



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

This newsletter is designed to provide information and news about NHLBI fellows to the NHLBI community. Increasingly, our scope has expanded, so we now include feature articles about the NHLBI cores as well as spotlight interesting activities within NHLBI DIR. While most of these articles are written by the Office of Education staff, we have welcomed and encouraged contributions from our Fellows. For example, we have featured the "Science Beat" column, pioneered by Nisha Narayan, which singles out a fellows paper as worthy of dissemination. With this issue, we now welcome Daniel Kraushaar, as both a new fellow and contributor to the newsletter. We hope that additional fellows will help with the newsletter by contributing columns of interest to them. For example - how about a review of a local affordable restaurant? Please contact the Office of Education if you are interested. Experience like this is also valuable for those of you seeking a non-academic career, as it demonstrates skills outside the laboratory.

We are now entering the Holiday season, and at this time of year and in this economy there are many who need our help. The Combined Federal Campaign is designed to efficiently collect funds that can be used to help the needy. So please consider donating some money for the less fortunate in our community.

How I transitioned from Studying Proteins to Studying Policy: My experience as a Science Policy Fellow at FASEB

By Anne Deschamps, Ph.D.

Have you ever wondered how the President, Congress, and government institutions make decisions and regulations related to biomedical research? If you have, you may be interested in learning what a career in science policy is like. Consider applying for the NHLBI-FASEB Science Policy Fellowship. Having

(cont'd on p.4)

Stress - How do I deal with it?

By Herbert Geller, Ph.D.

Stress is an intrinsic part of being a professional, including the graduate student and postdoctoral experience. Thus, learning appropriate responses to dealing with stress is an important part of your education. On the other hand, when stress reaches the point where it affects your performance or relationships, then it's time to assess whether your responses are appropriate or you need additional help. If so, there are many mechanisms available to you to deal with these stressors, (cont'd on p.5)

Recent Publications by NHLBI Fellows

- Anzinger, J. J., Chang, J., Xu, Q., Buono, C., Li, Y. F., Leyva, F. J., Park, B. C., Greene, L. E., & Kruth, H. S.** (2010). Native Low-Density Lipoprotein Uptake by Macrophage Colony-Stimulating Factor-Differentiated Human Macrophages Is Mediated by Macropinocytosis and Micropinocytosis. *Arterioscler. Thromb. Vasc. Biol.* *30*, 2022-U318.
- Berry, C., Kellman, P., Mancini, C., Chen, M. Y., Bandettini, W. P., Lowrey, T., Hsu, L. Y., Aletras, A. H., & Arai, A. E.** (2010). Magnetic Resonance Imaging Delineates the Ischemic Area at Risk and Myocardial Salvage in Patients With Acute Myocardial Infarction. *Circ. Cardiovasc. Imaging* *3*, 527-535.
- Fujiwara, I., Remmert, K., Hammer J.** Direct observation of the uncapping of capping protein-capped actin filaments by CARMIL homology domain. *J. Biol. Chem.* 2010; *285*(4):2707-20.
- Huang, H., Tang, Q. Z., **Wang, A. B.**, Chen, M. Y., Yan, L., Liu, C., Jiang, H., Yang, Q. L., Bian, Z. Y., Bai, X., Zhu, L. H., Wang, L., & Li, H. L. (2010). Tumor Suppressor A20 Protects Against Cardiac Hypertrophy and Fibrosis by Blocking Transforming Growth Factor-beta-Activated Kinase I-Dependent Signaling. *Hypertension* *56*, 232-U111.
- Kim, Y. C., **Kim, K. K.**, & Shevach, E. M. (2010). Simvastatin induces Foxp3+T regulatory cells by modulation of transforming growth factor-beta signal transduction. *Immunology* *130*, 484-493.
- Li, M., **Mazilu, D.**, & Horvath, K. A. (2010). Computer aided minimally invasive cardiac procedures. *Minerva Chir.* *65*, 439-450.
- Ma, M. C., Ding, S. L., Lundqvist, A., San, H., Fang, F., Konoplyannikov, M., Berry, C., Beltran, L. E., Chen, G. B., Kovacic, J. C., & Boehm, M.** (2010). Major Histocompatibility Complex-I Expression on Embryonic Stem Cell-Derived Vascular Progenitor Cells Is Critical for Syngeneic Transplant Survival. *Stem Cells* *28*, 1465-1475.
- Rousset, X., Vaisman, B., Auerbach, B., Krause, B. R., Homan, R., Stonik, J., Csako, G., Shamburek, R., & Remaley, A. T.** (2010). Effect of Recombinant Human Lecithin Cholesterol Acyltransferase Infusion on Lipoprotein Metabolism in Mice. *Journal of Pharmacology and Experimental Therapeutics* *335*, 140-148.
- Scheinberg, P., Cooper, J. N., Sloand, E. M., Wu, C. O., Calado, R. T., & Young, N. S.** (2010). Association of Telomere Length of Peripheral Blood Leukocytes With Hematopoietic Relapse, Malignant Transformation, and Survival in Severe Aplastic Anemia. *JAMA*. *304*, 1358-1364.
- Sung, H. J., Ma, W. Z., Wang, P. Y., Hynes, J., O'Riordan, T. C., Combs, C. A., McCoy, J. P., Bunz, F., Kang, J. G., & Hwang, P. M.** (2010). Mitochondrial respiration protects against oxygen-associated DNA damage. *Nat. Commun.* *1*.
- Wan, Z. H., Zhi, N., Wong, S. S., Keyvanfar, K., Liu, D. L., Raghavachari, N., Munson, P. J., Su, S., Malide, D., Kajigaya, S., & Young, N. S.** (2010). Human parvovirus B19 causes cell cycle arrest of human erythroid progenitors via deregulation of the E2F family of transcription factors. *J. Clin. Invest.* *120*, 3530-3544.
- Wan, C. K., Tse, A. K., Yu, Z. L., Zhu, G. Y., Wang, H., & Fong, D. W. F.** (2010). Inhibition of cytochrome P450 3A4 activity by schisandrol A and gomisin A isolated from *Fructus Schisandrae chinensis*. *Phytomedicine* *17*, 702-705.
- Yahiro, K., Morinaga, N., Moss, J., & Noda, M.** (2010). Subtilase cytotoxin induces apoptosis in HeLa cells by mitochondrial permeabilization via activation of Bax/Bak, independent of C/EBF-homologue protein (CHOP), Ire1 alpha or JNK signaling. *Microb. Pathog.* *49*, 153-163.
- Yi, L., **Rosales, T.**, Rose, J. J., Chaudhury, B., Knutson, J. R., & Venkatesan, S. (2010). HIV-1 Nef Binds a Subpopulation of MHC-I throughout Its Trafficking Itinerary and Down-regulates MHC-I by Perturbing Both Anterograde and Retrograde Trafficking. *J. Bio. Chem.* *285*, 30884-30905.

THE SCIENCE BEAT

By Daniel Kraushaar, Ph.D.

Ma, M. C., Ding, S. L., Lundqvist, A., San, H., Fang, F., Konoplyannikov, M., Berry, C., Beltran, L. E., Chen, G. B., Kovacic, J. C., & Boehm, M. (2010). Major Histocompatibility Complex-I Expression on Embryonic Stem Cell-Derived Vascular Progenitor Cells Is Critical for Syngeneic Transplant Survival. *Stem Cells* 28, 1465-1475.

Embryonic stem cells (ESCs) can differentiate into many cell types that can potentially be used for regenerative medicine including treatments for spinal cord injuries, diabetes and several neurodegenerative disorders. Only this year the first clinical trial of therapy with human ESC-derived neural progenitors has been initiated, and is primarily aimed at testing and evaluating the risks of cell transplantation. Despite great promise, ESC therapy comes with numerous

hurdles that have to be overcome and include the risk of spontaneous tumor formation and donor cell rejection. Immune-related destruction is one of the major causes for compromised survival of ESC-derived donor cells, in particular interactions between donor cells and recruited inflammatory cells are critical after transplantation. Major histocompatibility complex class I (MHC-I) molecules are involved in antigen presentation to cytotoxic T-cells and natural killer (NK) cells of the immune system. In some cases failure to express 'self' MHC-I molecules may result in NK cell attack of transplanted donor cells. Ma *et al.* investigated whether MHC-I expression in ESC-derived vascular progenitor cells plays any role in their susceptibility to NK-mediated transplant rejection.

To this end, the authors deployed a two-step differentiation protocol to differentiate ESCs into hemangioblast (early hematopoietic precursor)-like cells (Brachyury+Flk-1+; denoted as Bry+, Flk1+) and subsequently (cont'd on p. 6)

New NHLBI Fellows

Hiroko Endo, Ph.D., is a Visiting Fellow in the Translational Medicine Branch under Dr. Joel Moss. She received her Ph.D. in Animal Physiology from the Graduate School of Agricultural Science at Tohoku University, Japan. She was the recipient of the 2001 Burroughs Wellcome Fund Postdoctoral Travel award. Dr. Endo's current project is to investigate the function of Trim72 which is specifically expressed in ARH1 null mice.



Jinxí Li, Ph.D., is a Visiting Fellow in Laboratory of Kidney and Electrolyte Metabolism under Dr. Maurice Burg. She earned her Ph.D. in Analytical Chemistry from the University of Maryland, College Park. Dr. Li was previously an intern at the FDA

before coming to NIH. Her initial research project is undecided but will involve studies of relative quantitation of the proteins in the nuclear and cytoplasm of HEK293 cells and how the pattern changes when the cells are exposed to high salts.



Daniel Kraushaar, Ph.D., is a Visiting Fellow in the Laboratory of Molecular Immunology under Dr. Keji Zhao. He received his Ph.D. from the University of Georgia in Biochemistry and Molecular Biology. He was the recipient of the *Doctoral Travel*

Grant at the University of Georgia. Dr. Kraushaar initial research project includes the conversion of pluripotent embryonic stem cells and iPS cells into hematopoietic stem cells through induces expression of transcription and master regulators.



Dazhi Lai, Ph.D., is a Research Fellow in the Laboratory of Molecular Immunology under Dr. Warren Leonard. Dr. Lai earned his Ph.D. from the Academy of Military Medical Sciences in Beijing, China. He was involved in the development of numerous

patented drugs and vaccines such as those for SARS and HPV. Dr. Lai's current research is being done on the characterization of DUSP5/DUSP6 knockout mice in the immune system and miRNA regulated by IL-2.



Chien Nguyen, Ph.D., is a Visiting Fellow in the Laboratory of Cell Biology under Dr. Jian Liu. He earned his Ph.D. in Mechanical and Aerospace Engineering from Syracuse University, New York. Dr. Nguyen was the first place department winner at

the 2009 Nunan Research Day Poster Competition at Syracuse. His research project here at NIH deals with actin retrograde flow, focal adhesion dynamics.

attended many career symposia, I had always been attracted to the science policy arena but did not know exactly how to become involved. When the opportunity arose through the NHLBI Office of Education to participate in a rotation at the Federation of American Societies for Experimental Biology (FASEB) Office of Public Affairs as a Science Policy Fellow, I jumped at the opportunity.

I guess I should first explain what FASEB is and what we do. FASEB is an umbrella organization representing 23 different scientific societies – of which (like the American Physiological Society) some of you may be members – and functions in many different capacities. It publishes the *FASEB Journal*, provides management services to other societies, serves minority scientists through the Minority Access to Research Careers Program, sponsors scientific conferences, and advocates for the scientific community. You can find out more on the FASEB web site: www.FASEB.org

The Office of Public Affairs, from where our advocacy efforts originate, is where I spent my six-month rotation. In the Office of Public Affairs, we work with our 23 member societies to develop and promote policies to advance research and education in the biological and biomedical sciences through government liaising and community outreach. Some of the policy issues that we deal with include funding for scientific research, animals in research, peer review processes, stem cells, and training and career opportunities.

During my fellowship, I had the opportunity to work on a number of policy projects. One of my initial projects was assisting in the development of a symposium to encourage and facilitate the participation of basic scientists in translational research. In this capacity, I participated in developing

the agenda for the symposium, identifying potential symposium speakers, developing briefing books on translational research, and participating on multiple organizational conference calls. In doing so, I was able to partake in a number of meetings with NIH institute and center leadership and other interested parties.

I also became the point person on issues related to the humane care and use of animals in research and was appointed as the key staff liaison to FASEB's Animals in Research and Education committee, which is made up of scientists from all over the country. As the lead staff person for this committee, I drafted letters to Congressional members urging them to oppose the *Great Ape Protection Act*, which would prohibit any invasive research on great apes – including chimpanzees. On that same topic, I helped prepare the FASEB President for media interviews. Another major policy issue that I took the lead on was staying abreast of regulatory changes related to the use of animals in biomedical research, which provided me with the opportunity to attend policy meetings and participate in strategy discussions that shaped FASEB policy. Finally, I worked on a science education project that surveyed high school students, undergraduate students, and science educators about their experiences working in an NIH-funded lab for the summer. During this project I created survey methodology, developed a dissemination strategy and communicated with respondents. I will analyze these data and write up the report that will be a companion to a similar report that was released last year.

This fellowship afforded me other non-technical writing opportunities, as well. I was able to write stories for publication in our bi-weekly *Washington Update* newsletter, which is sent to subscribers who are interested in the

regulatory and legislative science policy issues, and write a column for *ASBMB Today* – a member society newsletter. The fellowship definitely kept me busy, but I learned so much about the science process of which I was not aware. It also provided me the opportunities to meet and network with people in the policy arena, added non-bench activities to my CV, provided me with career options that I would not have had otherwise, and ultimately prepared me to take on a full-time position as a science policy analyst.

If anyone has further questions about the NHLBI-FASEB Science Policy Fellowship program, please e-mail me at adeschamps@faseb.org. Additionally, if you are interested in becoming the next NHLBI-FASEB Science Policy Fellow, please contact Dr. Geller.

Additional information on the Fellows Rotation in Extramural Research (FRER) can be found at: <http://dir-intranet.nhlbi.nih.gov/oe/document.aspx?frer.htm>

The 9th Annual NHLBI DIR Scientific Retreat

**April 27-29, 2011
Cambridge, MD
Hyatt Regency**

Featured Speakers:
-Forest White, Ph.D.
*Associate Professor of Biological
Engineering, MIT*
-Donald Ingber, M.D., Ph.D.
*Professor of Bioengineering,
Harvard School of Engineering
and Applied Sciences*

starting with your own insights into causes and actions, talking to friends and family, escalating to conversations with the Office of Education, and, if severe enough, to seek counseling from a mental health professional.

Almost all of us have come to NIH from somewhere else, many from overseas. While some stress, such as deadlines for talks, data or manuscript submissions, are expected, when they are combined with other issues, such as money problems, illness or conflict in your family, or separation from your family and friends, they can seem insurmountable. Thus, while there is no one answer to all of these issues, the central features to many are communication and maintaining a balance of work and life. Communication also implies that you actively take steps to not feel 'isolated' either within your lab or outside the lab.

Within the lab, try to maintain active friendships with the other lab members; outside the lab, you need a circle of friends or family that can maintain the balance. If you are married with chil-

dren, this can both be a cause and a relief from stress, depending upon your circumstances, since you may be torn between research activities and home life. It would be important, for example, to let your family know that at critical times you need to spend extra time on research, while at others you will be able to be at home more. In addition, you need to establish a support system so that if you want to present your work at a meeting, or attend the NHLBI retreat, your family can maintain their activities without you. Otherwise, this can turn into a major source of stress that is not easily managed.

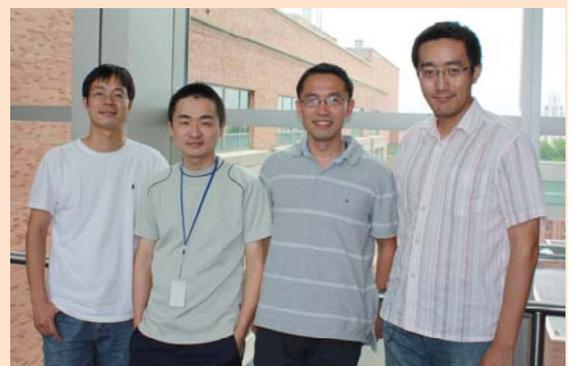
It is perhaps both easier and harder if you are unmarried and living alone – easier, because you control your own calendar and agenda, and harder, because there is no 'organic' friendship circle defined for you. There are many different clubs and activities at NIH, many sponsored by the the NIH Recreation & Welfare Association (<http://www.recgov.org/r&w/>). If you join, you can participate in physical fitness classes, trips and other activities.

If you are religious, there are opportunities to interact with people of your faith. In addition, being physically active and fit can serve as a stress reliever. Finally, though excess alcohol can impede your performance, you may want to take part in many of the 'Happy Hours' in Bethesda.

But sometimes all of these remedies are inadequate – you become overwhelmed and it is affecting your performance. Here is where each of us in the NIH community has a role. Your responsibility is to recognize this as an issue, and seek help. Your mentor's and lab mates responsibility is to help you seek the guidance and assistance you need. If neither works, the Office of Education is available to talk to you on a confidential basis, and will help you seek professional counseling if necessary. We should all keep in mind that needing support to deal with life is not a sign of weakness, just a signal that perhaps an outside voice can help you see the issues more clearly and adopt mechanisms to deal with the stress that is an inevitable part of life.

Introducing The NHLBI DIR DNA Sequencing Core (DSC) Facility

Having recently opened in October 2010, the DNA Sequencing Core is based on the Illumina platform, the DSC offers a wide range of sequencing services for basic and translational research, including but not limited to whole-genome sequencing, targeted sequencing, ChIP-Seq, RNA-Seq, and microRNA sequencing. The Core is operated on a cost-sharing basis, by which the investigator will cover half the sequencing reagent costs. In addition, the investigator is responsible for undertaking library construction in their own laboratory using standard protocols provided by the Core. All projects submitted to the Core require a project registration form for tracking and billing purposes. It is strongly recommend that the principal investigator meet with the Core staff before initiating a new project.



L to R: Ting Ni, Han Wu, Jun Zhu, Kang Tu

For detailed information, please contact Dr. Jun Zhu, Director of the DSC (Tel: 301-443-7927 or Email: jun.zhu@nih.gov) or visit the DSC web site (<http://dirweb.nhlbi.nih.gov/Cores/DNASC/Pages/Default.aspx>).

into endothelial progenitor cells (VE-Cadherin+; denoted as VE-CAD+). Both cell populations generally do not express MHC-I molecules; however as demonstrated in their study, Interferon γ (IFN γ) can induce expression of MHC-I in Bry+Flk1+ and VE-CAD+ cell populations without obvious interference with their differentiation potential. VE-CAD+MHC-I- and VE-CAD+MHC-I+ were evaluated for efficiency of transplantation in two syngeneic mouse models. Using matrigel plug assays, the authors show that significantly more vessel formation takes place in plugs containing VE-CAD+MHC-I+ cells than compared to matrigel plugs that were mixed with VE-CAD+MHC-I- cells. Immunostaining revealed CD31 and alpha-smooth muscle actin (α -SMA) positive cells in vessel structures indicating that VE-CAD+MHC-I+ cells integrate into vessels to form endothelial and smooth muscle cells during neovascularization.

In the other syngeneic model, Ma and co-workers injected VE-CAD+ cells derived from male ESCs into ischemic hind limb muscle of female mice and monitored initial inflammation and tissue degeneration that were typically observed after cell transplantation. A combination of histochemical methods, Y-chromosome FISH staining and FACS analysis revealed marked infiltration of macrophages and T-cells, increased tissue degeneration and compromised cell survival

as illustrated by abnormal FISH staining in the MHC-I- group. Further immunohistochemistry showed that substantially more NK cells infiltrated the tibialis muscle injected with VE-CAD+MHC-I- cells compared to VE-CAD+MHC-I+ cells, suggesting that increased attack by NK cells may be the underlying cause for tissue degeneration in the MHC-I- group.

To test this idea, *in vitro* chromium release assays showed that MHC-I expression directly protects VE-CAD+ cells from NK cell attack. Further support for this notion was provided by the observation that neutralization of NK attack by administration with an anti-NK cell antibody significantly enhanced survival of VE-CAD+MHC-I- cells. Importantly endothelial VE-CAD+/MHC-I+ continued to proliferate and differentiated into CD31 and α -SMA positive cells, suggesting successful engraftment of MHC-I+ cells. Together, Ma *et al's* study showed that IFN γ and associated MHC-I expression substantially enhanced graft survival of ESC- derived vascular progenitor cells by attenuation of NK cell attack.

The study highlights the importance of complex donor-recipient immune cell interactions, which, as this study shows can be manipulated by administration with exogenous factors prior to transplantation.

The NHLBI DIR Fellows Seminar Series presents:

“In the thick of it: MyBP-C in cardiac contraction”

Samantha Harris, Ph.D.

*Assistant Professor, Neurobiology, Physiology and Behavior
University of California, Davis*

Tuesday, November 23rd

11am-Noon

Building 50, Room 1328/1334

Please contact host, Attila Nagy (nagy@nhlbi.nih.gov),
to have lunch with the speaker.