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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. NHLBI has over 70 summer interns, and we hope that you are enjoying your stay here. We have had two of our summer lunchtime seminars, with two more to go. If you are an intern who has not attended, you should take advantage of this unique opportunity. In addition, if you are supervising a summer student, you should encourage them to go. Next Wednesday, the 13th, before the seminar we will have our Summer Intern picture, where interns can get their NHLBI Summer 2011 t-shirt. We hope to see you all there.

We are in the planning stages for our next DIR Scientific Retreat. We would very much like to get nominations from all of our fellows for potential speakers at the retreat. The major criteria are that they be a practicing scientist whose research has an impact on several areas that are found in the NHLBI Intramural program, and that they be an outstanding speaker. Send us your suggestions for consideration by the Fellows Advisory Committee ASAP.

Risk/Reward in Science

By Herbert Geller, Ph.D.

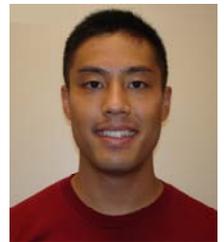
When it comes to athletic training, we are familiar with the expression "No pain, no gain". Or in skiing, "If you are not falling, then you are not trying hard enough". The parallel in scientific research is if you are not taking risks, then you are not likely to produce anything interesting. However, if you push yourself too hard in athletics, you can end up severely injured, and if you continually take on risky projects you could end up with no results to show for your efforts. So how do you judge and manage risk/reward for your scientific endeavors?

One answer is that the risk/benefit ratio is different at different stages of your career. For example, as a beginning graduate student, you have the

Building Your On-Line Image

By Jae Song

It has been said that "If you don't seem like you're bragging, then you are not doing enough for self-promotion." As scientists, we tend to believe that our work will speak for itself, and not require any advertisement. But, as many of you know, this is a different world – where most information is obtained through Google, rather than by PubMed. Towards that end, I was hired in January of 2010 by the Office of the Scientific Director to construct websites for the intramural component of NHLBI. I have worked with numerous PIs and Core Directors to



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option of doing some exploratory projects with the hope that one will produce an interesting result that can be followed up. Because tenure in graduate school is not fixed, it's possible to graduate in a reasonable amount of time even if you have had several false starts. The danger of a risky project gets higher for postdoctoral fellows. As a postdoc, you have a limited amount of time to demonstrate your productivity and ability. While a high-impact project can get you recognition and a start to a career, taking on

a project for which there is no clear path to a publication can also end up with nothing in a reasonable amount of time. Of course, from the perspective of a lab chief, having several fellows with high-impact projects can provide a cushion – you get the occasional publication, even if many of your fellows end up with nothing.

So what's a postdoctoral fellow to do? One approach is to have more than one project – one that is high risk, while the other is lower risk and is sure to

generate results. Another is to collaborate so that even if your primary publication is slower than you wish, you will have publications, even if not first author. What if you really like the project, but it's just not working? As we have addressed in a previous column, if things are not working, and time is flying by, you should be prepared to cut your losses and move on to another project. Time is too short to be in an unproductive situation.

THE SCIENCE BEAT

By Nisha Narayan, Ph.D.

Wang L, Yu CR, Kim HP, Liao W, Telford WG, Egwuagu CE, Leonard WJ (2011) Key Role for IL-21 in experimental autoimmune uveitis. Proc Natl Acad Sci U S A., 108(23):9542-7.

Interleukins are a group of cytokines produced by a variety of cells in the body. They play a pivotal role in the development and differentiation of T cells, B cells and hematopoietic cells and are essential to the proper functioning of the immune system. Many autoimmune diseases and immune deficiency syndromes are associated with deficiencies of interleukins, including Type 1 Diabetes, Systemic Lupus Erythematosus and Multiple Sclerosis. Among the interleukins, the genes encoding IL-21 and IL-2 are in close proximity with each other and are conserved in humans and mice. Though they are adjacent and IL-21 is most homologous to IL-2, these two interleukins are functionally distinct. To deduce their controversial roles in diseases such as uveitis and multiple sclerosis, the authors generated *il21-mCherry/il2-emGFP* dual-reporter transgenic mice as a model system. Experimental Autoimmune Uveitis (EAU) shares pathological features with human uveitis which is a group of sight-threatening intraocular inflammatory diseases.

After evaluating the expression of IL-21 and IL-2 in the reporter mice and their WT littermates by FACS, they immunized the mice with interphotoreceptor retinoid-bind-

ing protein (IRBP) and examined mCherry and emGFP expression at day 21 when the mice developed severe uveitis. Using cell-sorting, RT-PCR and intracellular staining, they found that both IL-2 and IL-21 were induced in autoreactive CD4+ T cells and cells expressing either or both cytokines were present in the inflammatory cells in the retina. In keeping with the role of IL-21 in the development of autoimmune diseases as well as its expression in the retina, they then investigated the development of EAU in WT versus *il21^{-/-}* mice by funduscopy. The WT retinas manifested severe signs of inflammation while the *il21^{-/-}* mice showed very modest fundoscopic changes with less inflammation, lower IL-17 and IFN- γ production. However there was more IL-10 production in the *il21^{-/-}* mice though IL-2 production was similar in both mice, indicating an overall shift from pro-inflammatory to anti-inflammatory cytokine signaling in the absence of IL-21.

Finally, they confirmed that the *il21^{-/-}* mouse defect occurred in the generation of IRBP-specific pathogenic T cells by adoptively transferring WT and *il21^{-/-}* IRBP-specific lymphocytes into WT mice. Accordingly, the *il21^{-/-}* cells produced less IL-17 and IFN- γ but similar levels of IL-2 and the mice receiving *il21^{-/-}* cells exhibited less severe EAU. To conclude, this study shows a primary role for IL-21 in the development of EAU, suggesting possible IL-21 dependent therapies. In addition, the generated mouse models can be potentially used to dissect and understand a broad range of other diseases.

Recent Publications by NHLBI Fellows

- Barbash, I. M., Saikus, C. E., Ratnayaka, K., Faranesh, A. Z., Kocaturk, O., Wu, V., Bell, J. A., Schenke, W. H., Raman, V. K., & Lederman, R. J.** (2011). Limitations of Closing Percutaneous Transthoracic Ventricular Access Ports Using a Commercial Collagen Vascular Closure Device. *Catheter. Cardiovasc. Interv.* *77*, 1079-1085.
- Barese, C. N. & Dunbar, C. E.** (2011). Contributions of Gene Marking to Cell and Gene Therapies. *Hum. Gene Ther.* *22*, 659-668.
- Foster, M. C., Hwang, S. J., Massaro, J. M., Hoffmann, U., Deboer, I. H., Robins, S. J., Vasani, R. S., & Fox, C. S.** (2011). Association of Subcutaneous and Visceral Adiposity With Albuminuria: The Framingham Heart Study. *Obesity* *19*, 1284-1289.
- Glancy, B. & Balaban, R. S.** (2011). Protein composition and function of red and white skeletal muscle mitochondria. *Am. J. Physiol. Cell Physiol.* *300*, C1280-C1290.
- Guzik-Lendrum, S., Nagy, A., Takagi, Y., Houdusse, A., & Sellers, J. R.** (2011). *Drosophila melanogaster* Myosin-18 Represents a Highly Divergent Motor with Actin Tethering Properties. *J. Biol. Chem.* *286*, 21755-21766.
- Kasamatsu, A., Nakao, M., Smith, B. C., Comstock, L. R., Ono, T., Kato, J., Denu, J. M., & Moss, J.** (2011). Hydrolysis of O-Acetyl-ADP-ribose Isomers by ADP-ribosylhydrolase 3. *J. Biol. Chem.* *286*, 21110-21117.
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- O'Seaghdha, C. M., Hwang, S. J., Bhavsar, N. A., Kottgen, A., Coresh, J., Astor, B. C., & Fox, C. S.** (2011). Lower Urinary Connective Tissue Growth Factor Levels and Incident CKD Stage 3 in the General Population. *Am. J. Kidney Dis.* *57*, 841-849.
- Pai, V. M., Rapacchi, S., Kellman, P., Croisille, P., & Wen, H.** (2011). PCATMIP: Enhancing Signal Intensity in Diffusion-Weighted Magnetic Resonance Imaging. *Magn. Reson. Med.* *65*, 1611-1619.
- Wang, L., Yu, C. R., Kim, H. P., Liao, W., Telford, W. G., Egwuagu, C. E., & Leonard, W. J.** (2011). Key role for IL-21 in experimental autoimmune uveitis. *Proc. Natl. Acad. Sci. U. S. A* *108*, 9542-9547.
- Wu, C. W. H., Vasalatiy, O., Liu, N., Wu, H. T., Cheal, S., Chen, D. Y., Koretsky, A. P., Griffiths, G. L., Tootell, R. B. H., & Ungerleider, L. G.** (2011). Development of a MR-Visible Compound for Tracing Neuroanatomical Connections In Vivo. *Neuron* *70*, 229-243.

New NHLBI Fellows



Sarah Herman, Ph.D. is a new IRTA fellow in the Hematology Branch under Dr. Adrian Wiestner. Dr. Herman earned her Ph.D. in Integrated Biomedical Sciences from Ohio State University. She was previously a Post doctoral fellow at the Ohio State focusing on Kinase signaling in leukocytes and regulation and mutation of BTK in CLL cells. She is currently studying the genetic profile of CLL cells after engraftment into a mouse xenograft model.



Dorothy Lerit, Ph.D. is a new IRTA fellow in the Cell Biology and Physiology Center under Dr. Nasser Rusan. Dr. Lerit earned her Ph.D. in Molecular Biology from Princeton University. She was previously a teaching assistant of Cellular Developmental Biology at Princeton. Her initial research project at NIH be to characterize the role of the pericentrin- like protein PLP in *Drosophila* testes development.

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assist in creating and updating their websites. It is my pleasure to announce that the project is almost complete. There are only a handful of labs, cores, and administrative offices who have not taken the opportunity to show off their new research data and progress since the old website discontinued its services in 2005. I am now available to help the postdoctoral population at NHLBI to do the same.

It was stated in the May issue of the newsletter that post-docs are now starting to leave NIH earlier than ever. The average time spent as a post-doc has decreased from 5 years to now only 3.5 years. This shift should provide even more reason for fellows to work on their staff sites. I firmly believe that having a professional website will give

our fellows an edge over other applicants when they transition into the next level of their careers, especially when the site is sponsored by NIH and NHLBI. Treat it like a professional online resume. PIs and Core Directors should encourage their fellows to build a website—it may help give them an edge on the next step in their career progression. Fellows can manage their own site as if it were their own laboratory/core site to bring attention to their research progress and accomplishments.

I would recommend posting links to your latest publications, uploading pictures that capture the attention of fellow researchers, and adding any additional content you feel is appropriate. Not only will this attract attention to

your research project, it could also help potential post-bac and post-doc students, as well as staff scientists become interested in your lab. Remember that this is your chance to share your research with the rest of the world.

Dr. Geller encouraged everyone to develop their “elevator speech” (which later turned into “ski lift speech”) at the last fellows retreat. I’m sure everyone mastered that skill. Now it is time to practice your “cyber speech” and build your website. If you need a hand to get started, just shoot me an email. Thanks, and I hope to hear from all of you soon.

Jae can be reached via email at songjh@mail.nih.gov, or by phone at (301) 594-7154.

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

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

The next meeting is Monday, July 11th at 4:00pm in Building 10/13S235. For more information, please email direducation@nhlbi.nih.gov