



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***

Happy New Year to All.

The Office of Education starts the New Year by opening up registration for the NHLBI Scientific Retreat. This year, the Retreat is an event for all scientific staff in DIR: fellows, staff scientists and investigators. It is intended to provide an opportunity for all of us to network and learn about the science going on at NHLBI. Our Keynote speaker, on opening night, is Dr. Ezekiel Emanuel, who is currently working at the Office of Management and Budget on Health Care Reform. I am sure that he will have lots of interesting information to share with us about the future of Health Care in this country. We have exciting scientific speakers from outside NHLBI, as well as talks chosen from the poster submissions. The information for registration is given below, and I hope to see all of you there.

**8th Annual NHLBI Scientific Retreat**

**Featuring:**

- Ezekiel J. Emanuel, Ph.D., M.D., Keynote Speaker
- Gerald Shulman, Ph.D., M.D., Scientific Speaker
- Peter Walter, Ph.D., Scientific Speaker

**April 14-16, 2010**  
**The Baltimore Tremonts**  
**Baltimore, MD**

**REGISTRATION IS NOW OPEN!**

**Fellows and Faculty, please follow the link below. The deadline for registration and abstract submissions is MARCH 12, 2010**

<http://dir-intranet.nhlbi.nih.gov/oe/retreat/>

**New NHLBI Fellows**

Jae-Hyuk (John) Yi, Ph.D., is a Postdoctoral Fellow in the Developmental Neurobiology Section under Dr. Herbert Geller. Dr. Yi earned his Ph.D. from the University of Montreal, Canada, and then was a Postdoctoral Fellow at the University of Wisconsin. He won the *Young Investigator Educational Enhancement Award* for American Society for Neurochemistry. Dr. Yi's initial research project deals with the role of proteoglycans in limiting recovery of function after traumatic brain injury,



Alexander Sodt, Ph.D., is a Post Doc IRTA Fellow under Drs. Bernard Brooks and Richard Pastor. Dr. Sodt earned his Ph.D. in Chemistry from the University of California at Berkeley. During his time at Berkeley, he was a teaching assistant for Chemistry. Dr. Sodt's is currently working on two research projects the first is the development of critical assessment of phase-space sampling algorithms for biophysical simulations, and the second being the study of tension of simulated lipid bilayers, as well as transmembrane helix binding motifs.



Roby Joehanes, Ph.D., is a Visiting Fellow in the Division of Prevention and Population Services under Dr. Daniel Levy. Dr. Joehanes earned his Ph.D. in Genetics from Kansas State University. He served at the workshop co-chair in the 2003 IJCAI *Learning Graphical Models on Computational Genomics*. Dr. Joehanes' current research project is to construct a gene interaction network for stratifying the risks of cardiovascular diseases.



Tae-Young Choi, Ph.D., is a Visiting Fellow in the Laboratory of Developmental Biology under Dr. Kenneth Kramer. Dr. Choi earned his Ph.D. in Dermatology from Chungnam National University, South Korea. He won the *Poster of Distinction* prize from Chungnam National University. Dr. Choi's initial research involves neural crest development of zebra fish by foxd3 promoter and phenotype-based screening by small compounds.



Dong Keun Rhee, Ph.D., is a Visiting Fellow in the Translational Medicine Branch under Dr. Vincent Manganiello. He earned his Ph.D. in Life Sciences and Biotechnology from Korea University in Seoul, Korea. Dr. Rhee served as a senior researcher at Catholic University before beginning at NIH. His initial research project is on cell signaling with a focus on PDE3A and PDE3B.

### **Featured CORE: The Protein Analysis Facility** **Duck-Yeon Lee**

Have you ever wanted to get an accurate mass on your newly produced recombinant protein? With results are in less than 30 minutes and only requires 1 minute of your time?

The Protein Analysis Facility (PAF) allows you to do this and more!

The mission of the PAF is to assist researchers at NHLBI, who want

1) Protein or peptide mass and metal content analysis, 2) Radioisotope labeled protein or peptide isolation,

3) Methods development designed to meet the rapidly evolving needs of researchers based on biochemical background

The PAF officially opened in May 2009 with eight operating instruments: ES-LC-MS (Agilent), MALDI-TOF HPLC equipped with In-line radiochemical detector (PerkinElmer), Liquid scintillation analyzer (PerkinElmer), HPLC equipped with In-line fluorescence detector (Agilent), Atomic absorption spectrometer (PerkinElmer), OFF Fel fractionator (Agilent), and Bio-Rad open column system

Most instruments are available for "walk-up" use although it is advised to check with Dr. Lee to see if there is a wait. When using the equipment for the first time, Dr. Lee will guide you through the procedures.

Instruction manuals for each instrument, along with screen shots, can be found at:

<https://dirweb.nhlbi.nih.gov/Cores/PAF/Pages/default.aspx>

PAF is located in Building 50/ 2224 & 2226. Dr. Lee's office: 50/ 2339.

Email: [leedy@nhlbi.nih.gov](mailto:leedy@nhlbi.nih.gov)

Phone: 301-435-8369

**Are you interested in an career in industry?**  
**Volunteer to help the Office of Education increase networking with industry!**

Send an email to:  
[direducation@nhlbi.nih.gov](mailto:direducation@nhlbi.nih.gov)

**THE SCIENCE BEAT**

By Nisha Narayan, Ph.D.

Hsieh MM, Kang EM, Fitzhugh CD, Link MB, Bolan CD, Kurlander R, Childs RW, Rodgers GP, Powell JD, Tisdale JF. *Allogeneic hematopoietic stem-cell transplantation for sickle cell disease. New England Journal of Medicine (2009) Dec 10;361(24):2309-17*

Sickle-cell disease is a genetic blood disorder resulting in sickle shaped red blood cells and a variety of consequent complications including, anemia, increased hemolysis and vaso-occlusive crisis resulting in multiple organ damage. Allogeneic stem-cell transplantation after myeloablative conditioning - a process by which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets, to allow successful transplantation - has been shown to be highly remedial in children with 95% showing disease-free survival, but harmful in adults with graft rejections further complicating the chances of effective treatment.

The authors of this study have developed a safe, non-myeloablative regimen to perform hematopoietic stem-cell transplantation in adults affected with sickle-cell disease that would allow engraftment and avoid graft-versus-host-disease (GVHD) in the presence of donor T cells. To do so, they used a low dose of radiation (300

cGy) followed by the drug Sirolimus, which acts by binding to the mammalian target of rapamycin (mTOR) and inhibiting T-cell proliferation. This leads to activated T-cells that cannot proliferate, hence promoting T-cell tolerance and graft acceptance. They showed the success of this novel approach in murine models where the sickle-cell disease phenotype was corrected in mice with the sickle cell gene.

In this publication, they describe their success with treating 10 adults with acute sickle-cell disease using this method. They chose 10 patients between the ages of 16-45 years of age based on three criteria – homozygosity for hemoglobin S or heterozygosity for hemoglobin S and C, identification of an HLA-identical family donor, and the existence of severe disease. After this, the donors underwent 5-6 days of granulocyte colony-stimulating factor (G-CSF) mobilization, followed by leukapheresis (the process of separating white blood cells from a sample of blood) to obtain  $10 \times 10^6$  CD34+ cells per kilogram of the recipient's body weight, which were then cryo-preserved. The procedure for the recipient consisted of gradually increasing doses of alemtuzumab (a monoclonal antibody directed against CD52, that depletes T cells and B cells) on days 7 to 3 before transplantation, 300 cGy of total body irradiation on day 2 before transplantation and oral Sirolimus starting the day before transplantation,

which is to be tapered off when donor chimerism reaches 100%.

The recipients tolerated the conditioning regimen fairly well and at a median follow-up of 30 months, all ten patients were alive. Nine out of ten retained the graft and among them, the mean percentage of circulating donor T cells was over 50% while that of donor myeloid cells over 75%. Since none reached 100% donor chimerism, Sirolimus administration was continued. Hemoglobin levels progressively improved after transplantation and markers of increased hemolysis decreased. Patients with histories of cerebrovascular injury or acute chest syndromes before transplantation were relieved of either. None of the patients developed acute or chronic GVHD, but there were some small adverse effects, including minor ankle arthralgia and nonpitting edema as well as pneumonitis as a response to Sirolimus, which were resolved in 3 months by lowering the dose of the drug.

This is a hallmark report in the field of stem cell transplantation to cure hemoglobinopathies like sickle-cell disease. This new conditioning regimen allows for stable transplantation with a mixed donor-recipient chimerism and successfully reverses the sickle-cell disease phenotype, not only transforming the lives of those affected positively, but also demonstrating the benefits of translational research.

### **Catching Up with Former Fellows: Luca Di Noto, Alexion Pharmaceuticals**

To kick off 2010 we've resurrected a column from the past which follows up with former fellows on where they are now. This month features Luca Di Noto, a former Re-

search Fellow in the Laboratory of Biochemistry with Dr. Rodney Levine from June 2002-July 2006. Luca currently works as a Purification Process Development Scientist II at Alexion Pharmaceuticals where he focuses on developing new purification processes for the manufacturing of biological drugs such as monoclonal antibodies.

*1) What was the hardest thing about transitioning from being a fellow to being a Scientist in industry?*

When I decided to make the transition to industry, I was not fully aware of the differences between academia and industry. This lack of knowledge about the world of drug manufacturing and

(cont'd on p.4)

<http://dir-intranet.nhlbi.nih.gov/oe/>

**Recent Publications by NHLBI Fellows**

- Chen, W. Y., Kim, M. S., Shanbhag, S., Arai, A., VanRyzin, C., McDonnell, N. B., & Merke, D. P. (2009). The Phenotypic Spectrum of Contiguous Deletion of CYP21A2 and Tenascin XB: Quadricuspid Aortic Valve and Other Midline
- Hsieh, M. M., Kang, E. M., Fitzhugh, C. D., Link, M. B., Bolan, C. D., Kurlander, R., Childs, R. W., Rodgers, G. P., Powell, J. D., & Tisdale, J. F. (2009). Allogeneic Hematopoietic Stem-Cell Transplantation for Sickle Cell Disease. *N. E. J. M.* 361, 2309-2317.
- Kang, Y. S., Zhao, X. H., Lovaas, J., Eisenberg, E., & Greene, L. E. (2009). Clathrin-independent internalization of normal cellular prion protein in neuroblastoma cells is associated with the Arf6 pathway. *J. Cell Sci.* 122, 4062-4069.
- Ma, X. F., Takeda, K., Singh, A., Yu, Z. X., Zervas, P., Blount, A., Liu, C. Y., Towbin, J. A., Schneider, M. D., Adelstein, R. S., & Wei, Q. Z. (2009). Conditional Ablation of Nonmuscle Myosin II-B Delineates Heart Defects in Adult Mice. *Circul. Res.* 105, 1102-U128.
- Rouhani, F. N., Brantly, M. L., Markello, T. C., Helip-Wooley, A., O'Brien, K., Hess, R., Huizing, M., Gahl, W. A., & Gochuico, B. R. (2009). Alveolar Macrophage Dysregulation in Hermansky-Pudlak Syndrome Type 1. *Am. J. Resp. Crit. Care Med.* 180, 1114-1121.
- Xu, J. H., Chen, J. J., Toptygin, D., Tcherkasskaya, O., Callis, P., King, J., Brand, L., & Knutson, J. R. (2009). Femtosecond Fluorescence Spectra of Tryptophan in Human gamma-Crystallin Mutants: Site-Dependent Ultrafast Quenching. *J. A. C. S.* 131, 16751-16757.
- Zhou, Y. F., Wang, S. N., Yu, Z. X., Hoyt, R. F., Sachdev, V., Vincent, P., Arai, A. E., Kwak, M., Burkett, S. S., & Horvath, K. A. (2009). Direct injection of autologous mesenchymal stromal cells improves myocardial function. *Biochem. Biophys. Res. Comm.* 390, 902-907.

the pharmaceutical industry (and the curiosity that spawned from it) was in fact one of the drivers behind my decision to make the jump.

In my case the change was even bigger as I transitioned not only from an academia-like environment (the NIH intramural research) to industry but also from research to development. As I settled in my new position the biggest challenge was changing my mind-set to a completely different way of thinking. I find industry structure a bit more rigid and more dead line oriented. I notice that creativity (a necessary tool in academia) is somewhat quenched by the need to work within pre-defined experimental spaces. On the other hand I have learned (a process that never ceases) a great deal by making this big jump.

*2) What advice do you have for fellows wanting to transition into a research position in industry?*

Be prepared for a different work philosophy. Always be aware of your

goals (what is expected of you), how you plan to deliver results within specific deadlines and always keep your focus on the bigger picture (understand how your work fits into a bigger project and what is the ultimate goal of that project).

*3) What was the best thing about your fellowship at NIH?*

Let me just say upfront that I had a fantastic experience at NIH. To this day, my mentor at NHLBI remains one of the reference figures in my professional career, even years after leaving the institute. Under his guidance I was provided all the tools necessary to nourish my growth as a scientist and to choose the career I wanted to pursue. I consider myself quite fortunate to have had this opportunity.

*4) What skills did you need to successfully perform at your present job that you wish you had acquired during your training years?*

I cannot think of any particular skill. I do not mean to say that my training years were perfect and that I acquired all the necessary skills, but simply that in ones career there will always be new skills that need to be learned from scratch. The important point is how you go about learning them, and in that sense I think my training years were a good practice.

*5) What is your mantra? (What gets you through the day)*

How does that work? (Never stop asking yourself questions)

*6) Any other advice you would like to impart to the fellows at NHLBI?*

Always keep your fascination with science alive. Nurture your curiosities, never stop wondering. Finally try to take full advantage of your experience in one of the most exciting and unique research environments in this country, the intramural research at NIH.

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