



March 2011

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***

Registration is open for the DIR Scientific Retreat, and I wanted to urge you all to attend and highlight some of the planned activities.

We would like all Fellows and Staff Scientists to present a poster. We will give awards for the best poster presentation in several different categories (Predoc/Postbac, Postdoc, Staff Scientist).

Communication is an essential skill, so our goal should be to be as effective as we can. We all give formal scientific presentations, normally using Powerpoint. But what happens when you meet a stranger and they ask about your work? Are you prepared to answer in a way that they understand, not using jargon? This type of interaction is often called the "elevator speech", but I recently went to a Keystone meeting, and got on a ski lift and was asked what I do, so I've renamed it the "ski lift speech", which gives a little more time. Because this interaction is so frequent, we're giving Fellows a chance to practice at the DIR Scientific Retreat at lunch on Thursday.

And we want to have some fun as well, so plan to participate in Scientific Trivia on Wednesday evening. The Fellows Advisory Committee has submitted a batch of questions that will draw on your scientific knowledge as well as your knowledge of NHLBI.

Registration closes on March 25<sup>th</sup>, so send in your abstract soon!

**9th Annual NHLBI DIR Scientific Retreat**

**April 27-29, 2011**

**Cambridge, MD • Hyatt Regency**

***\*Registration closes March 25th***

***Keynote Speaker:***

**Thomas Pollard, M.D.**

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

***Yale University***

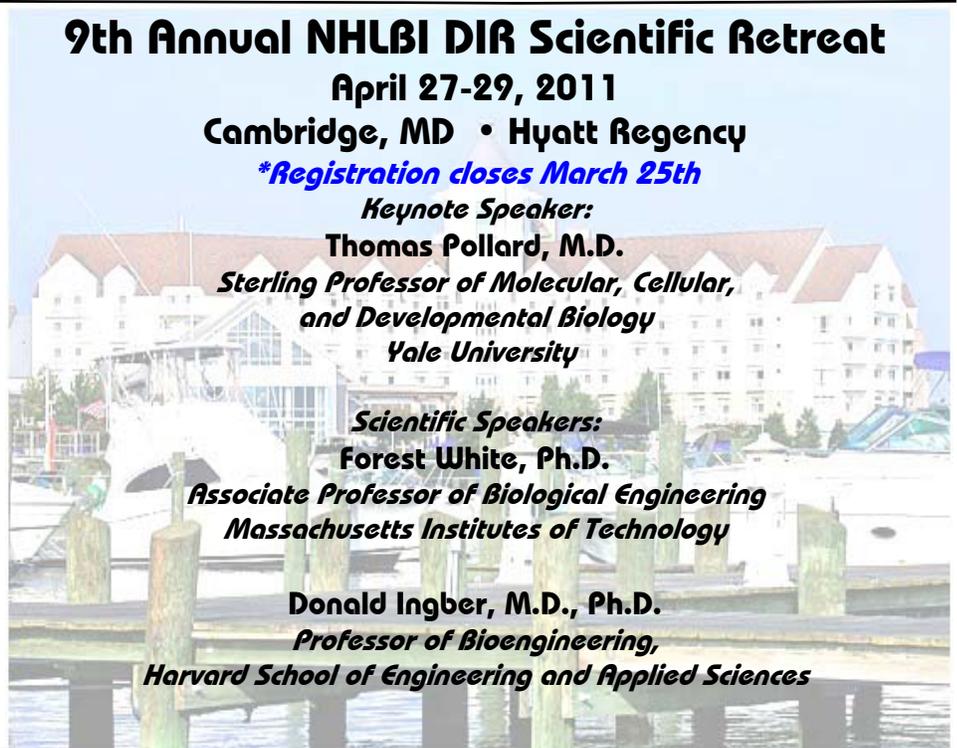
***Scientific Speakers:***

**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***



## **Communication Skills for Scientists**

By Herbert Geller, Ph.D.

**H**ow important is communication to your life? This seems like a very silly question: communication is essential, even more so in our chosen profession of science. So why aren't we good at it?

The recent STEP symposium entitled "Look Who's Talking: Communicating Your Message Fearlessly and Flawlessly" held in Masur Auditorium featured several excellent speakers who offered many different tips for communicating your message. Some were very practical, like "don't show too much data on a slide" or "make sure that you don't rush through your presentation". But these tips are probably known to many of us.

Because the symposium was Videocast, you have the opportunity to watch the entire program at your convenience at [videocast.nih.gov](http://videocast.nih.gov). However, if you are pressed for time, I want to recommend in particular the first and last presentations. The first, by Barrett Whitener, who is not only an excellent public speaker, but can be heard as the voice for many different books on tape.

Mr. Whitener's presentation focused on how to prepare an effective presentation, with the order of preparation being entirely different from the order of presentation. Thus, the first thing you want to establish (and this really applies to any communication) your take-home message. This then allows you to order the slides, with the next slide being the one that presents your main question, followed by the the one slide that you want people to remember. Once you have the skeleton in place, you add other slides that fill in the necessary details, finally picking a title only at the end. And don't make the title too informative – else your audience will think they know the punch line even before you get there.

The final segment of the symposium was led by Alan Alda, the well-known actor who also was the host for the Scientific American Frontiers series on PBS. As the host of a science TV show, who went around the world interviewing top scientists, Mr. Alda realized that many of them were unable to communicate their message, leading to the unfortunate consequence that the best communicators are not necessarily the best scientists. So he has taken it upon himself to alter this by helping establish a Center for Scientific Communication

at Stony Brook University. At the beginning of this segment, Mr. Alda spoke about in general about communicating. Interestingly, one of his main points was previously emphasized by Randy Olson at his talk here that if you really want to connect with your audience and get your point across, you need to appeal at an emotional level as well as at an intellectual level. He then went on to describe the types of programs offered at this center, which emphasized improving communication skills, and provided some tapes of actual presentations given by students before and after their participation in this program. Following his presentation, we participated in an actual demonstration of the techniques used to improve communication using improvisation techniques. In the exercises presented, improvisation requires that each participant communicate well with the others without formal rules or a prepared script. By doing so, you absorb the main principle that you need to be in touch with your audience if you expect them to absorb the information you are presenting. I urge you all to watch this entertaining and informative presentation, and perhaps think about how we can implement similar programs for NHLBI scientists.

## ***Congratulations to Lenfant Fellowship Recipient- Cynthia St Hilaire***



Congratulations to Cynthia St Hilaire, Postdoctoral fellow in the Center for Molecular Medicine under Dr. Manfred Boehm, who was awarded the Lenfant Biomedical Fellowship Award. This competitive award is granted to outstanding postdoctoral fellows in the NHLBI Division of Intramural Research (DIR). The fellowship is named after a past Director of the NHLBI, Dr. Claude Lenfant (1982-2003) who was a strong supporter of excellence in the DIR research program. The intent of this program is to recognize and provide additional support to those fellows committed to pursuing a career in research. The application deadlines for 2011 are: April 15, August 15, and November 15.

More information can be found at:

<http://dir-intranet.nhlbi.nih.gov/awards-and-grants/Default.aspx?lenfant.htm>

## New NHLBI Fellows



**Jahda Hill, Ph.D.**, is an IRTA fellow in the Genetics and Developmental Biology Center under Dr. Hong Xu. Dr. Hill earned her Ph.D. in Cell Biology and Molecular Development from the University of Maryland-College Park, Maryland. She has laboratory research experience from the University of Maryland where she also was a teaching assistant. Dr. Hill is a member of the Golden Key International Honour Society. Her current research project will focus on investigating selective mitochondrial degradation in *Drosophila*.



**Dinari Harris, Ph.D.**, is a Research Fellow in the Biochemistry and Biophysics Center under Dr. Justin Taraska. Dr. Harris earned his Ph.D. in Chemistry from the University of Michigan. He served as a Postdoctoral Research Associate at Northwestern University, Evanston, Illinois, during which time he received the Visual Sciences Training Grant. Dr. Harris will initially start his research here using several different fluorescent techniques to monitor conformational changes in the SID-1 protein.



**Benjamin Kidder, Ph.D.**, is a Research Fellow in the Laboratory of Molecular Immunology under Dr. Keji Zhao. He earned his Ph.D. in Molecular, Cellular, Developmental Biology and Genetics from the University of Minnesota, Minneapolis, MN. Dr. Kidder was the recipient of the 2010 EMD/Merck Spot Award. His initial research project involves stem cell genomics.



**Oscar Vidal, Ph.D.**, is a Visiting Fellow in the Center for Molecular Medicine under Dr. Haiming Cao. He earned his Ph.D. in Molecular and Cell Biology from the University of Sheffield, UK. He was awarded the "First Steps Funding Grant for a Business Idea" by the Enterprise Zone University of Sheffield. Dr. Vidal's initial project will be the analysis of micro RNA's in metabolism.



**Taha Bat, M.D.**, is a Visiting Fellow in the Hematology Branch under Dr. Cynthia Dunbar. Dr. Bat earned his M.D. from Hacettepe University in Turkey. He did a number of rotations at the University of Colorado, Stanford University, Hacettepe University in Turkey and Harvard University Beth Israel Deaconess Medical Center. Dr. Bat will be working to understand 2 dimensional architecture of HSC niche.



**Zhiping Jiang, Ph.D.**, is a Visiting Fellow in the Biochemistry and Biophysics Center under Dr. Jennifer Lee. Dr. Jiang earned her Ph.D. in Biochemistry from Kent State University, Kent, Ohio. She served as a lab instructor for a year while attending Kent State. Dr. Jiang's initial research project will be focused on if Alpha-synuclein is enriched in lipid rafts.

## New NHLBI Principal Investigator



**Nasser Rusan, Ph.D.**, is a new Principal Investigator in the Cell Biology and Physiology Center. Dr. Rusan earned his Ph.D. in Molecular and Cellular Biology from the University of Massachusetts, Amherst. Before starting at NIH, he held a post doc position at the University of North Carolina, Chapel Hill where he researched cell biology of *Drosophila* neural and germline stem cells, the role of centrosomes in asymmetric stem cell division, and much more. During his time at UNC, Dr. Rusan was awarded the UNC Postdoctoral Award for Research Excellence for 2009.

## **THE SCIENCE BEAT**

By Nisha Narayan, Ph.D.

*St Hilaire, C., Ziegler, S. G., Markello, T. C., Brusco, A., Groden, C., Gill, F., Carlson-Donohoe, H., Lederman, R. J., Chen, M. Y., Yang, D., Siegenthaler, M. P., Arduino, C., Mancini, C., Freudenthal, B., Stanescu, H. C., Zdebik, A. A., Chaganti, R. K., Nussbaum, R. L., Kleta, R., Gahl, W. A., & Boehm, M (2011) NT5E Mutations and Arterial Calcifications. N. E. J. M. 364, 432-442.*

The connection between deposits of calcium and heart disease has been well recognized for many years now. Calcium is now acknowledged as a marker for a diseased artery and rising evidence indicates that vascular calcification can be attributed to a process that is similar to bone remodeling. Idiopathic infantile arterial calcification is the only mendelian disorder of isolated vascular calcification known and is caused due to mutations in the ectonucleotide pyrophosphatase-phosphodiesterase 1 gene (ENPP1). This study aims to explain the genetic basis of the symptoms behind an adult-onset disease whose patients showed extensive calcifications of the arteries of the lower limbs and small joint capsules.

A total of nine patients from three families were identified with the lower-extremity artery calcifications and families 1 and 3 were admitted to the National Institutes of Health Undiagnosed Diseases Program. This program is organized by the National Human Genome Research Institute (NHGRI), the NIH Office of Rare Diseases Research (ORDR) and the NIH Clinical Center, and unites the expertise of scientists and physicians from many of the other NIH research centers and institutes. It pursues two goals - to provide answers to patients with mysterious conditions that have long eluded diagnosis and to advance medical knowledge about rare and common diseases. St Hilaire et al performed radiographic analyses to assess the extent of the calcifications in the patients, as well as clinical studies to rule out other conditions such as Type 2 diabetes mellitus, abnormal bone morphology or decreased kidney function. They then performed Single-Nucleotide-Polymorphism (SNP) analysis to identify biallelic nonsense, missense and frameshift mutations in the gene NT5E, which encodes the CD73 enzyme. This enzyme produces extracellular adenosine downstream of ENPP1 and is involved in extracellular

ATP metabolism, where it binds AMP and converts it to adenosine and inorganic phosphate.

Autosomal recessive inheritance was implied keeping in mind the consanguineous pedigree of Family 1. Hence, the group searched for a region of the genome homozygous in all the five siblings, but heterozygous in the parents of Family 1. One 22.4-Mb region with 92 genes was identified, of which 3 genes were evaluated : NT5E as its enzyme substrate is a product of the ENPP1 gene, and ATG5 and CASP8AP2, based on their involvement in degenerative cellular processes leading to calcification. Direct sequencing then revealed a homozygous nonsense mutation in exon 3 of the NT5E gene in all five siblings of family 1 as well as in both parents in the heterozygous state. Affected members of family 2 were homozygous for a missense mutation in exon 5 of NT5E and the affected member of family 3 was a compound heterozygote for the nonsense mutation founding family 1 as well as another mutation leading to a premature stop codon in exon 9 of NT5E. None of these mutations were found in 400 alleles of matched controls.

With the gene identified, further experiments were performed to examine protein and enzyme activity as well as on cellular studies. Western blots of fibroblast extracts from Family 1 revealed reduced expression of CD73 protein and nearly absent enzymatic activity. A CD73 encoding lentiviral vector could genetically rescue these anomalies. Cellular studies involved staining fibroblasts from patients for Tissue-nonspecific Alkaline Phosphatase (TNAP), a pivotal enzyme in tissue calcification in vitro and in vivo. Cells from patients showed very high levels of the enzyme after 3 days of calcific stimulation relative to control cells, and this could be abrogated by transducing the cells with a CD-73 coding lentiviral vector, as well as by treating the cells with Adenosine or with the TNAP inhibitor Levamisole.

Overall, this elegant study identifies for the first time, mutations in NT5E as one of the possible causes for adult onset symptomatic arterial and joint calcifications. Their work supports a role for the CD73 metabolic pathway in inhibiting ectopic tissue calcification. This work also showcases the unparalleled advantage of scientific collaboration in the NIH Undiagnosed Disease Program and how it tangibly contributes to helping families understand and possibly treat diseases.

**Recent Publications by NHLBI Fellows**

- Combs, C. A., Smirnov, A., **Chess, D.**, McGavern, D. B., **Schroeder, J. L.**, Riley, J., Kang, S. S., Lugar-Hammer, M., Gandjbakhche, A., Knutson, J. R., & Balaban, R. S. (2011). Optimizing multiphoton fluorescence microscopy light collection from living tissue by noncontact total emission detection (epiTED). *J. Microsc.* *241*, 153-161.
- Cuddapah, S.**, **Schones, D. E.**, **Cui, K. R.**, **Roh, T. Y.**, **Barski, A.**, **Wei, G.**, Rochman, M., Bustin, M., & Zhao, K. J. (2011). Genomic Profiling of HMGNI Reveals an Association with Chromatin at Regulatory Regions. *Mol. Cell. Biol.* *31*, 700-709.
- Hayakawa, J.**, **Hsieh, M. M.**, Anderson, D. E., Phang, O., **Uchida, N.**, Washington, K., & Tisdale, J. F. (2010). The Assessment of Human Erythroid Output in NOD/SCID Mice Reconstituted With Human Hematopoietic Stem Cells. *Cell Transplant.* *19*, 1465-1473.
- Herishanu, Y.**, **Perez-Galan, P.**, Liu, D. L., Biancotto, A., Pittaluga, S., Vire, B., **Gibellini, F.**, Njuguna, N., Lee, E., Stennett, L., Raghavachari, N., Liu, P. C., Mccoy, J. P., Raffeld, M., Stetler-Stevenson, M., Yuan, C., Sherry, R., Arthur, D. C., Maric, I., White, T., Marti, G. E., Munson, P., Wilson, W. H., & Wiestner, A. (2011). The lymph node microenvironment promotes B-cell receptor signaling, NF-kappa B activation, and tumor proliferation in chronic lymphocytic leukemia. *Blood* *117*, 563-574.
- Kengyel, A.**, Wolf, W. A., Chisholm, R. L., & Sellers, J. R. (2010). Nonmuscle myosin IIA with a GFP fused to the N-terminus of the regulatory light chain is regulated normally. *J Muscle Res. Cell Motil.* *31*, 163-170.
- Larochelle, A.**, Savona, M., Wiggins, M., Anderson, S., **Ichwan, B.**, Keyvanfar, K., Morrison, S. J., & Dunbar, C. E. (2011). Human and rhesus macaque hematopoietic stem cells cannot be purified based only on SLAM family markers. *Blood* *117*, 1550-1554.
- Li, L. Q., Jothi, R., **Cui, K. R.**, Lee, J. Y., Cohen, T., Gorivodsky, M., Tzchori, I., Zhao, Y. G., Hayes, S. M., Bresnick, E. H., Zhao, K. J., Westphal, H., & Love, P. E. (2011). Nuclear adaptor Ldb1 regulates a transcriptional program essential for the maintenance of hematopoietic stem cells. *Nature Immunology* *12*, 129-U38.
- Liu, H. J.**, Fergusson, M. M., **Wu, J. J.**, Rovira, I. I., **Liu, J.**, Gavrilova, O., Lu, T., **Bao, J. J.**, Han, D. H., Sack, M. N., & Finkel, T. (2011). Wnt Signaling Regulates Hepatic Metabolism. *Science Signaling* *4*.
- Perez-Galan, P.**, Mora-Jensen, H., **Weniger, M. A.**, Shaffer, A. L., Rizzatti, E. G., Chapman, C. M., Mo, C. C., Stennett, L. S., Rader, C., Liu, P. C., Raghavachari, N., Stetler-Stevenson, M., Yuan, C., Pittaluga, S., Maric, I., Dunleavy, K. M., Wilson, W. H., Staudt, L. M., & Wiestner, A. (2011). Bortezomib resistance in mantle cell lymphoma is associated with plasmacytic differentiation. *Blood* *117*, 542-552.
- Pfefferkorn, C. M.**, **McGlinchey, R. P.**, & Lee, J. C. (2010). Effects of pH on aggregation kinetics of the repeat domain of a functional amyloid, Pmel17. *Proc. Natl. Acad. Sci. U. S. A* *107*, 21447-21452.
- St Hilaire, C.**, Ziegler, S. G., Markello, T. C., Brusco, A., Groden, C., Gill, F., Carlson-Donohoe, H., Lederman, R. J., Chen, M. Y., Yang, D., Siegenthaler, M. P., Arduino, C., Mancini, C., Freudenthal, B., Stanescu, H. C., Zdebik, A. A., Chaganti, R. K., Nussbaum, R. L., Kleta, R., Gahl, W. A., & Boehm, M. (2011). NTSE Mutations and Arterial Calcifications. *N. E. J. M.* *364*, 432-442.
- Uchida, N.**, Washington, K. N., Lap, C. J., **Hsieh, M. M.**, & Tisdale, J. F. (2011). Chicken HS4 Insulators Have Minimal Barrier Function Among Progeny of Human Hematopoietic Cells Transduced With an HIV1-based Lentiviral Vector. *Mol. Ther.* *19*, 133-139.
- Vergarajauregui, S.**, **Martina, J. A.**, & Puertollano, R. (2011). LPTMs regulate lysosomal function and interact with mucolinin 1: new clues for understanding mucopolidosis type IV. *J. Cell Sci.* *124*, 459-468.