-dependent T cell differentiation and survival that is required for pathogen recognition and to overcome infection. Upon binding to cognate receptors, type I cytokines trigger receptor dimerization/oligomerization that allows for rapid transphosphorylation and activation of Janus kinases (Jak1, Jak2, Jak3 and Tyk2) that interact with these receptors. Activated receptor complexes provide docking sites for the SH2 domain of STAT transcription factors, which themselves become activated and subsequently translocate to the nucleus where target genes are transactivated.

A current NHLBI study by Rochman *et al.* investigated the role of thymic stromal lymphopoietin (TSLP), a type I cytokine that is produced by stromal cells, epithelial cells, fibroblasts, keratinocytes and basophils. Its secretion is associated with airway inflammatory disease and atopic dermatitis in humans and mice. TSLP is highly related to IL-7 and both cytokines signal through STAT5; yet the precise activators of the TSLP signaling cascade were unclear. The authors systematically examine the involvement of Jak proteins as downstream effectors of TSLP signaling using cell signaling assays combined with T-cells derived from knockout mice. TSLP promotes both proliferation and survival of CD4⁺ T-cells. Whether these functions are mediated by TSLP-induced STAT5 activation is addressed in experiments that utilize *STAT5a* KO CD4⁺ T cells stimulated with TSLP. *STAT5a* T-cells display both lower survival and proliferation as compared with their wild type counterparts demonstrating that STAT5 is coupled to TSLP-mediated functions that include proliferation and survival. Reduced proliferation and survival were also recorded from T-cells that are deficient in

STAT5 through Cre-mediated ablation of *STAT5a* and *STAT5b* confirming the previous results of the paper.

To identify activators upstream of STAT5 all members of the Jak family are examined by testing the short-term activation/phosphorylation of Jak1-3 and Tyk2 upon stimulation with TSLP. Jak1 and Jak2 become rapidly and substantially phosphorylated upon TSLP addition over a time course of 60 minutes. Using *Jak1* and *Jak2* KO T-cells, the authors show that STAT5 phosphorylation becomes disrupted in the presence of TSLP, extending their finding that TSLP signals via Jak1 and Jak2. In contrast, TSLP-mediated STAT5 activation requires neither Jak3 nor Tyk2 as demonstrated in *Jak3* and *Tyk2* KO cells respectively. Importantly, at this point, IL-7, used alongside TSLP, exhibited a requirement for Jak3 but not Jak1 in order to phosphorylate STAT5, illustrating a key difference between the two related cytokines that may account for some of the distinctly different biological effects on T-cells exerted by TSLP and IL-7. A question that remained to be answered was whether Jak1 or Jak2 associate with IL-7R and TSLPR, the two receptors of TSLP. Immunoprecipitation with antibodies against Jak1/Jak2 and TSLPR/IL-7R revealed interactions between Jak1 and IL-7R, and Jak2 and TSLPR. At last, the authors extend their findings from mouse to human T-cells and demonstrate that TSLP signals via the same Jak-STAT pathway in human T-cells.

Overall the study impresses through use of rigorous controls and execution of experiments in multiple cell lines. Based on the results of this study the authors propose a model whereby TSLP induces the dimerization of IL-7R α and TSLPR that are bound by Jak1 and Jak2 respectively, and which primarily results in activation of STAT5. An interesting aspect of the study is that IL-7 and TSLP, both share IL-7R and yet signal via a different set of Jak and STAT proteins. In contrast to TSLP, IL-7 activates Jak1/Jak3 and subsequently primarily STAT5 but also STAT3 and STAT1 to a lesser extent. In context with other cytokines, it is noted that even though activation of Jak1 and Jak2 by TSLP is shared with other cytokines such as IFN- γ and IL-6, a different set of STATs may be activated as a result. Therefore, this study and others highlight the importance of context-dependent cytokine signaling in immunity.

Comings and Goings: Annual Summary

At the end of 2010, there were 296 fellows at NHLBI (200 postdoctoral): 78 Visiting Fellows, 67 Research Fellows, 54 Post-Bac IRTAs, 35 Post-doctoral IRTAs, 25 Predoctoral Fellows, and 20 Clinical Fellows, not including those who are Special Volunteers. Each year, approximately 20% of our postdoctoral positions turn over. In 2010, 42 fellows arrived at NHLBI, and 34 departed. The average stay for departing fellows was 4 years, with a range of a little over a year to 8 years.

For the new arrivals, there were 4 new clinical fellows, 5 IRTA fellows, 21 visiting fellows and 17 research fellows.

Of the 42 new fellows, 32 held visas, with 15 from China, 2 from France, Japan and Korea, and 1 each from Austria, Belarus, Chile, Germany, Greece, Pakistan, Singapore, Sweden, Thailand, UK, and Vietnam. The others are either US citizens or permanent residents.

The trajectory of the departing fellows echoes this demographic: 12 returned to their home country for faculty positions in Australia, Canada, China, Japan (4), Korea, Singapore, Spain, Taiwan, and Thailand. Four fellows each obtained tenure-track positions at US Universities, became Staff Scientists, are working for a company in the US or went on to another postdoctoral position. One fellow is working in the

extramural program, and the other two are taking time off for family.

While it is hard to plan your career from demographic information, the take home message is that our fellows have a high degree of success in obtaining faculty positions, especially if they desire to return to their home country. Of the four fellows who obtained US faculty positions, half were US citizens and half were visa-holders. This same demographic held for those who went to US companies and obtaining Staff Scientist positions, with three being visa holders and one US citizen. Especially interesting is the fact that both of the fellows who took advantage of the NHLBI rotation program obtained permanent positions.

NHLBI DIR Fellows Seminar Series Presents

Daniel Rader, M.D. University of Pennsylvania

*"Functional Assessment and
Therapeutic Implications of New Lipid
Pathways Uncovered Through Human
Genetics"*

Tuesday, January 18th
11am-Noon
Building 50, Room 2328

Host: Kasey Vickers, Ph.D.
(vickerskc@nhlbi.nih.gov)

Thanks to all who attended the NHLBI DIR Holiday Dessert Potluck!

A cash prize was awarded to
the dessert with the most votes
and the winner was...

Zhongping Lu, Ph.D.
*Research Fellow from the
Cardiovascular Pulmonary Branch*



The above photo is similar to the dessert
brought by Dr. Lu.