Office of Education
Division of Intramural Research

Fellows Newsletter

February 2014

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From the Director of the Office of Education

This seems to be a very long winter, with cold and foul weather starting early and continuing for an much longer time than we would have predicted. Despite this, the Office of Education and the Fellows Advisory Committee have an ongoing series of activities to enhance the experience for NHLBI fellows. One of these is the Career Development Series, in which we invite a former NHLBI fellow to share their experiences and provide advice. Daniel Kraushaar reports on the first of these, a session with Dr. Zheng You, formerly in the Laboratory of Biochemistry and now at Dupont. Future sessions are planned with former fellows now serving in the NHLBI extramural program. Watch the newsletter for announcements of these events.

This year, we are trying something new instead of the Fellows Retreat, which we are unable to plan due to constraints on federal government meetings. Instead, we are holding a DIR Research Day in Natcher Auditorium on June 9th (announcement below). Research Day will give all DIR scientists a chance to present their research and interact with other members of the DIR. In addition, we'll be holding one of our periodic 'bakeoffs' during the afternoon break. This will give us a chance to show off our culinary skills alongside our scientific achievement. We'll be giving awards both for poster presentations as well as for baking skills, and maybe even the combination. So put it on your calendar!

NHLBI DIR Research Day 2014

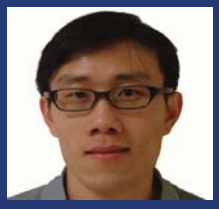
June 9, 2014

Building 45 - Natcher Auditorium and Atrium

More information to come

Meet the New Fellows

Dr. Komundi Singh is a new Visiting Fellow in the Cardiovascular-Pulmonary Branch under Dr. Michael Sack. Dr. Singh earned her Ph.D. at Ohio State University. Her initial project at NIH is to test the role of microglia and PARK2 gene in Parkinson's disease.



Dr. Wenchang Zhou is a new Visiting Fellow in the Biochemistry and Biophysics Center under Dr. Jose Faraldo-Gomez. Dr. Zhou earned his Ph.D. at the University of Konstanz. His initial project at NIH is to understand various molecular machines by using molecular simulations and cooperating the experimental data.

NHLBI DIR St. Patrick's Day Bake-Off

Tuesday, March 18th
3:00 PM - 4:00 PM
Building 10CRC, Room 2-3330

Please bring a dessert to share.
Must have green incorporated in the dish.
A prize will be given to the top voted dish.

THE SCIENCE BEAT by Dinari Harris, Ph.D.

Perrin, B. S., Jr., Tian, Y., Fu, R., Grant, C. V., Chekmenev, E. Y., Wieczorek, W. E., Dao, A. E., Hayden, R. M., Burzynski, C. M., Venable, R. M., Sharma, M., Opella, S. J., Pastor, R. W., & Cotten, M. L. (2014). High-Resolution Structures and Orientations of Antimicrobial Peptides Piscidin 1 and Piscidin 3 in Fluid Bilayers Reveal Tilting, Kinking, and Bilayer Immersion. J. Am. Chem. Soc.

Antimicrobial peptides (AMPs) are part of the innate immune response and are found among all classes of life. Fundamental differences exist between prokaryotic and eukaryotic cells that may represent targets for antimicrobial peptides. These peptides are potent, broad spectrum antibiotics which demonstrate potential as novel therapeutic agents. AMPs have been demonstrated to kill Gram negative and Gram positive bacteria, mycobacteria, enveloped viruses, fungi and event transformed or cancerous cells. AMPs are unique and diverse group of molecules, which are divided into subgroups on the basis of amino acid composition and structure. AMPs are generally: (1) smaller than 50 amino acids; (2) include specific amino acid composition like two or more positively charged residues (arginine, lysine) or histidine residues in acidic environments, and a large portion (generally >50) of hydrophobic residues. The secondary structure of AMPs vary depending on the conditions and environment but tend to be unstructured in free solution, and fold into □-helical structures upon partitioning into biological membranes. AMPs contain hydrophilic amino acid residues aligned along one side and hydrophobic residues along the opposite side of a helical molecule. This amphipathicity of the AMPs allows them to partition into the membrane lipid bilayer. The ability to associate with membranes is a definitive feature of AMPS although membrane permeabilisation is not necessary. The modes of action by which AMPs kill bacteria vary, however, the initial contact between the peptide and the target organism is electrostatic, as most bacterial surface are anionic or hydrophobic, such as the class of AMPs, Piscidin. Piscidins are found widely in teleost fish, was first discovered in mast cells, and have minimum inhibitory concentrations in the low micromolar (□M) range in bacteria. Members of the piscidin family contain up to 10 times as many histidines as do other AMPs and these residues act as a pH-sensitive switch that modulates the amphpathic character and antimicrobial activity of piscidin. Even though binding to biological membranes occurs through electrostatics the exact nature of these interactions is presently unclear.

High-resolution nuclear magnetic resonance (NMR) has contributed greatly to our understanding in this field and has provided insight about AMPs structure in aqueous solution, in organic solvents, and in micellar systems. Solid-state NMR can provide additional information about peptide-membrane binding. In the study by Perrin et. al, there researchers solved the high-resolutions structure and orientation of the Piscidin family of AMPs specifically in fluid bilayers. Their work makes clear how different kinds of lipid bilayer response to the attraction of membrane disrupting AMPs. They employed NMR experiments and molecular dynamics simulation to compare the behavior of two different mixtures of lipid bilayers, (phosphatidylcholine/phosphatidylglycerol (PC/PG) and phosphatidylethanolamine/phosphatidylglycerol (PE/PG), during the attraction of a model peptide into the membrane. They used the cationic 22-residue antimicrobial peptide called Piscidin-1 and Piscidin-3. By varying the lipid composition the researchers attempted to identify the molecular features important for membrane destabilization in bacterial cell membrane mimics. Using structural refinements of dipolar coupling and chemical shift analysis, along with MD simulations, the authors found that non-polar residues largely interact with the membrane model while charged residues favorably interact with the anionic membranes and that the both AMPs adopt a □-helical conformation. Thus, the presence of a critical threshold non-polar/charged residue ratio could be useful to design more effective antimicrobial peptides against infectious organisms in relation to their lipid composition. In our simulations, Piscidin has demonstrated the ability to cause disorder in acyl

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Recent Publications by NHLBI Fellows

Claxton, J. S., Sandoval, P. C., Liu, G., Chou, C. L., Hoffert, J. D., & Knepper, M. A. (2013). Endogenous carbamylation of renal medullary proteins. PLoS. One. 8, e82655.

Martina, J. A., **Diab, H**. I., Lishu, L., Jeong, A., **Patange, S**., Raben, N., & Puertollano, R. (2014). The Nutrient-Responsive Transcription Factor TFE3 Promotes Autophagy, Lysosomal Biogenesis, and Clearance of Cellular Debris. Sci. Signal. 7, ra9.

Mordini, F. E., Haddad, T., Hsu, L. Y., Kellman, P., Lowrey, T. B., Aletras, A. H., Bandettini, W. P., & Arai, A. E. (2014). Diagnostic Accuracy of Stress Perfusion CMR in Comparison With Quantitative Coronary Angiography: Fully Quantitative, Semiquantitative, and Qualitative Assessment. JACC. Cardiovasc. Imaging. 7, 14-22.

Murphy, E., Kohr, M., **Menazza, S., Nguyen, T., Evangelista, A.**, Sun, J., & Steenbergen, C. (2014). Signaling by S-nitrosylation in the heart. J. Mol. Cell Cardiol. 10.

Nguyen, K. L., Bandettini, W. P., Shanbhag, S., Leung, S. W., Wilson, J. R., & Arai, A. E. (2014). Safety and tolerability of regadenoson CMR. Eur. Heart J. Cardiovasc. Imaging.

Pattaradilokrat, S., Li, J., Wu, J., **Qi, Y**., Eastman, R. T., Zilversmit, M., Nair, S. C., Huaman, M. C., Quinones, M., Jiang, H., Li, N., Zhu, J., Zhao, K., Kaneko, O., Long, C. A., & Su, X. Z. (2014). Plasmodium genetic loci linked to host cytokine and chemokine responses. Genes Immun. 10.

Perrin, B. S., Jr., Tian, Y., Fu, R., Grant, C. V., Chekmenev, E. Y., Wieczorek, W. E., Dao, A. E., Hayden, R. M., Burzynski, C. M., Venable, R. M., Sharma, M., Opella, S. J., Pastor, R. W., & Cotten, M. L. (2014). High-Resolution Structures and Orientations of Antimicrobial Peptides Piscidin 1 and Piscidin 3 in Fluid Bilayers Reveal Tilting, Kinking, and Bilayer Immersion. J. Am. Chem. Soc.

Yin, F., Battiwalla, M., **Ito, S., Feng, X.**, Chinian, F., Melenhorst, J. J., Koklanaris, E., Sabatino, M., Stroncek, D., Samsel, L., Klotz, J., Hensel, N. F., Robey, P. G., & Barrett, A. J. (2014). Bone marrow mesenchymal stromal cells to treat tissue damage in allogeneic stem cell transplant recipients: Correlation of biological markers with clinical responses. Stem Cells. 10.

Outstanding Biotech Course by The American Society for Cell Biology (ASCB)

June 16 - 27
Keck Graduate Institute in Claremont, CA.
Selected graduate students and postdocs will receive free travel, room & board and tuition.

ASCB's own Ira Mellman, vice president at Genentech, and top instructors from the Keck Graduate Institute will introduce young scientists to the skills and competencies they need to be successful in the biotech industry.

-Classes on biotech management using case-based studies
-Scientific problem-solving cases
-Career-oriented workshops
-Networking events
-Team-based project

The deadline to apply is February 15, and you must be or become an ASCB member to apply. To apply, and get more information, visit: http://www.ascb.org/biotech-course

The Science Beat, continued

chains. The results show that the two model membranes used in this study have different behavior in the presence of Piscidin-1 and -3. The authors suggest that the membrane composition could be an important factor in determining the lytic ability of peptide drugs to kill a unique bacterial species. Using NMR analysis, the authors were able to accurately describe the piscidin peptides orientation and topology. Their work was even able to detect the presence of the helix-disrupting G(X)4G motif within the piscidin family, a motif that induces in a kink in the overall □-helical structure associated with this family of AMPs. The MD simulations that they conducted identified important peptide-lipid interactions and provide structural support of how this family of AMPs can remodel and disrupt lipid bilayers.

Overall, the research by Perrin et. al reveals that the piscidin-1 and -3 adopt disrupted □-helical structures that correct for the different amphipathicities of their N- and C-terminals. Bound to different bacterial mimics, piscidin is tilted, kinked, and immerse in the lipid bilayer, which enables its disruptive effects. This work provides the first atomic-level differences between two member of the piscidin family of AMPs and has shed new light on the modes of action of AMPs and how should ultimately facilitate the design of new drugs with enhanced antimicrobial activity and specificity for microbial membranes.

Career Development Networking Session

Presented by Fellows Advisory Committee's Career Development Subcommittee

1) February 28th from 4PM - 5PM (50/2nd fl libary) **Dr. Nisha Narayan** - Discuss her transition from NHLBI to the FDA.

2) March 7th from 1:30PM - 2:30PM (50/2nd fl library) **Dr. Renee Wong** - Program Officer in NHLBI Extramural Program to discuss her career transition.

Q&A with Investigator

Postdoc Kevin Ramkissoon interviews Dr. Tiffany Powell-Wiley, Assistant Clinical investigator, Social Determinants of Obesity and Cardiovascular Risk.

Dr. Tiffany Powell-Wiley joined the NIH in 2011, but the relationship began much earlier when she spent a year as a research fellow in the NIH's Clinical Research Training Program during her medical training. Her drive to understand the 'what', 'when' and 'why' of cardiovascular disease led to the completion of an M.P.H. in epidemiology from the University of North Carolina at Chapel Hill while earning her M.D. from the Duke University School of Medicine. Dr. Powell-Wiley completed a residency in internal medicine at Brigham and Women's Hospital in Boston, followed by a fellowship in cardiology at University of Texas Southwestern Medical Center where she served as chief cardiology fellow from 2010 to 2011. She received the Women in Cardiology Trainee Award for Excellence from the American Heart Association in 2009 and serves as a reviewer for multiple journals including Circulation and Annals of Internal Medicine, which named her one of the "Best Reviewers" for 2011. Dr. Powell-Wiley currently holds a joint appointment with the NHLBI and the Applied Research Program in the Division of Cancer Control and Population Sciences at the NCI and serves as a mentor to fellows through her position on the Board of Tutors for the NIH's Medical Research Scholars Program.

Your research focuses on the social, behavioral and environmental factors that contribute to obesity and cardiovascular disease. What were the primary motivating factors for your chosen area of focus?

My interest in cardiovascular disease stems largely from the patients I saw during medical school. The first patient that I took care of as a medical student was someone suffering from heart failure and in need of a transplant. That experience had an impact on me. It was always my intention to have a strong public health research component to my work, however I didn't decide what specific area of public health I wanted to focus my M.P.H. until, as a medical student, I became more aware of the wealth of data and treatment information available from cardiovascular clinical trials and cardiovascular epidemiologic research.

You have trained at some on the nation's top public and private universities and clinical centers. How does the academic and training environment at the NIH compare to other places you have worked and trained?

Many of the large academic institutions allocate time for medical students to engage in research, be it a summer or a year. A major benefit of training at the NIH is that this is where a majority of research and national health policies are determined. Many of the nation's best investigators are based here, and much of the NIH's work is done in collaboration with the top academic and clinical centers across the country and around the world. Being here facilitates access to all of it! From cutting edge basic research to major clinical studies, the development of novel

Q&A with Postdoc Amarjit Mishra

Postdoc Kevin Ramkissoon interviews Dr. Amarjit Mishra, Visiting Fellow in the Cardiovascular-Pulmonary Branch.

When did you decide that you wanted to become a scientist?

My childhood was based on asking questions and wondering why things happen the way they do. I had good teachers during high school and college who kept fueling this curiosity which led me down a path in science. After gaining a degree in Veterinary Medicine, I worked on finding solutions to practical problems in animal health, but the underlying cause of some diseases were still unknown so I pursued a PhD in Biomedical Sciences to better understand human systems and look at complex processes - particularly lung diseases.

What factors were most important in your decision to come to the NIH?

I believe there are four phases in the life of any professional: learning, establishment, accomplishment and achievement. The learning phase requires you surround yourself with the right environment and people. The establishment phase is better suited to a place where you have organized infrastructure to do what you want to do. In the accomplishment phase you begin setting your own goals and focus on what you want to do. Achievement relates in part to a social acknowledgement of your accomplishments. The NIH is a great training environment that provides the intellectual and physical resources for any scientist focused on this type of journey and I knew from the very beginning that my goals for a productive postdoctoral training would be best served here.

What do you enjoy most about your experience and the research environment here?

The best part of doing research at NIH is the collaborative environment. The support, scientific and technical guidance available from peers, mentors and core facilities help make doing research here enjoyable. I feel proud and enlightened to work with and under the aegis of highly touted intellectuals with common visions and goals. The focus of my current research is to develop novel treatment strategies for asthma and inflammation, as well as to identify new mechanisms and pathways that mediate the pathogenesis of asthma. I feel privileged to be at the NIH and part of a team working on a clinically relevant problem.

In addition to research, have you participated in additional career building activities during your time at NIH?

I would highly recommend the grant writing workshops and other specialized training courses offered at the NIH. Presenting each year at the American Thoracic Society conference has been a wonderful experience and a way to keep track of cutting-edge research, as well as build a professional network in my scientific field and beyond.

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

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Summary of NHLBI development and networking session
By Daniel Kraushaar

On January 17th , the first in a series of NHLBI career development and networking sessions kicked off. Dr. Zheng You, formerly a NHLBI postdoctoral fellow in the lab of Dr. Rodney Levine, and now at DuPont, discussed her successful transition into a biotech career. Here is some of the information and advice that Dr. You passed on in this small-group event:

1. Although Dr. You stressed the importance of networking in landing your first job in industry she pointed out that she successfully applied to an advertised position without prior networking. Hence she still encourages the old-fashioned job search on job boards such as monster.com and others.

2. Dr. You pointed out that her expertise in protein crystallography and her background in enzymology provided the right fit for her position at DuPont. She advised that technical skills beneficial for one's job search should ideally be reflected in the shape of publications.

3. Dr. You spends about 50% of her time in meetings and 50% at the bench. Her research focus revolves around developing biocatalysts from renewable sources.

4. Dr. You stresses the importance of self-motivation and diligence to deadlines. Much of the performance pressure in her position originates from meeting deadlines. Therefore, although work on weekends is not typical, it may be required in times of intense deadline pressure.

5. Dr. You admitted that the publishing of results was not a priority at DuPont , and that continuing to build one's resume is certainly not as easy as at an academic institution. Nonetheless once proprietary information has been patented, publication of results is doable as long as one is prepared to initiate the process.

NHLBI DIR Seminar Series

Pere Puigserver, Ph.D.
Professor, Cell Biology, Harvard Medical School

" Metabolic Reprogramming in Type 2 Diabetes "
Tuesday, February 25th
11:00 AM - 12:00 PM
Building 50, Room 1227/1233

Featured Article

Getting to a Mentor
By Herbert M. Geller, Ph.D.

When I ask our fellows about who is doing their mentoring, most would tell me that their PI supervisor is also their mentor. However, if I ask the follow question "So is your PI capable of guiding you in all aspects of your career development?", the answer is invariably "No". So where should the other mentoring come from? This, of course, depends upon your intended career path. If your intention is to have an academic appointment as a faculty member, then it would be appropriate to have a mentor from academia in addition to your NIH mentor. Likewise, if your goal is to seek a job in industry, then having a mentor who knows how to enter and survive in that environment could only help.

The question then arises as to how to find such a mentor? There are several ways, depending upon your field. Many society meetings have a mentoring program, where they fill requests by trainees to be matched up with a potential mentor. My own experience in this role at the Neuroscience Society has been very positive: I've managed to mentor a graduate student with whom I was matched in 2004 go through her graduate work, two postdoctoral positions, and now advise her as an Assistant Professor.

If your society meeting does not have a formal program, then you need to be more pro-active in finding a mentor. The Science Careers Web site at: http://tinyurl.com/qxbxkf4 has a number of tips for doing this, but the essentials are that you need to seek out potential mentors, and conduct an "audition", more like a conversation, to see if the person is someone whose advice you can trust. If your potential mentor is not at NIH, then the optimal situation is to ask to sit down with them sometime during the meeting. Their response to this will immediately indicate their interest: if they have no time for you at the meeting, they are unlikely to have time when they are back at work. Moreover, once you initiate the conversation, because the role of a mentor is to be responsive rather than directive, you need to keep up the relationship with active communications.

Finally, just as a corporation has a Board of Directors to help guide its future, you should consider that you may need several mentors, each with a different set of expertise, to provide guidance.

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Building 10, Room 7N218
DIReducation@nhlbi.nih.gov
301-451-9440

Q&A with Dr. Tiffany Powell-Wiley, continued

treatments, and some of the best surveillance data available are all generated here. The NIH has a strong influence in what becomes standard policy nationwide and it's a privilege to be a part of that.

Do you think there is enough appreciation amongst the medical community for the significant role that public health plays in their patients' well being?

The understanding of and appreciation for the importance of social determinants, such as behavioral and environmental factors or access to primary care, to human health has grown significantly in both the medical and research communities since I started my training. On the medical side, this is evident in the increasing number of medical students interested in incorporating research on social determinants of health into their training. There has been somewhat of a paradigm shift in my experience, with the question "how do we promote and maintain cardiovascular health?" gaining more parity with the question of "how do we treat the disease?". It's definitely a good time to be involved in this type of research!

You have a track record of translating your research findings into community programs and interventions to combat obesity and cardiovascular disease. What common challenges have you encountered in implementing programs across different communities?

Implementation science, or "bedside to community" research as some may call it, always poses challenges. One challenge I have encountered is countering misperceptions that some in the community may have about the work being carried out. A common example is the view that the research or program being implemented will be of primary benefit to the researcher or institution rather than the community. A key component of overcoming such challenges is building a trusting relationship with the community in which you plan to work, which we have achieved this in the past by working closely with individuals and community organizations such as churches, to understand and take into account the community's needs.

You currently serve on the Medical Research Scholars Board of Tutors. What is your approach to mentoring the next wave of physician researchers?

I try to draw from my own experience as a NIH fellow and be a mentor who helps fellows identify and take the steps necessary to move to the next phase in their careers. In addition to providing advice and helping them find solutions to any challenges they face, one of my goals as a member of the MRSP Board of Tutors is to help fellows get the most out of their 1 year of research training.

What one key piece of advice would you give to fellows to help maximize their research training experience during their time at the NIH?

Probably one of the most important pieces of advice I can give is to adequately consider the scope of their chosen research project and their ability to not only get the desired training, but also to reach a meaningful conclusion in the allotted 1 year timeframe, be that a publication or conference presentation or otherwise.

You received a number of early-career recognitions and served as chief cardiology fellow during your time at UT Southwestern Medical Center. What aspect of your personality, or characteristic have you learned during your training, has helped you to be successful?

I enjoy working with others, which has definitely been very helpful in a field where actively seeking out collaborations and being a team player helps to advance one's career. It is also important to realize and accept that no one is perfect. Many of the professional decisions we make each day, be they at the bench or in the clinic, impact both ourselves and others. For many, this can be a source of a lot of stress and disappointment, particularly when things don't go as planned. While the importance of careful planning and thoughtful consideration cannot be emphasized enough, you can't expect perfection. Even in cases where the correct decision is made, the outcomes can be unpredictable. One thing I learned, particularly during my residency, is that keeping your composure, both outwardly and inwardly, is important to problem solving during challenging situations either on your own or as part of a team.

When not focused on work, what hobbies or activities do you enjoy?

My husband and I are currently expecting our first child so everything that you can imagine that goes into preparing for that currently takes up a lot of my free time. I practice yoga and enjoy taking Zumba classes. I also really enjoy visiting the many museums and historical sites in the area.

Q&A with Dr. Amarjit Mishra, continued

A high caliber research career involves being a leader in your scientific arena and being able to form successful collaborations with colleagues. If your goal is an academic position you should tackle an exciting, high-impact problem that will provide you with opportunities for discovery and independence. Don't be afraid take on high-risk projects because therein often lie big rewards. It is prudent however to have a less risky, back-up project or component. Inter- or intra-lab collaborations at NIH can be very productive while learning collaborative skills which will be valuable as your scientific inquiries becomes more complex. This won't happen overnight! Expect downtime and struggles as you establish and familiarize yourself with new research areas at NIH.

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

Music. I'm very fond of playing rhythm instruments and percussions. Apart from lab work I spent a lot of time listening to different kinds of natural and simulated sounds and songs and trying to mimic them.