



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***

Summer is upon us, and that means an infusion of new and enthusiastic summer interns. We have the largest class ever (you can find the roster on our web site), and this means a major opportunity for our scientific staff, especially postdocs and graduate students, to practice their mentoring skills. Because the summer experience is so short, mentoring has to be intense and focused. The major advice is that students should engage in a project that builds upon their existing skills and interests, and that mentors should provide a project that can generate rapid results. In addition the research experience, the Office of Education provides a series of pizza lunches and talks, which provide an opportunity for NHLBI summer interns to meet each other and learn about ongoing research at NHLBI. They are scheduled for every other Wednesday at Noon, beginning June 15th. The complete schedule is on our web site. I hope to see you all there! Of course, we hope that our interns take advantage of the cultural and social environment in DC, which becomes a virtual youth festival during the summer because of all the summer interns. Enjoy!

### **Congratulations to the Recipients of the 2011 FARE Award**

<b>Brian Abraham</b>	<i>(Mentor: Keji Zhao)</i>
<b>Shaad Ahmad</b>	<i>(Mentor: Alan Michelson)</i>
<b>Melanie Barzik</b>	<i>(Mentor: John Hammer)</i>
<b>Mark Kohr</b>	<i>(Mentor: Elizabeth Murphy)</i>
<b>Cynthia St. Hilaire</b>	<i>(Mentor: Manfred Boehm)</i>
<b>Kasey Vickers</b>	<i>(Mentor: Alan Remaley)</i>
<b>Bradley Webster</b>	<i>(Mentor: Michael Sack)</i>

The Fellows Award for Research Excellence began in 1995 to provide recognition for the outstanding scientific research performed by intramural postdoctoral fellows. Fellows submit an abstract of their research, which is peer reviewed in a blind study section competition.

\*FARE applications are accepted every year in March.  
For more information, please visit  
<http://felcom.od.nih.gov/subCommittee/fare.aspx>

**Recent Publications by NHLBI Fellows**

- Berezin, M. Y., Guo, K., Akers, W., Northdurft, R. E., Culver, J. P., **Teng, B.**, **Vasalatiy, O.**, Barbacow, K., Gandjbakhche, A., Griffiths, G. L., & Achilefu, S. (2011). Near-Infrared Fluorescence Lifetime pH-Sensitive Probes. *Biophys. J.* *100*, 2063-2072.
- Cleveland, S. B., **Davies, J.**, & McClure, M. A. (2011). A Bioinformatics Approach to the Structure, Function, and Evolution of the Nucleoprotein of the Order Mononegavirales. *Plos One* *6*.
- El-Chemaly, S.**, Ziegler, S. G., Calado, R. T., Wilson, K. A., **Wu, H. P.**, Haughey, M., Peterson, N. R., Young, N. S., Gahl, W. A., Moss, J., & Gochuico, B. R. (2011). Natural History of Pulmonary Fibrosis in Two Subjects With the Same Telomerase Mutation. *Chest* *139*, 1203-1209.
- Feng, X. M.**, Scheinberg, P., Wu, C. O., Samsel, L., Nunez, O., Prince, C., Ganetzky, R. D., McCoy, J. P., Maciejewski, J. R., & Young, N. S. (2011). Cytokine signature profiles in acquired aplastic anemia and myelodysplastic syndromes. *Haematologica* *96*, 602-606.
- Huang, J.**, **Johnson, A. D.**, & O'Donnell, C. J. (2011). PRIME: a method for characterization and evaluation of pleiotropic regions from multiple genome-wide association studies. *Bioinformatics* *27*, 1201-1206.
- Johnson, A. D.**, Newton-Cheh, C., Chasman, D. I., Ehret, G. B., Johnson, T., Rose, L., Rice, K., Verwoert, G. C., Launer, L. J., Gudnason, V., Larson, M. G., Chakravarti, A., Psaty, B. M., Caulfield, M., van Duijn, C. M., Ridker, P. M., Munroe, P. B., & Levy, D. (2011). Association of Hypertension Drug Target Genes With Blood Pressure and Hypertension in 86 588 Individuals. *Hypertension* *57*, 903-U99.
- Kendrick, A. A., Choudhury, M., Rahman, S. M., McCurdy, C. E., Friederich, M., Van Hove, J. L. K., Watson, P. A., Birdsey, N., **Bao, J. J.**, Gius, D., Sack, M. N., Jing, E. X., Kahn, C. R., Friedman, J. E., & Jonscher, K. R. (2011). Fatty liver is associated with reduced SIRT3 activity and mitochondrial protein hyperacetylation. *Biochem. J.* *433*, 505-514.
- Kim, H. K., **Chung, Y. W.**, Chock, P. B., & Yim, M. B. (2011). Effect of CCS on the accumulation of FALS SOD1 mutant-containing aggregates and on mitochondrial translocation of SOD1 mutants: Implication of a free radical hypothesis. *Arch. Biochem. Biophys.* *509*, 177-185.
- Kim, K. K.**, Kim, Y. C., Adelstein, R. S., & Kawamoto, S. (2011). Fox-3 and PSF interact to activate neural cell-specific alternative splicing. *Nucl. Acid Res.* *39*, 3064-3078.
- Le, R. Q., Melenhorst, J. J., Battiwalla, M., Hill, B., Memon, S., Savani, B. N., **Shenoy, A.**, Hensel, N. F., Koklanaris, E. K., Keyvanfar, K., Hakim, F. T., Douek, D. C., & Barrett, A. J. (2011). Evolution of the donor T-cell repertoire in recipients in the second decade after allogeneic stem cell transplantation. *Blood* *117*, 5250-5256.
- Li, T. W.**, Santockyte, R., Yu, S. Q., Shen, R. F., Tekle, E., Lee, C. G. L., Yang, D. C. H., & Chock, P. B. (2011). FAT10 modifies p53 and upregulates its transcriptional activity. *Arch. Biochem. Biophys.* *509*, 164-169.
- Markello, T. C., Pak, L. K., **St Hilaire, C.**, Dorward, H., Ziegler, S. G., **Chen, M. Y.**, Chaganti, K., Nussbaum, R. L., Boehm, M., & Gahl, W. A. (2011). Vascular pathology of medial arterial calcifications in NT5E deficiency: Implications for the role of adenosine in pseudoxanthoma elasticum. *Molecular Genetics and Metabolism* *103*, 44-50.
- Olkhanud, P. B., **Rochman, Y.**, Bodogai, M., Malchinkhuu, E., Wejksza, K., Xu, M., Gress, R. E., Hesdorffer, C., Leonard, W. J., & Biragyn, A. (2011). Thymic Stromal Lymphopoietin Is a Key Mediator of Breast Cancer Progression. *J. Immunol.* *186*, 5656-5662.
- Roussel, X.**, Shamburek, R., **Vaisman, B.**, **Amar, M.**, & Remaley, A. T. (2011). Lecithin Cholesterol Acyltransferase: An Anti- or Pro-atherogenic Factor? *Current Atherosclerosis Reports* *13*, 249-256.
- Sung, H. J.**, **Ma, W. Z.**, Starost, M. F., **Lago, C. U.**, Lim, P. K., Sack, M. N., **Kang, J. G.**, Wang, P. Y., & Hwang, P. M. (2011). Ambient Oxygen Promotes Tumorigenesis. *Plos One* *6*.
- Wang, H., Ge, G. N., **Uchida, Y.**, Luu, B., & Ahn, S. (2011). Gli3 Is Required for Maintenance and Fate Specification of Cortical Progenitors. *J. Neurosci.* *31*, 6440-6448.
- Wu, V., **Barbash, I. M.**, Ratnayaka, K., **Saikus, C. E.**, Sonmez, M., Kocaturk, O., Lederman, R. J., & Faranesh, A. Z. (2011). Adaptive Noise Cancellation to Suppress Electrocardiography Artifacts During Real-Time Interventional MRI. *J. Magn. Reson. Imaging* *33*, 1184-1193.

## **THE SCIENCE BEAT**

*By Daniel Kraushaar, Ph.D.*

*Kim, K. K., Kim, Y. C., Adelstein, R. S., & Kawamoto, S. (2011). Fox-3 and PSF interact to activate neural cell-specific alternative splicing. Nucleic Acids Research 39, 3064-3078.*

Alternative splicing allows for the production of more than one protein isoform from a single gene by inclusion or exclusion of exons from pre-messenger RNAs, which, once processed to mature mRNA will determine the final protein sequence. This post-translational regulation of gene expression has the potential to increase the diversity of gene products that is needed to orchestrate development and protein expression in tissue- and cell type specific fashion. Over the past decade it has been recognized that the phenomenon of alternative splicing is not an exotic event but actually occurs in about 95% of human genes. Both RNA-binding proteins and *cis*-elements regulate alternative splicing. Two relatively well-understood classes of RNA-binding proteins are SR proteins and hnRNPs, which are involved in both regulation of splicing and selection of splice sites. However, other classes of RNA-binding proteins are being identified, yet their roles in the regulation of splicing are not yet known.

The current NHLBI study carried out by Kim *et al.* takes a closer look at the family of FoxI (Fox) proteins and their function in alternative splicing of the nonmuscle myosin heavy chain II-B (NMHC II-B) gene in the central nervous system. NMHC II-B is ubiquitously expressed, however inclusion of an alternative exon, N30, only occurs in a subset of neural cells. Deploying a variety of biochemical assays Kim and co-workers revealed a striking correlation between Fox3 expression levels and N30 inclusion: separation of Fox3+ and Fox3- cells by FACS from cerebellum and brain stem/spinal cord respectively, showed that N30 expression

is substantially higher in Fox3+ cells. *In situ* hybridization confirmed that N30 is expressed together with Fox3 in motor neurons but not Purkinje cells where Fox3 was absent. Evidence that N30 inclusion is directly dependent upon expression of Fox3 was inferred from *in vitro* differentiation experiments with pluripotent embryonic carcinoma P19 cells that were coaxed into neural cell types *via* retinoic acid treatment. Neural differentiation triggered Fox3 expression, which once again was accompanied by inclusion of N30. Inhibition of Fox3 expression through shRNA expression during differentiation abolished the expression of N30 and thereby established a direct functional relationship between Fox3 and alternative splicing of NMHC II-B. Mass spec analysis of endogenous Fox3 and subsequent binding assays with recombinant tagged fusion proteins identified PTB-associated splicing factor (PSF) as a direct interacting factor of Fox3. Neural-specific inclusion of N30 is mediated by two copies of a UGCAUG element, which is present downstream of the N30 exon and is recognized by Fox proteins. Incubation of tagged fusion proteins Fox3 and PSF together with radiolabeled RNA that contained two UGCAUG elements showed that the PSF-Fox3 interaction enhanced recruitment of Fox3 to RNA. RNA-protein Co-IP assays extended the idea to live cells that were expressing exogenous Fox3 and PSF, and showed an increase in binding of Fox3 to endogenous NMHC II-B RNA when expressed together with PSF. Knockdown of PSF in P19 cells inhibited N30 inclusion as did the previous knockdown of Fox3 and suggests that both components are essential for alternative inclusion of N30.

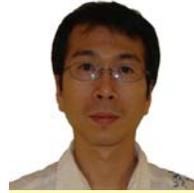
In summary, Kim and co-workers identified a Fox3-PSF complex, which bears a critical role in activating alternative splicing of the N30 exon of NMHC II-B. It will be interesting to see whether other Fox proteins act in much the same manner in other tissue types and their work will likely prompt further studies aimed at investigating the interactions of the Fox-PSF complex with the splicing machinery of the cell.

Join the **NHLBI Fellows and Alumni** group in LinkedIn. It's a great way to network with past and current fellows.

## New NHLBI Fellows



**Xin Pan, Ph.D.**, is a new Visiting fellow in the Molecular Biology Section under Dr. Toren Finkel. Dr. Pan earned his Ph.D. in Cell Biology from the National Center of Biomedical Analysis, Beijing, China. He was previously a Research Associate at NCBA department of Cell Biology. Dr. Pan's initial research project will be on a new gene's function in mitochondria and its molecular mechanisms.



**Takehiro Torisu M.D., Ph.D.**, is a new Visiting fellow in the Molecular Biology Section under Dr. Toren Finkel. Dr. Torisu earned his M.D. and Ph.D. from the Molecular and Cellular Immunology Division, Kyushu University, Japan. He was previously an assistant professor in the Department of Health Promotion at Kyushu Dental College. Dr. Torisu's initial project involves sirtuins as tumor suppressors.



**Hasina Akter, Ph.D.**, is a new Visiting Fellow in the Laboratory of Mitochondrial Biology in Cardiometabolic Syndromes under Dr. Michael Sack. Dr. Akter earned her Ph.D. in Biochemistry from the University of Hyogo, Japan. She worked as an Assistant Professor at Jahangirnagar University in Bangladesh before coming to the NIH. Dr. Akter will initially be studying the correlation between Parkinson disease and metabolic disorders.

## NHLBI Fellow Wins the Young Investigator Competition



L to R: Tiffany Nguyen (second), Mark Kohr (last)

The Young Investigator Competition was held at the International Society for Heart Research Meeting in Philadelphia on May 22-25. Mark Kohr, Laboratory of Cardiac Physiology, won the award. Tiffany Nguyen, also from the Laboratory of Cardiac Physiology, was the runner-up.

## Help plan the 2012 NHLBI DIR Scientific Retreat by becoming a part of the Fellows Advisory Committee

The next meeting is Monday, June 13th at 4:00pm in Building 10/13S235.  
For more information, please email [direducation@nhlbi.nih.gov](mailto:direducation@nhlbi.nih.gov)