National Heart, Lung, and Blood Institute

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Office of Education
Division of Intramural Research

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

We hope that you have been enjoying your summer. The Office of Education has been busy with our activities for summer students as well as welcoming our new class of post-bac fellows, some of who are introduced in this newsletter.

NHLBI has over 70 summer interns, and we hope that you are enjoying your stay here. We have had three of our summer lunchtime seminars, with our last one on Wednesday the 24th. Before the seminar we will have our Summer Intern picture. Finally, we will have our NHLBI Summer Intern Poster Session on Wednesday, August 7th at 4 PM in Natcher. This is a special session for NHLBI interns and their mentors, where we will serve light refreshments and present Summer Intern Certificates. We hope to see all summer interns and their mentors.

This MOOCs for you!

By Herbert M. Geller, Ph.D.

We'd like to think that the NHLBI DIR provides an environment for learning. While most learning here is informal, during the course of doing our science, or attending a lecture, there are ways to participate in courses. Examples are the many courses offered through the FAES or Biotrac, or the course in Glycobiology taught by the Glycobiology Interest Group. However, these courses are oriented towards the biomedical sciences. In addition, they are offered on rigid schedule, and the course you would like might not be available. In that case, you should consider taking a MOOC!

So what's a MOOC? Six months ago, I would not have been able to even tell you what that stands for – Massive Open Online Course – and now, having taken one, I would highly recommend them to anyone. MOOCs have quickly become the paradigm for life-long learning. They are generally free (if you don't need credit), available on your own schedule, and often come with a way for students in a class to communicate with each other online, take exams on line (and grade each other's exams), and even facilitate in-person conferences on the subject of the class.

The subject matter for MOOCs is just about everything taught. Many colleges and universities have signed agreements to have their courses on line. The major providers of MOOCs are Coursera (www.coursera.org), Udacity (www.udacity.com) and edX (www.edx.org). Each has their own affiliations with particular universities, course offerings and rules. Thus, coursera courses have a fixed start and end date, while udacity courses can be taken any time. EdX also has fixed dates, and is supported by MIT, Harvard, Berkeley and the University of Texas. Coursera Cont'd, page 2

Recent Publications by NHLBI Fellows

E. Guirguis, S. Hockman, Y. W. Chung, F. Ahmad, O. Gavrilova, N. Raghavachari, Y. Yang, G. Niu, X. Chen, Z. X. Yu, S. Liu, E. Degerman, and **V. Manganiello**. A Role for Phosphodiesterase 3B in Acquisition of Brown Fat Characteristics by White Adipose Tissue in Male Mice. *Endocrinology.*, 2013.

D. Hafez, **T. Ni**, S. Mukherjee, **J. Zhu**, and U. Ohler. Genome-wide identification and predictive modeling of tissue-specific alternative polyadenylation. *Bioinformatics.* 29 (13):i108-i116, 2013.

J. Pantin, X. Tian, A. A. Shah, R. Kurlander, C. Ramos, L. Cook, H. Khuu, D. Stroncek, S. Leitman, J. Barrett, T. Donohue, N. S. Young, N. Geller, and **R. W. Childs**. Rapid donor T-cell engraftment increases the risk of chronic graft-versus-host disease following salvage allogeneic peripheral blood stem cell transplantation for bone marrow failure syndromes. *Am J Hematol.*:10, 2013.

S. Perl, **J. Perlman**, **R. P. Weitzel**, O. Phang, **M. M. Hsieh**, and **J. Tisdale**. Addition of Rapamycin to Anti-CD3 Antibody Improves Long-Term Glycaemia Control in Diabetic NOD Mice. *PLoS One.* 8 (6):e67189, 2013.

W. R. Proctor, M. Chakraborty, **L. S. Chea, J. C. Morrison, J. D. Berkson**, K. Semple, M. Bourdi, and **L. R. Pohl**. Eosinophils Mediate the Pathogenesis of Halothane-Induced Liver Injury in Mice. *Hepatology* 57 (5):2026-2036, 2013.

T. Rosales, Z. Nie, V. Kapoor, R. Casellas, Jr., **J. R. Knutson**, and D. Levens. Partition of Myc into Immobile vs. Mobile Complexes within Nuclei. *Sci Rep.* 3:1953. doi: 10.1038/srep01953.:1953, 2013.

S. K. Sarkar, A. Bumb, M. Mills, and **K. C. Neuman**. SnapShot: Single-Molecule Fluorescence. *Cell.* 153 (6):1408, 2013.

Y. Seol and **K. C. Neuman**. SnapShot: Force Spectroscopy and Single-Molecule Manipulation. *Cell* 153 (5):1168-+, 2013.

S. Topanurak, J. D. Ferraris, J. X. Li, Y. Izumi, C. K. Williams, M. Gucek, G. H. Wang, X. M. Zhou, and **M. B. Burg**. High NaCl- and urea-induced posttranslational modifications that increase glycerophosphocholine by inhibiting GDPD5 phosphodiesterase. *Proceedings of the National Academy of Sciences of the United States of America* 110 (18):7482-7487, 2013.

T. Winkler, **S. G. Hong**, J. E. Decker, **M. J. Morgan, C. F. Wu, W. M. Hughes**, Y. Q. Yang, D. Wangsa, H. M. Padilla-Nash, T. Ried, **N. S. Young, C. E. Dunbar**, and R. T. Calado. Defective telomere elongation and hematopoiesis from telomerase-mutant aplastic anemia iPSCs. *Journal of Clinical Investigation* 123 (5):1952-1963, 2013.

X. Yao, M. Gao, C. Dai, K. S. Meyer, J. Chen, K. J. Keeran, G. Z. Nugent, X. Qu, Z. X. Yu, P. K. Dagur, J. P. Mccoy, and S. J. Levine. Peptidoglycan Recognition Protein 1 Promotes House Dust Mite-Induced Airway Inflammation in Mice. *Am J Respir.Cell Mol Biol.*, 2013.

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courses are in just about any area that you find in a college curriculum, while udacity and edX are more oriented towards the sciences.

I took a course from The Hong Kong University of Science and Technology entitled "Science and Technology in China" which was quite informative. One offering on coursera from Johns Hopkins University is entitled "Mathematical Biostatistics Boot Camp 1" starts on July 29th, but you could also take a course entitled "Elementary Statistics" on udacity at any time. If you are into science and cooking, you could take a Harvard course "Science & Cooking: From Haute Cuisine to Soft Matter Science" on edX or "The Science of Gastronomy" from The Hong Kong University of Science and Technology on coursera. For those of you doing clinical research, a course from Harvard on edX entitled "Fundamentals of Clinical Trials" features world-class faculty. And many of these courses provide certificates if you need additional credentials.

As you can see, how and when you use MOOCs is only a function of your particular interest, enthusiasm and imagination. From technical courses in specialized areas (e.g., Network Analysis in Systems Biology from Mt. Sinai on coursera), to more general interest topics, you can find a MOOC to fit your needs.

New NHLBI PostBacs

Nicholas Chedid is a new Postbaccalaureate IRTA in the Laboratory of Imaging Physics headed by Dr. Han Wen. Nicholas is a recent graduate of Tulane University where he received a Bachelor of Science degree in Biomedical Engineering.

Katherine Harmon is a new Postbaccalaureate IRTA in the Laboratory of Imaging Physics headed by Dr. Han Wen. Katherine is a recent graduate of University of California at Berkeley where she received a Bachelor of Arts in Physics.

Holly Jordan is a new Postbaccalaureate IRTA in the Laboratory of Molecular Machines and Tissue Architecture headed by Dr. Nasser Rusan. Holly is a recent graduate of Lee University where she received a Bachelor of Science degree in Biochemistry.

Michael McClurkin is a new Postbaccalaureate IRTA in the Social Determinants of Obesity and Cardiovascular Risk headed by Dr. Tiffany Powell-Wiley. Michael is a recent graduate of State University of New York at Buffalo where he received his Bachelor of Science degree in Biological Sciences.

Ashlea Morgan is a new Postbaccalaureate IRTA in the Developmental Biology Section headed by Dr. Herbert Geller. Ashlea is a recent graduate from the College of William and Mary where she received her Bachelor of Science degree in Neuroscience.

Ramon Rodriguez is a new Postbaccalaureate IRTA in the Laboratory of Cellular Physiology. Ramon is a recent graduate of Brown University where he received his Bachelor of Science degree in Human Biology.

Fellows Award for Research Excellence

Congratulations to the NHLBI recipients of the 2013 Fellows Award for Research Excellence (FARE)! The below fellows are recognized for their research and will present their work at the NIH Research Festival and serve as judges for the next FARE competition. FARE began in 1995 to provide recognition for the outstanding scientific research performed by intramural postdoctoral fellows.

So Gun Hong, DVM, Ph.D.
Gangqing Hu, Ph.D.
Lymarie Maldonado-Baez, Ph.D.
Sara Menazza, Ph.D.
Kim-Lien Nguyen, M.D.
Chuanfeng Wu, Ph.D.

FARE applications are accepted every March. For more information, please visit https://www.training.nih.gov/felcom/fare.

THE SCIENCE BEAT

By Zhiyun Ge, Ph.D.

D. Hafez, **T. Ni**, S. Mukherjee, **J. Zhu**, and U. Ohler. Genome-wide identification and predictive modeling of tissue-specific alternative polyadenylation. *Bioinformatics.* 29 (13):i108-i116, 2013.

Polyadenylation refers to an post-transcriptional process that adds a poly(A) tail to an RNA molecule at the 3'-end. When the transcription of a gene terminates, the 3'-most segment of the newly synthesized RNA is first cleaved off by a number of proteins at specific sites (polyA sites), followed by the synthesis of the poly(A) tail at the RNA's 3' end. In eukaryotes, polyadenylation is not only part of the process that produces mature messenger RNAs (mRNAs) for translation, but also defines the length of the 3'-untranslated region (3'UTR) of mRNAs, which contains various regulatory sequence elements. Earlier studies have shown that a large number of protein-coding genes have more than one functional polyadenylation sites, resulting in alternative polyadenylation(APA) events. APA can affect the nuclear export, cytoplasmic localization, translation, and stability of mRNAs, and therefore can directly regulation gene expression. There is also evidence suggesting that the polyadenylation events are regulated differently in different human tissues. As a result, understanding the specific regulation of APA and identifying tissue-specific APA events is of particular importance.

With the recent development of several high-throughput sequencing protocols, differential preferences for APA usage in different tissues have been reported. However, only small samples or non-mammalian genomes have been analyzed using these technologies so far. In this article, the authors aim at thoroughly analyzing the polyadenylationevents in different human tissue types and deciphering the tissue-specific APA regulation.Due to the lack of adequate methodology to specify the significance of APA biases in different tissues, it is particularly challenging to distinguish the mere presence of multiple APA and their specific up- or down- regulation in different conditions. To address these challenges, the authors first utilized a newly developed RNA-seq protocol that specifically probes the 3'-end of mRNAs, PA-seq, to accurately identify poly(A) sites with high resolution in three different human adult tissue types: brain, liver, and kidney. The next step is to establish an appropriate statistical framework to identify tissue-specific APA sites across multiple deep sequencing libraries. By using a fixed-effects linear model and permutation tests, the authors were able to distinguish between constitutive, alternative and alternatively regulated polyadenylation sites and assess the significance of differences between samples from different tissue types.

mRNApolyadenylation is normally controlled by the presence of specific cis-regulatory sequence elements around poly(A) sites, due to the lack of substrate specificity of the poly(A) polymerase. The authors then set out to investigate the local sequence features around poly(A) sites. Consistent with previous findings that one of the main element described to be responsible for polyadenylation is a conserved hexamer with consensus AWUAAA, located 10-35nt upstream of the poly(A) site, the authors founds that motifs around constitutive poly(A) sites are highly conserved in both sequence and locationHowever, the canonical polyadenylation signal (PAS) used for constitutive sites is absent in 20-30% of human genes, where polyadenylation regulation is achieved by non-canonical sequences. The sequence motifs responsible for APA, especially for tissue-specific APA, remain largely unknown. Further investigation of specifically regulated subsets identified a highly enriched motif (AAAAAAAAAA) starting just downstream of the PASspecifically in brain APA sites. In contrast, the canonical poly(A) signal was not found near brain-specific APA site, and was found at lower conservation in liver and kidney.

In summary, this article described a versatile strategy to identify and distinguish significant condition-specific polyadenylation events, and therefor can be used for the identification for new post-transcriptional regulatory features.

For the Summer Interns!

NHLBI DIR Summer Seminar Series

"Adipokine, Cytokine and Lipokine: the Language of Fat Cells"
Haiming Cao, Ph.D.

Wednesday, July 24th
11:45 AM- 1:30 PM
Building 10-CRC, Room 2-3330