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Office of Education, Division of Intramural Research
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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

Writing an submitting a manuscript is one of the most important skills in science. We want to make sure that all NHLBI fellows gain this experience. While this takes the cooperation of both the fellow and the mentor, fellows have the primary responsibility to make this happen by taking charge of the process. In my article below, I present certain tips on how planning your experiments can lead to a smoother process for getting your publication out.

The NHLBI DIR congratulates our Lenfant Fellowship winners. These are the last Lenfant fellowships given out under the old rules. We will soon announce the new Lenfant Fellowship competition, which is open to all NHLBI fellows with less than two years of postdoctoral experience. The new Lenfant fellowships will be awarded based on an application very similar to the NIH Individual NRSA format. They will be judged by an extramural review committee, and anonymous feedback will be provided to the applicants. Winners will receive an increase in their stipend. Writing the Lenfant application gives you a head start on writing one of the Career Transition Grants, K22 or K99.

The Office of Education wishes you all the best for the coming year.

My Grant Writing Experience

By Jule Wu, Ph.D.

Are you thinking about an academic career? If your answer is yes, you should consider applying for either one of the transition grants, K99 or NHLBI K22. Both of these grants include a mentored phase where you will continue to work in your current postdoctoral lab and a three year supported independent phase at any academic institution. Having just submitted my application, I can say that applying for either one of these grants is a challenge and will mean sacrificing around two months of bench work and submerging yourself in stressful (cont'd on p.4)

Writing your first Manuscript

By Herbert M. Geller, Ph.D.

Writing and submitting high-quality publications is an essential part of research training in DIR. While most publications are joint efforts of many people in the lab, one is traditionally designated as "first author" which gives them the major responsibility for organizing the data, writing the first draft, and coordinating the editing and submission process to the journal. This can be either an exhilarating or debilitating experience. Of course, once the paper gets accepted, you begin to forget the pain and effort that went into its production, and focus (cont'd on p.2)

on the next one. But there are certain rules and procedures that you can follow to ensure that the process flows smoothly.

The first rule is to plan your manuscript as early as possible. Here, as in your career choices, the earlier you define the goals of your research, the easier it will be to evaluate whether you have achieved them or need to do more experiments. A manuscript should tell a story. Many research papers begin as a series of probe experiments, either hypothesis based, to evaluate whether a narrow hypotheses has some validity and whether data can be collected in a reasonable amount of time to evaluate it, or exploratory, to collect data, such as array data, which may provide clues for future investigations. In either case, once the data from these probe experiments is analyzed, it's important to sit down with your mentor and make some firm plans about the direction of the research. This should include an outline of the story, including sketches of the kinds of figures will be necessary to tell the story. This is similar to a Hollywood script. Having this information, you can then plan and execute the experiments that will complete the story.

As you do the specific experiments, you should think about how the data will look in a finished product. For example, the order of lanes in a gel should be chosen to best illustrate the findings. If you are doing a dose-response curve, choose enough of a range and enough points to make sure that your data falls in the middle. Finally, always include enough replicates to ensure that you have adequate statistics, even if one or two of your samples accidently get washed away. It's always easier to include an extra sample at the beginning as compared to finding out that you didn't have enough at the end and need to repeat. Finally, put your data in a secure place and label it carefully and keep accurate notebooks so that, in a year's time, you can go back and understand what you did. Once you have done the experiments, make your final figure as early as possible. Show the figures at meetings and seek feedback from your lab group to make sure that they understand the figures and they fits in with your story.

Even before the final figures are complete, it's time to begin to write. Writing the first draft is often the hardest part of the process, and while your mentor may be more experienced, the only way a fellow can acquire the necessary skill is if they do it themselves. We'll continue next month with some tips on the writing process.

THE SCIENCE BEAT

By Nisha Narayan, Ph.D.

***Kang YS**, Zhao X, Lovaas J, Eisenberg E, Greene LE. Clathrin-independent internalization of normal cellular prion protein in neuroblastoma cells is associated with the Arf6 pathway. Journal of Cell Science (2009) Nov 15;122(Pt 22):4062-9.*

Prions are infectious agents consisting mainly of proteins that cause spongiform encephalopathies in sheep, goats, cows and humans. The specific protein that the Prion is made of is called the Prion protein or PrP, and it can be found in both the non-infectious (PrP^{c} or cellular Prion protein) and the infectious isoforms (PrP^{Sc}, named for the Prion disease in Sheep, Scrapie). The infectious isoform converts a normal PrP^{c} protein into PrP^{Sc} by changing its conformation altering the way in which these proteins interact. Accumulation of the abnormal isoforms form highly ordered amyloid plaques that aggregate in cells leading to the pathogenesis of the disease.

To understand the development of the disease, it is essential to know how the cell internalizes the PrP^{c} protein and it has been widely accepted that it is ingested in Clathrin-coated pits at least in neuronal cells. The authors of this study have established that PrP^{c} can be internalized independently of Clathrin in N2a cells - a common cellular model used to study scrapie propagation and the movement of PrP^{c}. They use RNA interference to knock down Clathrin and show through fluorescence microscopy that PrP^{c} can still be internalized through lipid rafts. Using inhibitors to lipid rafts such as Nystatin and Filipin, and inhibitors such as dynasore, to the molecular transport motor dynamin, the authors show that the endocytosis of PrP^{c} is lipid raft and dynamin-dependent but Clathrin independent. They further go on to show that these rafts are regulated by Arf6 – a small GTP-biding protein that regulates vesicular trafficking in cells - by transfecting cells with the Arf6 dominant-positive mutant Arf6Q67L and finding that PrP^{c} localizes to the large Arf6Q67L-expressing vacuoles formed in the cell.

This study therefore confirms the possibility that the PrP^{c} protein can be internalized through cellular pathways other than the one dependent on Clathrin. However, it does not explain whether these pathways come into play as a compensation for the missing clathrin or whether these can operate independent of its presence. The authors acknowledge that finding the carrier protein for the PrP^{c} protein might be key to understanding this phenomenon.

New NHLBI Fellows

Gang-Qing Hu, Ph.D., is a Visiting Fellow in the Laboratory of Molecular Immunology under Dr. Keji Zhao. Dr. Gang- Qing earned his Ph.D. in Biochemical Engineering at Peking University in Beijing, China. He was given the Leo Koguan Scholarship: Innovation Award in Academic Reaseach. Dr. Gang- Qing currently working on the genome-wide profile histone variant H2A.Z and the chromatin remodeling factor Brg1 in mouse ES cells and neural cells, to study their function in neuron

Jennifer James, Ph.D., is a Post- Doc IRTA Fellow in the Laboratory of Developmental Biology under Dr. Yosuke Mukoyama. Dr. James earned her Ph.D. in Biology from the University of North Carolina, Chapel Hill, North Carolina. Dr. James is currently working on two projects the first focuses on mechanisms of nerve vessel alignment in the limb skin in mouse and the other focuses on the mechanisms of lymphatic vessel suppression in the spinal cord.

Izumi Onitsuka, Ph.D., is a Visiting Fellow in the Translational Medicine Branch under Dr. Yosuke Mukoyama. Dr. Onitsuka earned her Ph.D. in Biophysics from the University of Tokyo, Japan. Her initial research projects is investigating the interaction between vasculature and nerve system in mouse coronary development.

Gerrit Weber, M.D., is a Research Fellow in the Hematology Branch under Dr. John Barrett. Dr. Weber earned her M.D. in Hematology and Oncology from Goethe University Frankfurt, Germany. Dr. Weber's current research project is to analyze immune responses to WT1/tumor antigen peptides.

Recent Publications by NHLBI Fellows

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thought provoking paper research. Despite the sacrifice, you may even accelerate in your research. This is a unique opportunity to temporarily halt experimental research and reevaluate your work, and will allow you to see your research in a whole new light.

The K99 is open to every fellow who has five or less years of postdoctoral research experience, while the NHLBI K22 is similar to the K99, but it does not have the time limit and is restricted to NHLBI fellows who have green cards or are American citizens. Both of these transition grants have the same goals and formats. The first step is to download the application from the http://grants.gov web site. It is one of the most complex and intimidating websites you will ever visit. Accessing the correct application is not direct. On the grants.gov home page, you will see a link at the left called "Find Grant Opportunities". You click on this link, and then click the "Basic Search" Link, which then presents several search boxes. Entering either "K99" or "K22" then takes you to yet another web page which lists a whole bunch of grant types and their next closing date. You then would click on the appropriate grant name which then takes you yet another web page which provides specific information on that grant, including a link to "Application". To create more problems, clicking on the "Application" link requires that you have the right version of Acrobat reader to be able to download the grant instructions and forms. You can find out what version you have by starting Acrobat and then clicking on "Help" and then "About Adobe Acrobat". I had to have tech support come to my computer to update the Acrobat Reader to the required version. Once you finally find the instructions and the grant application, don't be scared or feel overwhelmed. The instructions are, surprisingly, very helpful and contain details that will walk you through the grant application line by line.

NHLBI is well equipped with the resources to help with the grant writing process. Take advantage of the grant writing workshop run by the NHLBI Office of Education. Participants of the workshop critique one another's work. Not only is it very helpful to read other fellows' work, it is just as nice to have others to comment on your ideas and share in your misery. Also, try to get a copy of a funded K grant. This will allow you to see what a funded K grant looks like. However, don't be offended if your request is denied; grants often ideas that are still works in progress.

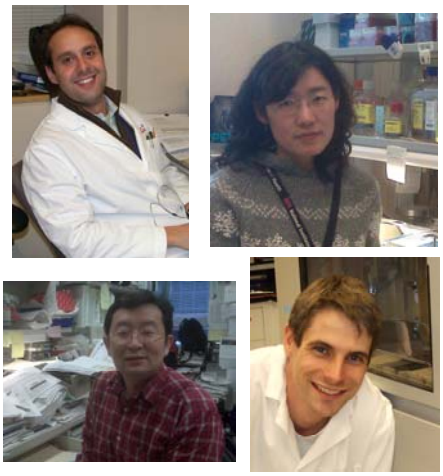
Writing the research sections of the grant is only part of the whole grant process. The K grants require letters of support from references, your mentor and the NHLBI DIR. You must consider who to ask for references – the best are people with international reputations who know you well. Letters of support are required from collaborators. Using your list of collaborators as references is not advised.

Since the entire grant application is electronic, you cannot wait until the last minute to begin the grant registration process. First, you must be registered with eRA commons (http://era.nih.gov/) and it is recommended you do this at least 2-4 weeks before your grant deadline. This requires you to contact someone from the Intramural Administrative Management office to establish an eRA comments account for you. The eRA commons login name is needed for the reference letter forms that are to be sent to your referees. Since you are with NHLBI, you will not need to register with Grants.gov.

Although you upload your grant when you complete the forms, when you are ready to submit, someone from the Intramural Administrative Management Office will use the NHLBI Grants.gov account to officially submit

your grant. Don't procrastinate and wait until the due date to fill out the grant form since this task can take many hours in itself. Important considerations include that all your attachments are in the PDF format and to put your eRA commons name in the "Credential, e.g., agency login" field under the "RESEARCH & RELATED Senior/Key Person Profile" section. Also, try not to wait until the last moment to hit the submit button on your grant application. If there are errors on your grant, it may not be submitted. Give yourself plenty of time to work through unforeseen issues. Call the grants help desk if you encounter a problem you cannot figure out. These people are extremely nice and well equipped to deal with frazzled investigators and will calmly guide you through whatever issues you may have. I would never have gotten my grant compiled and submitted without their support. Once you have successfully submitted your grant, don't celebrate yet. If there are errors with your grant application, you will receive an email from Grants.gov or eRA commons with any potential errors found on your grant. Some are serious and can affect the submission of your grant, such as attachments not being in the correct format. Some are minor and may not need to be fixed. One error warning that other fellows and I received is that our grants may exceed the page limit. The grant website still sent out this warning despite the fact that when all the sections of my grant were compiled together, it was within the page limit. You will have 48 hours from the time of the grant submission to fix any potential issues. Whenever you need to resubmit, you will need the Intramural Administrative Management Office to submit your grant. By this point, I had the number of my contact person from the Intramural Administrative Management Office on speed dial. I was very grateful to her for bearing with me through this hectic submission process.

The whole grant process is very complex and confusing, but there are many experienced and helpful people to help guide us through. During these months of intense reading and writing, you may ask yourself why you are subjecting yourself to this taxing and challenging process or if all your efforts are even worth it. Let me tell you, it is completely worth all the stress, anxiety, and sleepless nights. It will allow you to evaluate your current research in a completely new light and learn invaluable grant writing skills. It will allow you to see if an academic career, which generally involves grant writing, is right for you. Regardless if you will receive the grant or not, this grant process is worth enduring.



Clockwise (from top): In Hye Lee, Andrew Johnson, Zhibin Wang, Rodrigo Calado

Lenfant Fellowship Winners

Congratulations to Drs. Roberto Calado, In Hye Lee, Andrew Johnson, and Zhibin Wang, who are the most recent recipients of the NHLBI Lenfant Fellowship. This award, named in honor of the former Director of the NHLBI, was given n recognition of their research achievements early in their career.

In 2010, DIR implements a new process for selection of Lenfant Fellows. NHLBI Fellows with less than two years of experience are eligible to apply. The application will consist of a standard postdoctoral NRSA fellowship application, with some modifications. Applications will be judged by an NHLBI Extramural committee. More details will be presented in the January newsletter.

NHLBI Fellows Holiday Party
December 17th
1-2pm
10/9s235b
Come join us for light refreshments!
Sponsored by the Fellows Advisory Committee and OE