



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

Although summer has not yet officially begun, we welcome 88 summer researchers to NHLBI this year. While the summer interns are officially working with the NHLBI PIs, we know that most, if not all, the direct supervisors are either Fellows or Staff Scientists. We encourage this arrangement, because it provides an opportunity for each NHLBI scientist to sharpen their skills as a mentor. In addition, it is often the fellows and staff scientists who are the closest to the bench, so they can transmit their technical knowledge more easily. So if this is your first time as a supervisor, please take adequate time to make sure that your summer researcher receives all the guidance that they need. And if you are an intern, you should expect appropriate guidance and attention from the fellows and staff scientists in your lab. Summer researchers are also reminded that NHLBI sponsors a series of pizza lunches every other week this summer, beginning on June 16th. See the complete schedule on Page 4.

Elsewhere in this issue, I also discuss how you can learn more about career opportunities and the possibilities for doing a rotation or a detail outside the intramural program. Fellows who have taken advantage of this are in many different careers. These are a great resource if you are entertaining thoughts about leaving the lab. We are happy to meet with you if you want further information.

Advice. What does it mean?

By Herbert M. Geller, Ph.D

It's graduation season, and commencement speakers are full of advice. What's the best piece of advice that you've ever received? Use sunscreen? Do not smoke tobacco? Avoid junk food? Each of these can increase your health, but they probably do not address the key issue that you are facing – what can I do to improve my chances of “success” in my career? If I were such a speaker, I would argue that it is essential to maintain an open mind, explore as many different opportunities

(cont'd on p.2)

The Fellows Seminar Series presents:

Characterization of an In Vivo Model of LEOPARD Syndrome: the Effects of an Shp2 Mutation on Cardiac Development and Disease

**Maria Kontaridis, Ph.D.
Harvard Medical School**

**Tuesday, June 15th, 2010
11:00am to 12:00pm
Building 50, room 1328/1334**

as you can, and realize that you are not likely to end up as you start off.

While many fellows at NHLBI go on to research careers, many others have come to the realization that lab work is not in their future – either as a principal investigator or in a laboratory at all. This is the time to heed the advice above about keeping an open mind. There are many different careers that use your scientific knowledge. While they are sometimes referred to as “alternate” careers, they are, in fact, becoming the majority career for Ph.D. graduates in the medical sciences. With that in mind, a major effort of the NHLBI Office of Education is to help you in with the second bit of advice, which is to explore opportunities. Our

web site has a page with a long list of potential careers and links to information about each one. In addition, NHLBI is prepared to support rotations or details to organizations, both government and private, that can provide valuable experience in learning what the career is all about. While we have already established several formal rotations for fellows (see box), we are prepared to assist any fellow or displaced Staff Scientist in obtaining an extended experience with a particular organization. Fellows who have done these rotations in the past have found them to be extremely valuable to help them guide their future.

The last part of the advice is that things don't often end up as they start

off. This is especially true of an academic research career, where, even if you stay in the lab, the questions that you address and the techniques that you use are constantly evolving. More often, there is a migration from the lab to other areas that build on your knowledge; this change can take place at any point, with the postdoc only being the most obvious. Many research scientists in industry move over to the development side or to the business side. Many faculty find rewards in academic administration. Each of these transitions builds on your present knowledge and skills. So don't be afraid of change – it's inevitable.

Science Rotations for NHLBI Fellows

Have you thought about leaving the bench? Are you interested in a career which takes advantage of your scientific and analytical skills? If so, you may be interested in participating in NHLBI DIR Rotations with any of the organizations listed below. Rotations typically last 3 – 6 months, most often full-time, and are scheduled at the end of your NHLBI fellowship. Rotations or details can also be arranged for displaced Staff Scientists. Contact the Office of Education if you are interested.

Fellows Rotation in Extramural Research –

<http://dir-intranet.nhlbi.nih.gov/oe/document.aspx?frer.htm>

- With the NHLBI Extramural Program to focus on Research Administration or Review

Battelle National Laboratories – <http://dir-intranet.nhlbi.nih.gov/oe/documents/battelle.htm>

- With any of several National Labs administered by Battelle

Technology Transfer Rotations — <http://www.nhlbi.nih.gov/resources/tt/index.htm>

- With the NHLBI Office of Technology Transfer

The FASEB Public Policy Research Fellows Program –www.faseb.org

- With the FASEB in Bethesda to focus on Science Policy

Center for Innovative Technology — www.cit.org

- To focus on Business Development With Virginia's Center for Innovative Technology in Herndon, Virginia

Adjuvant Global Partners – www.adjuvant.com

- To focus on Venture Capital and Business Development in their Bethesda, MD office.

Recent Publications by NHLBI Fellows

Bao, J. J., Lu, Z. P., Joseph, J. J., Carabenciov, D., Diamond, C. C., Pang, L. Y., Samsel, L., McCoy, J. P., Leclerc, J., Nguyen, P., Gius, D., & Sack, M. N. (2010). Characterization of the Murine SIRT3 Mitochondrial Localization Sequence and Comparison of Mitochondrial Enrichment and Deacetylase Activity of Long and Short SIRT3 Isoforms. *Journal of Cellular Biochemistry* 110, 238-247.

Barski, A., Chepelev, I., Liko, D., Cuddapah, S., Fleming, A. B., Birch, J., Cui, K. R., White, R. J., & Zhao, K. (2010). Pol II and its associated epigenetic marks are present at Pol III-transcribed noncoding RNA genes. *Nature Structural & Molecular Biology* 17, 629-632.

Johnson, A. D. (2010). An extended IUPAC nomenclature code for polymorphic nucleic acids. *Bioinformatics* 26, 1386-1389.

Winkler, T., Cantilena, A., Métais, J. Y., Xu, X. L., Nguyen, A. D., Borate, B., Antosiewicz-Bourget, J. E., Wolfsberg,

T. G., Thomson, J. A., & Dunbar, C. E. (2010). No Evidence for Clonal Selection Due to Lentiviral Integration Sites in Human Induced Pluripotent Stem Cells. *Stem Cells* 28, 687-694.

Ye, H., Jeong, S. Y., Ghosh, M. C., Kovtunovych, G., Silvestri, L., Ortillo, D., Uchida, N., Tisdale, J., Camaschella, C., & Rouault, T. A. (2010). Glutaredoxin 5 deficiency causes sideroblastic anemia by specifically impairing heme biosynthesis and depleting cytosolic iron in human erythroblasts. *Journal of Clinical Investigation* 120, 1749-1761.

Zhou, X. M., Gallazzini, M., Burg, M. B., & Ferraris, J. D. (2010). Contribution of SHP-1 protein tyrosine phosphatase to osmotic regulation of the transcription factor TonEBP/OREBP. *Proceedings of the National Academy of Sciences of the United States of America* 107, 7072-7077.

THE SCIENCE BEAT

By Nisha Narayan, Ph.D.

[*Winkler T, Cantilena A, Métais JY, Xu X, Nguyen AD, Borate B, Antosiewicz-Bourget JE, Wolfsberg TG, Thomson JA, Dunbar CE. No evidence for clonal selection due to lentiviral integration sites in human induced pluripotent stem cells. Stem Cells \(2010\) Apr;28\(4\):687-94*](#)

In 2006, Yamanaka and colleagues from Kyoto, Japan revolutionized the world of stem cell research by publishing their findings that normal murine fibroblasts can be reprogrammed into induced pluripotent (iPS) stem cells by the ectopic expression of certain defined transcription factors. A year later, Yu et al showed separately that selected factors could reprogram human somatic cells into iPS cells. Since then, similar techniques where the transgene was introduced into a variety of different target cell types using replication-deficient murine retroviruses or lentiviruses have been used widely and all though the reprogramming procedure itself is very vigorous, the overall success in obtaining fully functional iPS cells is very low. This alludes to the possibility that the integration of the viral vector into the genome might activate assisting endogenous proto-oncogenes and the turning on of certain loci in this manner might be necessary to achieve effective reprogramming. This matter of insertional activation contributing to iPS generation influences

the assessment of the tumorigenic capacity of clones derived from iPS clones and raises questions about the use of these vectors to create iPS cells for research purposes.

In this study by Winkler et al, they examine the distribution of integration sites (IS) in eight human iPS cell lines acquired by transduction using lentiviral vectors expressing the Oct4, Nanog, Sox2 and Lin28 transcription factors. Using a combination of different kinds of PCR techniques, Southern blotting and expression analyses, they address the question of whether these integration events disturbed the expression of the interrupted or nearby genes. An integration site analysis of four iPS clones each derived from the IMR90 fetal fibroblasts and foreskin fibroblasts, revealed no common target genes. Moreover, the clones were tested for their ES cell-like phenotype, including potential to differentiate into derivatives of all three primary germ layers, telomerase activity and cell surface markers. Using microarray data, they determined the impact of the lentiviral insertions on the differential expression of interrupted or nearby genes in each individual clone relative to either the profile of the remaining three clones from the same parental cells or all seven iPS clones combined, and found that out of 45 genes evaluated, only 3 had increased expression levels and only 2 genes expressed reduced levels. Next, they used bioinformatics tools from MetaCore and Ingenuity Pathway Analysis to investigate the effect of the lentiviral-tagged genes in functional pathways. They con-

cluded from the analysis that no functional pathways were preferentially targeted by the lentiviral integrations. Even though they did not detect any IS shared between autonomous iPS clones, six of the eight clones were found to have unusual "double" insertions, i.e. with two proviral insertions located in close proximity to each other on the same chromosomal allele. This is a very novel, previously unreported finding and the authors suggest that it is an epiphenomenon of the reprogramming procedure with no direct

functional link to neither the success rate of the reprogramming nor the attainment of pluripotency.

In conclusion, this study shows that reprogramming of human somatic cells most probably does not depend on the lentiviral integration-induced activation or deactivation of specific genes. The authors provide rather conclusive evidence and support for the sustained employment of the lentiviral vectors for the generation of iPS cells due to their higher efficiency, as opposed to most non-integrating vector or protein transfer approaches.

NHLBI Summer Students: Lunchtime Seminar Series

*Seminars held in Building 10, Room 7S235 from 11:30-1:30

6/16

Herbert M. Geller, Ph.D.

Office of Education and Developmental Neurobiology Section

"The Scientific Method and Success in Research"

6/30

Julie Dondaldson, Ph.D.

Laboratory of Cell Biology

"Adventures Traveling on New Endocytic Pathways"

7/14

Nico Tjandra, Ph.D.

Laboratory of Molecular Biophysics

"Structural Studies of Actin Cytoskeleton Regulation"

7/28

Michael Sack, M.D., Ph.D.

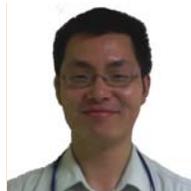
Translational Medicine Branch

"Diabetes, Mitochondria, and Insights Gained from 'Anti-Aging' Research"

New NHLBI Fellows



QiuSo Gun Hong, Ph.D., is a Visiting Fellow in the Hematology Branch under Dr. Cynthia Dunbar. Dr. Hong earned her Ph.D. in Theriogenology and Biotechnology from Seoul National University's Veterinary Graduate School. In 2009 she won the Larry Ewing Memorial Trainee Travel Fund Award from the Society for the Study of Reproduction. Dr. Hong is currently working on the establishment of rhesus induced pluripotent stem cells.



Yun Qi, Ph.D., is a Visiting Fellow in the Genetics and Development Biology Center under Dr. Hong Xu. He earned his Ph.D. in Biology at Tsinghua University in Beijing, China. Dr. Qi interned at a Ph.D. candidate at New Summit Biopharma in Shanghai, China. Dr. Qi is currently working on two projects. The first project is identifying the mitochondrial histone 3, the other is about mitochondrial turn over.