

Office of Education  
Division of Intramural Research

# Fellows Newsletter

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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

Welcome back! As you now know, funding for the NIH, like much of the United States Government, is through the annual appropriations process. Both the US House of Representatives and the US Senate must pass bills allocating funds, and the bills must then be signed by the President. Normally, many different bills are passed, each for a specific agency or government function. However, when congress cannot pass these bills on time, they normally resort to a “continuing resolution”, which simply says to keep funding the government at last year’s levels. This year, it took until last night for Congress to approve such a “C.R.”, and so the NIH was forced to curtail many of our activities. While any break is not good, hopefully, you can all get your research back on track very quickly and make up for lost time. One positive note for FTE fellows is that the C.R. included payment for your salary during the shutdown, essentially meaning we’ve all had a two-week paid vacation. Funding for IRTA and VF s was already guaranteed. When and whether contractors will get paid depends upon the exact wording of your contract and your contractor, but the DIR will aim for fairness.

The OE had several activities planned, and we will keep you informed about rescheduling. In particular, the review of the Lenfant Fellowships was disrupted, which will likely delay the next submission date as well in order to give fellows a chance to reapply. We will have more information in the November newsletter. Happy Halloween to all of you!

## Opinion: Government Shutdown

While the shutdown caused much frustration and anxiety, were you able to find a silver lining? How did you cope? What activities did you partake in?

Email us at [direducation@nhlbi.nih.gov](mailto:direducation@nhlbi.nih.gov). We will compile your experiences and include them in next month’s newsletter. If you would like to remain anonymous, please mention that.

## Meet the New Postdoc Fellows



**Martin Lang, Ph.D.**, is a new Visiting Fellow in the Center for Molecular Medicine under Dr. Hong Xu. Dr. Lang earned his Ph.D. in Human Genetics at the Università di Torino. His initial project at NIH is finding a way to perform a targeted mutagenesis of the mitochondrial genome.



**Mitsunori Nomura, Ph.D.**, is a new Visiting Fellow in the Center for Molecular Medicine under Dr. Toren Finkel. Dr. Nomura earned his Ph.D. at École Polytechnique Fédérale de Lausanne. His initial project at NIH is on the role of necroptosis in adipocyte and macrophages.



**Lingdi Wang, Ph.D.**, is a new Visiting Fellow in the Center for Molecular Biology under Dr. Michael Sack. Dr. Wang earned her Ph.D. in Biochemistry and Molecular Biology at the Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Science. Her initial project at NIH is to research the function of this gene in lipid metabolism, especially cholesterol metabolism.

**Hu G, Tang Q, Sharma S, Yu F, Escobar TM, Muljo SA, Zhu J, Zhao K (2013) Expression and regulation of intergenic long noncoding RNAs during T cell development and differentiation. Nat Immunol 10.**

Long non-coding RNAs (long ncRNAs, lincRNA) are defined as non-protein coding transcripts longer than 200 nucleotides. Previous studies have shown that only one-fifth of transcription across the human genome is associated with protein-coding genes, indicating unanticipated abundance of non-coding RNAs. Intergenic long non-coding RNAs (lincRNAs) refer to long non-coding RNAs that are transcribed from non-coding DNA sequences between protein-coding genes. LincRNAs have been shown to play essential roles in the regulation of mammalian gene expression both transcriptionally and post-transcriptionally, thus modulating various important biological processes during development and pathological conditions. The function of lincRNAs in the immune system is becoming an increasingly popular field of study. So far, there is evidence supporting roles of lincRNAs in the responses of helper T cells to various pathogens, the pathogenesis of several immunological diseases, and the differentiation and activation of lymphocytes. However, the mechanism of how lincRNAs regulate gene expression during the development and differentiation of T cells remains largely unclear, partially due to the lack of knowledge in the expression profiles of lincRNAs in cells of the immune system.

In this article, the authors comprehensively analyzed the expression profiles of lincRNAs in 42 subsets of thymocytes and mature peripheral T cells at multiple time points during their differentiation by high-throughput sequencing of the cDNAs (RNA-seq) from these cell types. Both total RNA and polyadenylated RNA were analyzed. A total of 1524 lincRNA-expressing genome regions were identified in all the T cell subsets, possibly leading to a larger number of lincRNAs because each cluster may encode more than one lincRNA. Interestingly, 73% of the clusters identified by the authors were not annotated in

public databases. To facilitate the systematic identification of new lincRNAs, the authors then proposed a nomenclature that specifies the relative location and distance of a lincRNA to a protein-encoding gene, and the directionality of the lincRNA in the genome. A thorough assessment of the coding potential of these putative lincRNA-coding gene clusters revealed that the majority of the identified lincRNA genes have limited protein coding potential. Further analyses of the cellular specificity of lincRNA expression demonstrated that lincRNA expression differs significantly in any two T cell subtypes, while overall mRNA expression remains similar. Comparison of the RNA-seq data obtained from total RNA and polyadenylated RNA suggests that a subset of lincRNAs is polyadenylated. Further analysis of the polyadenylated lincRNA profile in one specific T cell type at different time points during T cell differentiation revealed that they are dynamically regulated and their levels fluctuate throughout the T cell differentiation process.

Next, the authors reasoned that the tissue specific expression of lincRNAs in T cells suggests that their expression is tightly regulated during differentiation. Therefore, the roles of several key T cell transcription regulators in the regulation of lincRNA expression during T cell differentiation were investigated. The results show that STAT4 binds to and activates TH1-specific lincRNA-encoding genes in TH1 cells, while STAT6 regulates the activation of TH2-specific lincRNA expression in TH2 cells. Another transcription factor T-bet activates the expression of certain lincRNAs and represses the expression of different lincRNAs in TH1 cells. GATA3 also contributes to the regulation of lincRNA expression in TH2 cells. Furthermore, the authors showed evidence that proximal lincRNAs and protein-coding genes are coregulated by the same transcriptional factor. Further investigation of the [Cont'd on next page](#)

## Recent Publications by NHLBI Fellows

**Hill SA**, Kwa LG, Shammass SL, Lee JC, Clarke J (2013) Mechanism of assembly of the non-covalent spectrin tetramerization domain from intrinsically disordered partners. *J Mol Biol*10.

**Hu G**, Tang Q, Sharma S, Yu F, Escobar TM, Muljo SA, Zhu J, Zhao K (2013) Expression and regulation of intergenic long noncoding RNAs during T cell development and differentiation. *Nat Immunol*10.

**Lee IH, Yun J**, Finkel T (2013) The emerging links between sirtuins and autophagy. *Methods Mol Biol* 1077:259-71.

**Sandoval PC**, Slentz DH, Pisitkun T, **Saeed F**, Hoffert JD, Knepper MA (2013) Proteome-Wide Measurement of Protein Half-Lives and Translation Rates in Vasopressin-Sensitive Collecting Duct Cells. *J Am Soc Nephrol*.

**Shim B**, Pacheco-Rodriguez G, Kato J, Darling TN, Vaughan M, Moss J (2013) Sex-specific lung diseases: effect of oestrogen on cultured cells and in animal models. *Eur Respir Rev* 22:302-311.

**Torisu T, Torisu K, Lee IH**, Liu J, Malide D, Combs CA, Wu XS, Rovira II, Fergusson MM, Weigert R, Connelly PS, Daniels MP, Komatsu M, Cao L, Finkel T (2013) Autophagy regulates endothelial

cell processing, maturation and secretion of von Willebrand factor. *Nat Med*10.

**Wu JJ**, Liu J, **Chen EB**, Wang JJ, Cao L, **Narayan N**, Fergusson MM, Rovira II, Allen M, Springer DA, Lago CU, Zhang S, Dubois W, Ward T, Decabo R, Gavrilova O, Mock B, Finkel T (2013) Increased Mammalian Lifespan and a Segmental and Tissue-Specific Slowing of Aging after Genetic Reduction of mTOR Expression. *Cell Rep* 4:913-920.

**Yao YG**, Kajigaya S, Samsel L, McCoy JP, Jr., Torelli G, Young NS (2013) Apparent mtDNA sequence heterogeneity in single human blood CD34 cells is markedly affected by storage and transport. *Mutat Res*10.

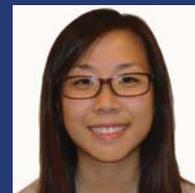
**Yi J**, Wu X, Chung AH, Chen JK, Kapoor TM, Hammer JA (2013) Centrosome repositioning in T cells is biphasic and driven by microtubule end-on capture-shrinkage. *J Cell Biol* 202:779-792.

**Zhang X**, Johnson AD, Hendricks AE, Hwang SJ, Tanriverdi K, Ganesh SK, Smith NL, Peyser PA, Freedman JE, **O'Donnell CJ** (2013) Genetic Associations with Expression for Genes Implicated in GWAS Studies for Atherosclerotic Cardiovascular Disease and Blood Phenotypes. *Hum Mol Genet*.

### Beat, continued

relative position of the lincRNA-encoding genes revealed that many lincRNA-encoding genes are located adjacent to genes encoding proteins that are known to exert important immunological functions, suggesting possible co-evolution of lincRNAs and protein-encoding genes for the regulation of specific immunological processes. The authors then provided evidence supporting the roles of lincRNAs in T cell differentiation and function, ribosome biogenesis, and cell cycle regulation. Finally, the function of a specific lincRNA, LincR-Ccr2-5'AS, in TH2 cells was studied. LincR-Ccr2-5'AS regulates the expression of several chemokine receptors and affects the chemokine-mediated signaling pathways, which in turn affects the migration of TH2 cells. Consistent with previous observations, LincR-Ccr2-5'AS also regulates the expression of a number of co-expressed protein-encoding genes.

In summary, the findings reported in this article will not only provide valuable resources for future studies of transcriptional regulatory networks during T cell development and differentiation, but also contribute to the characterization of new lincRNAs in their functions immune systems.



**Clare Sun, M.D.**, is a new Clinical Fellow in the Hematology Branch under Dr. Charles Bolan. Dr. Sun earned her M.D. at the University of British Columbia.

### Meet the New Postbac Fellows



**Joshua Okonkwo** is a new Postbaccalaureate IRTA in the Center for Molecular Medicine under Dr. Michael Sack. Joshua is a recent graduate of Yale University where he received his Bachelor of Science in Biochemistry and Biophysics.



**Connie Lerma** is a new Postbaccalaureate IRTA in the Genetics and Development Biology Center under Dr. Robert Adelstein. Connie is a recent graduate of Texas A&M International University where she received her Bachelor of Science in Chemistry.

## Featured Article



### Elizabeth Weiner

is a new Postbaccalaureate IRTA in the Cardiovascular-Pulmonary Branch under Dr.

Nehal Mehta. Elizabeth is a recent graduate of Pennsylvania State University where she received her Bachelor of Science in Kinesiology.



### Charlotte Platner

is a new Postbaccalaureate IRTA in the Hematology Center under Dr. John Tisdale. Charlotte is a recent

graduate of College of William and Mary where she received her Bachelor of Science in Chemistry.

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### How to Succeed at Science Without Going Crazy

By Herbert M. Geller, Ph.D.

In any discussion of strategies for success in a career, work/life balance is a hot topic. A recent Scientific American Blog post, <http://tinyurl.com/l57oqys>, The Awesomest 7-Year Postdoc or: How I Learned to Stop Worrying and Love the Tenure-Track Faculty Life, presents the strategy used by an Assistant Professor at Harvard to remain sane while being on the tenure track. Radhika Nagpal (who ultimately got tenure in the Computer Science Department) decided that she would treat her time as a tenure-track faculty member as "a 7-year postdoc". Of course, she was, in reality, not a postdoc, and while she did her job as a Faculty member and mother, her overriding consideration was maintaining her sanity while not specifically doing everything that she was told to would be required for tenure. While her circumstance might be somewhat unique, it would seem that some of her coping strategies would be applicable to anyone in a demanding career. Let's look at some of them:

- Work fixed number of hours and in fixed amounts

According to some, success requires working 80 hour weeks. That's about 11 hours a day, 7 days a week. She figured out, quite correctly, that this is incompatible with having a life. So she picked a number, 56, that was compatible with her family. As you can see, 56 is already 20% more than the stan-

dard US Government work week of 40 hours

- No weekend work  
Weekends were to recover from the week and also to provide for quality family time. In her case, this meant no e-mail or professional reading on the weekend. While this might not be possible for those with laboratory experiments that need tending, the overall strategy of having time off is important
- Limit activities that are not essential for your career  
This meant that she set strict limits on professional travel - at most 5 times a year, and quotas on non-research items such as grant and manuscript reviewing.
- Balance child care  
In her case, she and her husband shared child care responsibilities 50/50, and when one was doing child care, the other could do whatever they wanted - work, play, etc.

She also gave several other tips, such as it's OK to ignore advice, and to find friends and mentors who can help you over the rough spots. Overall, while her coping strategies are not for everyone, the overall tenor of her blog was that it is impossible to satisfy every master, and by establishing rules and priorities a priori, and not focusing on the process of getting tenure, she was able to control her lifestyle, and ultimately achieved tenure anyway.

**NHLBI DIR Halloween Dessert Potluck  
Monday, October 28th  
3PM- 4PM  
Building 10, 1SE Patio**

**All NHLBI Fellows,  
Investigators and Staff are invited.  
Bring a dessert for a chance to win the top prize!**

Sponsored by the Fellows Advisory Committee and the Office of Education