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From the Director of the Office of Education

As you can see in the box below, this year we will have a new format for bringing together the DIR: Research Day, taking place in Natcher on June 9th. The Natcher location will make it easy for all DIR researchers to attend and participate, especially our PIs. The deadline for submitting your abstract is May 16th. Board positions this year are being assigned in order of submission, so that the sooner you get your abstract in, the better your location will be! I expect to see all NHLBI Fellows and Staff Scientists at your posters!

My extended commentary this month highlights the value of the Progress Report in enhancing communication between you and your mentor. We have established this as a requirement for renewal because it makes sure that all of us – Fellow, Mentor, and the Office of Education are all on the same page about your career goals and how we can help you get there. So the more honest the report the better we can serve you.

NHLBI DIR Research Day 2014
June 9th
Natcher Conference Center and Auditorium

*Abstracts due May 19th*
Meet the New Fellows

Dr. Marcus Corat is a new Research Fellow in the Hematology Branch under Dr. Cynthia Dunbar. Dr. Corat earned his Ph.D. at the State University of Campinas. His initial project at NIH is to work with genetic barcoding track clonal contribution for hematopoiesis in Rhesus and to work with CRISP/CAS9 technology to produce genome modification to generate a Paroxysmal nocturnal hemoglobinuria model in Rhesus.

Dr. Agila Somasundaram is a new Visiting Fellow in the Biochemistry and Biophysics Center under Dr. Justin Taraska. Dr. Somasundaram earned her Ph.D. at Northwestern University. Her initial project at NIH is investigating membrane processes including endocytosis and exocytosis, specifically to gain insight into membrane protein behavior at high spatial and temporal resolutions using advanced microscopy techniques.

THE SCIENCE BEAT by Nazmul Haque, Ph.D.


The low-density lipoprotein (LDL) receptor plays a central role in lipid metabolism by picking up the circulating cholesterol-rich LDLs from the bloodstream by endocytosis. There are seven members of LDL receptor family; one of them is the very low-density lipoprotein receptor (VLDLR). Similar to LDL receptors, VLDLR has an important role in cholesterol uptake, and metabolism of apoprotein-E-containing triacylglycerol-rich lipoproteins. Unlike LDLR, VLDLR is almost ubiquitously expressed throughout the body. However, VLDLR is particularly highly expressed in tissues with high content of its primary ligand, triglycerides, that include heart, skeletal muscle, lung and brain. According to its broad body distribution, VLDLR is reported to be involved in various other functions; for example, the VLDLR is found to play a very important role in the development of the mouse central nervous system. Consistent with this, mutation of the VLDLR gene is found to be associated with severe developmental disorders in the CNS in both mouse and humans.

The house dust mite (HDM) is a major source of indoor allergens, and highly associated with the development and pathogenesis of asthma. HDM can evoke a direct non-allergic inflammatory response in mice. Interestingly, a recent study showed that LDLR expressed in lung epithelial cells can negatively regulate HDM-induced airway hyperresponsiveness (AHR) and mucous cell metaplasia in murine asthma. As VLDLR is highly similar to LDLR both functionally and structurally, the authors hypothesized that VLDLR may also regulate the immune response in HDM-induced asthma. In this paper, the authors have tested the notion using homozygous knockout mice for VLDLR gene (VLDLR-/-), and later extended their observation in human samples.

The authors initially observed that nasal administration of HDM causes significant increase in leucocytes in the alveolar fluid of VLDLR-deficient mice compared to normal animals. Similar increases in IgE, an early indicator of inflammation, as well as a set of Th2 derived cytokines were observed. Lung histology of the HDM challenged animals also revealed increased lung inflammation compared to normal animals, suggesting an important role of VLDLR in regulation of lung inflammation induced by HDM.

To understand the mechanism how Th2-mediated inflammation was enhanced in VLDLR-deficient animals, the authors studied gene expression on a genome-wide scale in the lung samples. By looking at gene expression data, they found that CD209e had the highest level of expression in the mutant mice. Taking account of the previous observation that the human homolog of CD209 is primarily expressed in dendritic cells (DC), and that they observed increased levels of Th2 derived cytokines upon HDM challenge in VLDLR deficient mice, the authors hypothesized that VLDLR expressed in DCs may attenuate the Th2 response during HDM-induced inflammation. To test this theory, they studied the VLDLR expression in human dendritic cells, and found that VLDLR expression was highly increased in human monocyte-derived DCs by HDM stimulation. In addition, individuals hypersensitive to common allergens expressed VLDLR on the surface of peripheral CD11c+ DCs under basal conditions, suggesting that VLDLR expressed in DCs may negatively regulate HDM-induced inflammation in human. By in vivo transplantation and ex vivo culture method, the authors further assessed the direct role of VLDLR in HDM-induced inflammation. The CD11c+


Q&A with Investigator

Postdoc Kevin Ramkissoon interviews Dr. Adrian Ferré-D’Amaré, Senior Investigator, RNA Biophysics and Cellular Physiology

Dr. Adrian R. Ferré-D’Amaré earned a B.S. in chemistry from the Instituto Tecnológico y de Estudios Superiores de Monterrey in Mexico before completing his Ph.D. in molecular biophysics at the Rockefeller University. He was a Jane Coffin Childs postdoctoral fellow at Yale University from 1995 to 1999, and moved on to become a Member of the Fred Hutchinson Cancer Research Center and an Affiliate Professor of Biochemistry at the University of Washington, Seattle from 1999 to 2011. Within this period, he was also a Rita Allen Foundation Scholar (2001–2004), a Distinguished Young Scholar in Medical Research of the W.M. Keck Foundation (2003–2008), and served as an Investigator of the Howard Hughes Medical Institute (2008–2011). In 2004 Dr. Ferré-D’Amaré was awarded the Eli Lilly and Company Research Award from the American Society for Microbiology, the organization’s oldest and most prestigious prize. He joined the NHLBI in 2011 as a Senior Investigator and Chief of the Laboratory of RNA Biophysics and Cellular Physiology. Here he leads a group that, amongst other endeavors, develops and exploits fundamental biophysical approaches to understand the function of catalytic RNAs, and atomic-level interactions between RNA and proteins. Dr. Ferré-D’Amaré has authored or coauthored more than 80 papers and sits on the editorial board of the journal RNA. He additionally serves as an ad hoc reviewer of the NIH’s Biological Chemistry and Macromolecular Biophysics Study Section and the National Science Foundation’s Biophysics and Chemistry of Life Sciences Programs.

When did you decide that you wanted to pursue science as a career?

It was sometime around the age of 10. My initial interests were in marine biology and ecology, and by my 12th summer, I had found a mentor, and started helping with work in his marine biology lab on the island of Ishigaki, in southern Japan. I made my first presentation at an international meeting when I was sixteen. I started college with the intention of majoring in marine biology (my interest was coral reef ecology), but I gradually found the pace of field-based research, where it can take years to do a single experiment, too slow. Also, as I learned more physical chemistry and biochemistry, my interests became more molecular. After my sophomore year, I changed my major to Chemistry, and I have been studying biological molecules ever since.

You have trained and worked at a number of prestigious scientific institutions. What are the similarities and differences in the research environment amongst the places you’ve worked?

The research environment here at NIH is fantastic! What I like most is the engaging seminars we have in our cell biology and physiology center (CBPC), and the NIH wide seminars like the WALS. In CBPC, post-docs and grad students invite and host top scientists in cell biology for a Thursday seminar series. This gives us a great opportunity for networking and collaboration. I also like our Wednesday seminars a lot, where every CBPC researcher gets a chance to present their research and receives constructive comments and ideas from PIs and fellows. Last but not the least, there are several career development courses and workshops offered here at NIH that are truly helpful to young scientists.

How would you compare and contrast your research and training experiences here in the US and in India?

I did my undergraduate work in India and had a couple of years of research experience there as well. Compared to my experience here in the US, there are stark differences in terms of opportunities and facilities. It’s very competitive to get into a great lab in India due to sheer volume of good students. You also have to plan your research very well since reagents from overseas companies can take a while to arrive. Doing good research is not too difficult however, due to increasing government funding. Here in the US, and at the NIH in particular, very high caliber research can be done on a wider scale due to the availability of state of the art equipment, rapid availability of the best reagents, and a great collaborative environment.

In addition to research, what professional/career building opportunities have you participated in that are important to your career development?

I have already been at NIH for 1 year and 5 months. I earned my PhD in the laboratory of Dr. Rong Li, at Stowers Institute for Medical Research in Kansas City, MO. My research focused on understanding actin cytoskeleton and RhoGDI mediated cell polarization in budding yeast. My decision to come to the NIH was primarily driven by the fantastic research environment the NIH provides, and the research I planned to do during my post-doc, which involved understanding actin cytoskeletal dynamics and mechanosensation in living cells using high resolution light microscopy. Clare M. Waterman is one of the world leaders in this field, and a fascinating microscopist, and the reason I am here at the NHLBI. Clare is a wonderful supervisor who gives me a lot of independence to drive my project, which is helping me to become an independent scientist.

What do you enjoy most about the research environment here?

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Q&A with Postdoc Dr. Arupratan Das

Postdoc Kevin Ramkissoon interviews Dr. Arupratan Das Postdoc Fellow in the Cell Biology and Physiology Center

How long have you been at the NIH?

I have been at NIH for 1 year and 5 months.

What was your path to the NIH and what factors were most important in your decision to come here?

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Honesty is the best policy

By Herbert M. Geller, Ph.D.

I t stands to reason that fellows come to NHLBI to gain additional training to achieve their goals. Presumably, fellows choose their lab and their mentor based on the skills they wish to learn to move on to their desired position. Once on board, the process of training and mentoring becomes a collaborative effort between the fellow and the mentor. Each incoming NHLBI fellow gets a copy of the NIH Handbook on Training and Mentoring, which specifically addresses the responsibilities of the mentor and the trainee. NHLBI reinforces these practices through the use of the Fellow's Progress Report, which is signed by both the trainee and the mentor.

In order to have value, the information in the Progress Report has to be accurate and informative. Yet I have heard from some fellows that they are afraid to list their actual career goal on their Progress Report, because they feel that their mentor will not agree. My response is that it is essential to be honest at every step of the way if you hope to profit from a relationship with your mentor. Thus, if you say on your Progress Report that you are aiming for a P.I. position, but you actually would like a position away from the bench, you are losing in several different ways. The first is that expectations from a mentor are clearly dependent upon the aspirations of the fellow. If you say you want to be a P.I., your mentor is going to expect that you are fully invested in your project, and will be looking to you to provide leadership and creativity that will help you to be a P.I. This requires a significant investment of time and energy. You are also losing because, if you actually intend to move away from the bench, you would be better off taking advantage of the many different opportunities on campus for learning about these career paths, and perhaps even take advantage of a rotation. However, such activities would not be considered productive if your mentor expects you to be a P.I. Finally, there is no question that your true career goals will ultimately surface, and then the discussion with your P.I. will be much, much harder.

So what to do if you cannot share your career goals with your mentor? You are in the wrong place. Move to a position where you can. Moreover, if your goal is ultimately a non-research position, such as tech transfer, law, business, the sooner you leave the lab, the more successful you will be. In your relationship with your mentor, as in all of life, honesty is the best policy.

The main similarity between all the places I’ve trained and worked at is that you “publish or perish”. While I agree that, in the long run, the best science may be appreciated even if it is published in obscure venues (Gregor Mendel’s work would be a great example of this), a scientists’ career is sustained through peer recognition. Publishing in highly visible places is not sufficient to be held in high regard by your field, but it certainly helps. As for the differences, they have mainly to do with the varying emphasis on prospective vs. retrospective review. At the Fred Hutchinson Cancer Research Center (FHCRC), where I was faculty for a dozen years, the bulk of funding came from NIH R01 grants. To get these, one has to write a proposal for work that one intends to do in the future, and be evaluated favorably (prospective). In contrast, as an Investigator of the Howard Hughes Medical Institute or of the DIR of the National Heart, Lung and Blood Institute, my primary reviews take place after the work has been done (retrospective). These distinctions are not absolute however. The tenure process at FHCRC involved mostly retrospective evaluation, and at the DIR, I have obtained funding (e.g. the Director’s Challenge Award) by writing proposals for research for which I only had preliminary data at the time of application. The same goes for my fellows, who I encourage to write R22 or K99/R00 proposals (a mixture of retrospective and prospective evaluation). When they go out for jobs, they will be evaluated by selection committees that will evaluate them both retrospectively (Ph.D. and post-doc track records) and prospectively (research proposal, teaching plan, etc.)

How would you compare or contrast the training program for postdoctoral fellows at these institutions?

My experience is that the training program for postdoctoral fellows is pretty much the same in any competitive, conscientious lab, regardless of the institution. For those who want to be scientists (and I don’t see why I would do a post-doc, if my goal were to become a patent lawyer or a management consultant), the post-doc is a time to get as much excellent science done as possible, in order to be competitive in the job market. Insofar as there is a “training program”, it consists of having access to excellent resources, great colleagues and fantastic mentors. That is the definition of a good lab, no matter the institution.

What do you enjoy most about working at the NIH?

The fact that my colleagues are not constantly beleaguered by funding concerns, so that the first topic of discussion in a social context is not invariably how the grant situation is terrible, and the first thing that needs to be settled in a scientific context is not whether our exchange has a potential to form part of a new grant application.

What advice would you give to current fellows to ensure they get the most out of their training experience?

Cont’d on page 6
activities have you taken part in during your time at NIH?
As a part of my continuing education and career building, I was selected for and participated in a microscopy course, “Quantitative imaging from cells to molecules”, at Cold Spring Harbor Laboratory, which is run by world leading microscopists and cell biologists. I attended the Pennsylvania Muscle Institute Symposium on Cytoskeletal Regulation at U. of Penn, Philadelphia, PA and discussed science with renowned cell biologists like Tom Pollard, Yale E. Goldman and others. Recently, I also served as a judge in the poster competition for Postbac Poster Day 2014.

What advice would you give to a first year fellow entering the NHLBI training program?
Research wise, my advice to a newcomer would be to stay unbiased, complete the requisite preliminary experiments necessary to build confidence in your project, and rigorously test how solid your results and observations are. In my experience, this sets up a solid foundation for future success. I strongly recommend attending at least one seminar every week. Attending, and actively participating in the discussions, will help you broaden your knowledge and build your professional network.

When did you decide that you wanted to become a research scientist?
That decision came during my MSc in biochemistry at Calcutta University in India. I attended presentations from biology speakers from around the world where I was exposed to beautiful images of cells, dynamic organelles inside live cells, and learned how major human diseases are often associated with the microscopic cellular defects. Those experiences were thrilling and motivated me to become a part of the research scientist community.

Had you not chosen a career in scientific research, where do you think you would be today and what would you be doing?
Perhaps I would have ended up playing professional soccer. I used to play soccer routinely until my graduation, and won intra college championship and runner up for two consecutive years during my undergrad. I still love playing this game.

What other hobbies or activities do you enjoy away from the lab?
I love spending time with friends whenever I get time. In addition to playing soccer, I love doing outdoor activities such as hiking, playing cricket, and swimming. But above all, I most enjoy spending time with my 11-month-old daughter.

DCs taken from HDM-challenged VLDLR-deficient mice showed increased pathogenesis of airway inflammation when transplanted onto the airways of normal mice, suggesting that VLDLR negatively regulates airway inflammation induced by HDM.

This study identifies an unprecedented role of VLDLR in regulating pathogenesis of lung inflammation. This observation is also consistent with their previous study that LDL receptors have a similar role in limiting HDM-induced asthma. By studying the pathogenesis of lung inflammation in murine model, elucidating the mechanism by genome-wide transcriptome analysis, and extending the studies further into human samples the author systematically identified a novel role for VLDLR in suppression of the DC-mediated adaptive immune response in HDM-induced airway inflammation.

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