

Office of Education
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Fellows Newsletter

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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

We are now in the middle of fall, and I hope that you took some time to enjoy the fall scenery. Our fall event, the NHLBI Halloween Bake Off was a major success. A big thank you to all the bakers who contributed to the success of the! Well over 80 people attended and enjoyed a wide variety of baked goods. Based on this, the Fellows Advisory Committee is planning several events for the NHLBI DIR to enjoy each other's culinary talents.

My column this month highlights the iBiology web (www.ibiology.org) site, started by Dr. Ron Vale of the University of California San Francisco, but now supported by the NSF, NIGMS, and HHMI. As I note below, the web site has material of interest to any one in DIR from beginning postbac to Senior Investigator. Check it out!

FEATURED ARTICLE

iBiology and you

By: Dr. Herbert Geller

Dr. Ron Vale gave an outstanding talk on The Mechanisms of Cytoskeletal Motor Proteins in his October 29th WALS lecture. While Dr. Vale's major scientific interest is motors, he and other colleagues have taken an interest in "open source" science – scientific tools that are freely accessible and useful. He introduced us to two of them at the

beginning of his talk - μ Manager, a program for the acquisition and control of microscopes, and iBiology, a web site that contains a collection of interesting scientific videos. While I will leave a review of μ Manager for a future issue, I will focus this column on iBiology.

iBiology has several different sections. The largest section is iBioSeminars, a collection of talks that span the entire field of biology. While some of these are likely to be useful, most were recorded in 2006-

Meet the New Fellows



Dr. Crystal Fagan is a new IRTA Fellow in the Biochemistry and Biophysics

Center under Dr. Adrian Ferre-D'Amare. Dr. Fagan earned her Ph.D. at Emory University. Her initial project at NIH is studying the ASH1 mRNA transport machinery.



Dr. Luigi Alvarado is a new Visiting Fellow in the Hematology Branch under

Dr. Andre LaRoche. Dr. Alvarado earned his Ph.D. at The University of Maryland, College Park. His initial project at NIH is Genetic correction of diseased induced pluripotent-derived hematopoietic stem cells for subsequent autologous bone marrow transplantation.



Dr. Ye Yan is a new Research Fellow in the Center for Molecular Medicine under Dr.

Toren Finkel. Dr. Yan earned her Ph.D. at the Shanghai Institute of Biochemistry and Cell Biology. Her initial project at NIH is studying the role of vascular autophagic flux on neurodegenerative disease.

THE SCIENCE BEAT by Nazmul Haque, Ph.D.

Gabl, R. F., He, Y., Yu, S., & Tjandra, N. (2014). Conformational Rearrangements in the Pro-Apoptotic Protein, Bax, as it inserts into mitochondria: A Cellular Death Switch. J. Biol. Chem. jbc

Mammalian cells encompass a highly conserved mechanism to terminate its life, termed programmed cell death or apoptosis. Apoptosis is considered to be a major component of various cellular and physiological processes, including normal cell turnover, proper development and function of immune system, embryonic development, chemical-induced cell death and so on. Consistent with its importance, aberration in apoptosis pathway causes severe physiological consequences, such as neurodegenerative diseases, autoimmune diseases, numerous types of cancers etc. Considering that components of apoptosis pathway is considerably well-studied biochemically, very little is known in structural point of view. In this article authors studied the conformation of pro-apoptotic protein Bax in live cells during apoptosis activation, and identified the conformational changes that dictates commitment of activation.

Apoptotic stimulation occurs through distinct signaling cascades. The intrinsic or mitochondrial pathway is activated by DNA damage, UV, activation of tumor suppressor (p53 or c-Myc), cytoskeletal damage, or endoplasmic reticulum stress. The activation of mitochondrial pathway requires permeabilization of mitochondrial outer membrane (MOM), which releases a number of pro-apoptotic soluble proteins from inter-membrane space of the mitochondria, an event considered to be “commitment to cell death” or “point of no return”.

Center to the mitochondrial pathway is the Bcl-2 family of proteins. Each members can be classified as either pro- or anti- apoptotic, based on their role in permeabilization of outer mitochondrial membrane (OMM). While opposing in functions, they are structurally similar; they have four conserved Bcl-2 homology (BH) domains. In addition, there is a subclass of protein with only one BH domain, thought to modulate interaction between pro- and anti-apoptotic proteins. Here, the authors monitored the conformational changes of Bax associated with its translocation from cytosol to mitochondria during Staurosporine induced apoptosis. Utilizing Forster Resonance Energy Transfer (FRET) in Bax domains relative to BH3 in live mouse embryonic fibroblasts, they identified intermolecular conformational changes and intra-molecular contacts in Bax during translocation. They used a novel correction method for FRAT analysis in living cells that allowed identifying conformational changes of BH3 domain. In addition, fluorescence correlation microscopy (FCM) showed that cytosolic Bax diffuse at much slower rate during apoptosis activation, suggesting possible complex formation or transient interaction with membrane. Furthermore, FRET measurement showed that Bax molecules formed oligomers in mitochondria through two distinct interfaces involving the BH3 domain and the C-terminal domain.

FEATURED ARTICLE CONT.

2009, which suggests that they may be a bit outdated for those interested in recent progress in the field. On the other hand, the more recent talks, such as the one on Ion Channel Signaling by William Catterall, Circadian Biology by Joseph Takahashi or microRNAs by David Bartel are outstanding.

The next part is iBiomagazine, an irregularly-issued collection of talks in sections entitled “Discoveries”, “Science and Society”, “Careers”, “Education” and “Professional Development”. The Discoveries section. The most recent issue contains a talk by Joe Gall on In Situ Hybridization, and Gary Rivkun entitled The Small RNA Revolution: A Perfect Storm, both of which are highly informative. Talks from previous issues are archived by section, and you will likely find several of interest as you scroll through them. Thus, the “Careers” section will have talks on different careers – science writing, public service, science museum

curator, etc., by people who are actually engaged in those careers.

I actually found the “Professional Development” section to be the most interesting, with talks that ranged from the practical – such as how to give a scientific talk and the best use of Powerpoint by Sue McConnell of Stanford University – to the inspirational – a talk by Nobel Laureate Avram Hershko reflecting on his life in science and some useful insights into scientific success and a talk by Jeremy Nathans on mechanisms to increase creativity. One that I recommend to all is a talk by Bruce Alberts on Learning from Failure (his personal history in this area is incredibly important to learn).

There are too many other talks for me to list them individually, but this web site offers something for each of us – undergraduate, postbac, postdoc, and investigator and it would be worth your spending some time there.

CRITICAL READING BLOG: OPEN INVITATION TO PARTICIPATE! BY: JULIANE CAVISTON

Have you ever wondered about the world of extramural NIH and how it all works to fund research at universities and institutes around the globe? I am guessing the answer is not so much, aside from your own grant proposal, perhaps.

Here in the intramural world of NHLBI we tend not to give the extramural side much thought (most of the offices are off campus, so it's not like a fellow could even accidentally stumble upon them. And don't act like you've never been lost on campus.) With this unfortunate divide in mind, some extramural scientist administrators would like to foster more unity between the two “sides” of NHLBI. To this end, they created the Critical Reading Blog.

On the NHLBI Intranet home page, if you page all the way down, you will find the Blog section. Started by Keith Mintzer, a Scientific Review Officer and Pablo Gersten, Lead Program Specialist, the Critical Reading Blog is a multipurpose platform that is updated frequently. It is useful as an information source on NIH funded studies that are making headlines and it can also serve as a quick summary of what is currently hot in heart, lung and blood research. Importantly, it is also interactive. You need to sign on to the intranet using your NIH username and password (I know, I didn't even notice there was an option to sign in either), and then you can leave comments on the blog posts.

The creators of the blog are interested in content contributions from intramural scientists, particularly fellows. The blog could be a way to popularize your colleague's most recent publications (we can all use a little promotion sometimes!) Additionally, it is a great opportunity for fellows who are interested in flexing their writing muscles to get some experience blogging about science, careers in science, or experiences at the NIH. For more information on contributing, please contact Keith Mintzer, mintzerk@nhlbi.nih.gov

Meet the New Fellows



Dr. Chingiz Underbayev is a new Visiting Fellow in the Hematology Branch under

Dr. Adrian Wiestner. Chingiz earned his Ph.D. at Rutgers University, Department of Pathology and Laboratory Medicine. His initial project at NIH is a study of human CLL using xenograft mouse model.



Dr. Heather Huntsman is a new IRTA Fellow in the Hematology Branch under Dr. Andre LaRoche.

Dr. Huntsman earned her Ph.D. at the University of Illinois Urbana-Champaign. Her initial project at NIH is determining the hematopoietic stem cell (HSC) purity, and transfection and engraftment potential of the CD34+CD38-CD90+CD45RA-CD49f+Rhoglo subpopulation in human mobilized peripheral blood.



Dr. Haihui Pan is a new Visiting Fellow in the Center for Molecular Medicine under Dr. Toren

Finkel. Dr. Pan earned his Ph.D. at the University of Texas at San Antonio. His initial project at NIH is Bmi-1's role in cardiac regeneration.

QUESTION & ANSWER WITH AN INVESTIGATOR

Postdoc Nuo Sun interviews Dr. Manfred Boehm, Senior Investigator, Laboratory of Cardiovascular Regenerative Medicine, Center for Molecular Medicine.



Manfred Boehm, M.D., is a renowned scientist and senior investigator in the Center for Molecular Medicine. Dr. Boehm's primary research interests are in

vascular biology and the genetics of vascular remodeling in human diseases. Dr. Boehm received his Doctor of Medicine in 1993 from the University of Heidelberg, Germany and did a residency in internal medicine at the Franz-Volhard-Clinic in Berlin. Then he became a research fellow at the Max Delbrück Center for Molecular Medicine, Berlin (1996-1997) and the University of Michigan, Ann Arbor (1997-1999). He joined the NHLBI as a research fellow in 1999 and has been an Investigator since 2003.

Dr. Boehm has authored numerous original scientific articles, reviews and book chapters, and has received many honors, including an NHLBI Star Award for Excellence in Laboratory Basic and Clinical Research, and a Foundation for Advanced Education in the Sciences Award for Re-

search Excellence from the NIH. He serves on the editorial boards of Trends in Cardiovascular Medicine, ISRN Stem Cells, Atherosclerosis, and Journal of Molecular Medicine. Dr. Boehm holds two patents, has participated in cooperative research and development agreements with biotechnology companies and has several active clinical protocols.

Dr. Boehm investigates vascular injury and remodeling in order to understand the underlying molecular mechanisms and to develop new treatment methods. Recently, Dr. Boehm and his colleagues identified a novel disease, Arterial Calcification due to a Deficiency in CD73 (ACDC) in patients seen at the NIH Clinical Center. A clinical study has been initiated for treatment of these patients with an oral bisphosphonate based on their work characterizing the ACDC disease mechanism. In 2014, Dr. Boehm identified a biological pathway that contributes to the high rate of vein graft failure following bypass surgery.

When did you decide to pursue a career in science?

It was in the medical school of the University of Heidelberg, since my initial plan was to be a doctor to treat patients with heart diseases. I was involved in a general pharmacology class with a really characteristic instructor. I was fascinated as he en-

couraged us to develop our own program to solve some medical problems. We need to run it logically and scientifically. He became my mentor for the doctor thesis and also encouraged me to be a scientist in the NIH.

How do you like NIH to start your own lab?

I really like NIH and appreciate NIH for providing so many resources so that I can focus on research and related clinical work. I started my research by doing animal models of cardiovascular diseases and vascular injury. We have demonstrated that the cyclin-dependent kinase inhibitors, including p27Kip1 and p21Cip1, mediate the complex interactions between local vascular and circulating immune cells during vascular wound repair. Then the question would be how to study the disease mechanism in human. When I wanted to translate my study to human diseases, I can find many collaborators and patient samples within the NIH. For example, we developed patient-specific induced pluripotent stem (iPS) cells to establish cellular models to study vascular disease mechanisms. These cells can be used to test drugs or small molecules to interfere with the disease process. I was also involved in the NIH Undiagnosed Diseases Program (UDP), which recruits and selects patients who suffer from dis-

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QUESTION & ANSWER WITH A POST-DOC

Postdoc Nuo Sun interviews Dr. Zhiyun Ge, Laboratory of Ribonucleoprotein Biochemistry, Biochemistry and Biophysics Center.



What factors influenced your decision to come to the NIH?

Right before I was getting ready to defend my Ph.D. dissertation, I came to the NIH to attend the "National Graduate Students Research Conference". At

the conference, I was introduced to the exciting, cutting edge research being conducted here. I also came to learn about the resources available to help scientists identify and prepare for a career after their postdoc, including academic and non-academic career paths. So I decided the NIH would be a great place to obtain further training after Ph.D. for a future career.

What do you enjoy most about the research environment at NIH?

I enjoy most the open, sharing, and collaborative atmosphere. If you need anything

(reagent, protocol, equipment, constructive criticism of your research, etc), there are people who are more than happy to and have the ability to help you.

In addition to research, what activities have you taken part in during your time as an NHLBI postdoc?

In terms of other activities, I have been writing the "Science Beat" for the NHLBI newsletter and I'm on the NHLBI fellow advisory committee. For career building, I have attended several NIH-wide career symposiums as well as

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Q&A WITH AN INVESTIGATOR

eases of unknown etiology, and studies their causes at the clinical, genetic and cellular levels. With my collaborators from the NIH clinical center, we have identified a novel disease, Arterial Calcification due to a Deficiency in CD73 (ACDC). By characterizing the ACDC disease mechanism, we found treatment with bisphosphonates could be a potential therapy; therefore, we have initiated a clinical protocol to test this.

What advice would you give to fellows with aspirations of running their own lab to help them launch their independent careers?

First of all, you need to be passionate about what you are doing. When you struggle, you need to love your research. There is not a single day that I am not passionate about my job and I work hard to achieve my goals. I love to do experiments and currently, I am testing some patient samples.

But definitely, only passion is not enough. You also need proper environments as a driver. You need nice colleagues and good connections to them to know how the field is going. I also suggest the new PIs to apply for as many grants as you can. Then you will think in a proper way about what you are doing and develop some critical ideas about why you are do-

ing this. Writing is very important for a scientist and I believe the skill is learnable and need to be trained.

Besides, young PIs should have reasonable research directions. It's kind of balance between freedom to do science and restrictions of research areas. If there are too many directions to go at the beginning, it could be too broad to get into deep studies. And it's hard to form a solid foundation for the research.

Have you ever thought of taking another career route?

Not really. I love my research and my job. I like the NIH very much. I am passionate to study diseases and use my skills to treat patients, which drives me almost everyday to work hard.

What do you enjoy most other than doing science?

I have two kids and I really enjoy being with my family. I spent as much time as I can in my spare time. We like ski, volleyball and tennis. Sometimes I take my kids to the swimming pool. We also spend some time in Germany for a vacation.

Meet the New Fellows



Scott Stegemann is a new Post-Baccalaureate Fellow in the Hematology Branch under Dr. John

Barrett. Scott earned his BS in Biology at Syracuse University. His initial project at NIH is studying CD4 T cell polarization and Th17 cells.



Andrea Dickey is a new Post-Baccalaureate Fellow in the Biochemistry and Biophysics Center

under Dr. Justin Taraska. Andrea earned her BS in Bioengineering at the University of California, Berkeley. Her initial project at NIH is focusing on complex analysis of three-dimensional microscopy data to better understand how vesicles within cells move.



J.T. Ahearn is a new Post-Baccalaureate Fellow in the Cell Biology and Physiology Center under

Dr. Lois Greene. J.T. earned his BA in Molecular Biology at Colgate University. His initial project at NIH is researching the mechanism by which yeast heat shock protein Hsp104 cures psi yeast prions.

Q&A WITH A POST-DOC

the career development seminars at the NHLBI. I am also taking FAES classes to learn more about other career paths.

What advice would you give to a first year fellow entering the NHLBI?

Think about your goals in life, short-term or long-term goals and orient your work/daily life towards them. As a post-doc, your most important task at hand is no doubt your research project. But you must identify as early as possible what you want your career to be like after the postdoc and prepare yourself for it. If

you have a clear goal, plan your days/weeks/months ahead so that you are getting closer to your goal. If you don't know, start learning about your options and talking to people with different experiences.

What hobbies or activities do you enjoy away from the lab?

Having a very young child, my life outside the lab largely revolves around her.

RECENT PUBLICATIONS BY NHLBI FELLOWS

Barese, C. N., Felizardo, T. C., Sellers, S. E., Keyvanfar, K., Di, S. A., Metzger, M. E., Krouse, A. E., Donahue, R. E., Spencer, D. M., & Dunbar, C. E. (2014). Regulated Apoptosis of Genetically-Modified Hematopoietic Stem and Progenitor Cells via an Inducible Caspase-9 Suicide Gene in Rhesus Macaques. *Stem Cells*. 10.

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Tao, P., Sodt, A. J., Shao, Y., Konig, G., & Brooks, B. R. (2014). Computing the Free Energy along a Reaction Coordinate Using Rigid Body Dynamics. *J. Chem. Theory. Comput.* 10, 4198-4207.

Meet the New Fellows



Oimin Ng is a new Post-Baccalaureate Fellow in the Cardiovascular-Pulmonary Branch under

Dr. Nehal Mehta. Oimin earned his BS in Chemical and Biomolecular Engineering at Johns Hopkins University. His initial project at NIH is developmental cardiology.



Lisa Eshun-Wilson is a new Post-Baccalaureate Fellow in the Cell Biology and Physiology Center under Dr. Julie Donaldson.

Lisa earned her BA in Biological Chemistry at Grinnell College. Her initial project at NIH is performing an RNAi screen with an siRNA library of ~100 human de-ubiquitinating proteases (DUBs) to identify mediators of clathrin-independent endocytosis (CIE) cargo sorting in HeLa cells.



Katherine Delaney is a new Post-Baccalaureate Fellow in the Center for Molecular Medicine

under Dr. Hong Xu. Katherine earned her BS in Biochemistry at William Smith College. Her initial project at NIH is looking at different genes that are involved with mitochondrial replication.

The NHLBI Halloween Bake-Off was a HUGE success! Thank you for all that attended and participated!

Congrats to the winners: Javier Traba & Elizabeth Mushaben (CPB)

