

Office of Education  
Division of Intramural Research

# 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

Summer has arrived in spades early this year. While the weather pattern has been somewhat atypical, there are a lot of special events in and around town. Tomorrow is the 4th of July, US Independence Day, and the major celebration is on the National Mall, where there will be a major concert and fireworks display. While the mall tends to be crowded, you can get a good view of the fireworks from many points on the Virginia side of the Potomac River. Other ongoing events include lots of free outdoor concerts and movies. Liz Cox, our new Program Coordinator, provides you with a list of concert venues in her new “About Town” column which debuts in this newsletter. We hope that you find time to take advantage of them. Lots of fellows come to me with the same question “What are my chances of becoming a PI. While there is no certainty, a new widget, described in my column, can help you make this evaluation. The newsletter takes a break in August, so look for the next one right after Labor Day in September.

## FEATURED ARTICLE

What are my chances of being a PI?  
By: Herbert M. Geller, Ph.D.

Many NHLBI Fellows want to be a PI, only some of whom achieve their goal. So what if there were a way of measuring what your chances are? A new widget ([www.pipredictor.com](http://www.pipredictor.com)), arising from

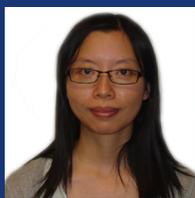
a recent paper in Current Biology (van Dijk, et al, 24:R516-R517, 2014) offers one approach based on data mining. The method they used was to identify a group of authors who published their first paper in recent years, and then classified them as a PI if they then became last authors on publications in following years. They could then determine the factors that best predicted whether the author would become a PI.

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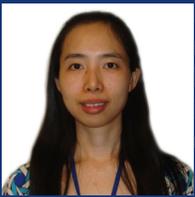
## Meet the New Fellows



Dr. Maddy Davison is a new Visiting Fellow in the Biochemistry and Biophysics Center under Dr. Nico Tjandra. Dr. Davison earned her Ph.D. at the University of Bristol. Her initial project at NIH is using NMR to investigate structural biology questions, such as studying specific interactions between proteins, peptides, and drug candidates



Dr. Ye Chen is a new Postdoctoral Fellow in the Systems Biology Center under Dr. Keji Zhao. Dr. Chen earned her Ph.D. at West Virginia University. Her initial project at NIH is analysis and mathematical modeling on Next Generation Sequencing data.



Dr. Jessica Tang is a new Postdoctoral Fellow in the Center for Molecular Medicine under Dr. Hong Xu. Dr. Tang earned her Ph.D. at the University of Maryland. Her initial project at NIH is genetic screens of nuclear factors that affect mitochondrial DNA replication in *Drosophila*.



Dr. Julia Liu is a new Postdoctoral Fellow in the Center for Molecular Medicine under Dr. Toreen Finkel. Dr. Liu earned her Ph.D. at Harvard University. Her initial project at NIH is characterizing the phenotype of mitochondrial calcium uniporter (MCU) in knockout mice, in particular studying whether they have defects in mitochondrial unfolded protein response, inflammation, and/or other processes.

## THE SCIENCE BEAT by Dinari Harris, Ph.D.

McGlinchey, R. P., Jiang, Z., & Lee, J. C. (2014). *Molecular Origin of pH-Dependent Fibril Formation of a Functional Amyloid*. *ChemBiochem*. 10.

Protein misfolding and functional amyloids have emerged as important regulators of human diseases. Peptides or proteins are converted under some conditions (eg: changes in pH) from their soluble forms into highly ordered fibrillar aggregates. Such transitions can give rise to pathological conditions ranging from neurodegenerative disorders to systemic amyloidoses. Pmel17 is a melanocyte protein necessary for melanin deposition in mammals and found in melanosomes in a filamentous form. The luminal part of human Pmel17 includes a repeat domain (RPT) region with 10 copies of a partial repeat sequence, known to be essential *in vivo* for filament formation. Pmel17 is highly regulated *in vivo*, undergoing a series of post-translational and proteolytic modifications that control the formation of amyloids. In the work done by McGlinchey et al., the researchers use a combination of mutation analysis, tryptophan fluorescence, circular dichroism (CD), and transmission electron microscopy to determine which amino acid residues are responsible for mediating the reversibility, aggregation of functional amyloids at different pH levels.

One interesting aspect of pH-dependent fibril formation is that RPT form amyloids under mildly acidic, melanosomal pH of ~5, but these fibrils completely dissolve at pH levels above 6. This reversible polymerization behavior contrasts with those exhibited by disease-related amyloids, which disassemble only upon harsh treatments (eg: chemical denaturants and non-physiological pH). The molecular basis for reversible pH-dependent amyloid formation of the Pmel17 repeat domain has been revealed by mutational analysis. Wild-type (WT) RPT aggregated in a pH-dependent manner as expected and with fibrillation occurring only below pH 6. In contrast, mutation of essential glutamic acid (Glu, E) residues within RPT can significantly alter the aggregation time of fibril formation. The authors specifically then asked if these mutated residues could change the pH sensitivity of amyloid formation. Of the 16 carboxylic acids, only E422 impacts its strict pH regime to form amyloid. Neutralization of E422 is vital for self-assembly and shifts the pH dependence by one pH unit. Based on their findings, the authors proposed a putative model in which E422 side chains within the filament core, suggesting that upon protonation, both intra- and inter-sheet contacts are facilitated and essential in stabilizing the filament structure.

Overall the work by McGlinchey et al. offer new insight into the molecular basis that governs the formation of a functional amyloid. Consistent with their results, the authors suggest an important pH switch which might be a simple yet elegant way controlling fibril assembly and maintaining the benign nature of other amyloid-like structure. From an application perspective, a reversible amyloid formation mechanism could have potential applications in the areas of nano-biotechnology including tissue engineering and/or drug delivery.

Not surprisingly, authors who published more papers in high-impact journals had a higher probability of being a PI, but they also noted that the probability of being a PI increased based on the total number of first-author publications, as well as the citations to those publications as measured by the h-index. They also noted a negative correlation with middle author publications, but note that this could simply be due to publications by staff scientists and technicians, who do not have aspirations to become a PI. One other predictive factor was the number of citations for a paper compared to the impact factor of the journal – papers that got cited more than the average, even in low-impact journals, are predictive of achievement.

Two other factors had a high predictive value. One is the ranking of the universities the author was associated with, and whether the postdoctoral university was better than the graduate one. (It is not clear how NIH was ranked or whether it was included in these calculations). The second

was sex: males had a higher probability of becoming a PI after correcting for all other variables. These two factors don't have a ready explanation.

The authors note that all their data are correlative, so that they cannot claim causality, but it would seem that many of the factors, such as quality and number of first author publications confirm many of our preconceived notions. The fact that middle author publications are not predictive would seem to be a disincentive to collaborations. Moreover, the model appears not to recognize equal contributions as being equivalent to first authorship. Finally, their result that women with equal records to men are not getting the same level of achievement is something that needs to be addressed.

## Outdoor Lounging in the District: Films and Concerts in the D.C. Area

By: Liz Cox, Program Coordinator

Summer has arrived in DC! And besides people standing on the left on metro escalators, summer brings a number of outdoor activities open to the public – including outdoor movie screenings and live music performances. Generally free and taking place at night, outdoor movies and concerts are a great low-cost way to relax after work or on the weekends. Most places allow picnic dinners and snacks (making it even more budget-friendly) or have a variety of food options nearby.

Live music lovers looking for free summer concerts, look no further than NIH's own neighborhood. The Bethesda Urban Partnership puts on a summer concert series, featuring every type of music you could want. The BUP series runs every Thursday until August 14th, from 6pm – 8pm in Veterans Park.

Jazz aficionados, and those looking to explore a bit more, should not miss the "Jazz-O-Scope" summer series on the mall. "Jazz-O-Scope" takes place at the Smithsonian's Hirshhorn Museum and Sculpture Garden every Thursday from 5:30pm – 7pm. Several concerts will highlight African influences on the world of jazz – July 31st, August 14th (a double concert!) and August 28th. "Jazz-O-Scope" is definitely not to miss.

Movie buffs, we've got you covered too. Taking place in every section of the city, from Rockville to Rosslyn to the Capitol Riverfront, there is sure to be a movie shown close to you. New releases, such as *Gravity* and *The Hunger Games* are screened alongside classics like *Top Gun* and *Feris Bueller's Day Off* (anyone?...anyone?). Those looking for family-friendly flicks fear not – *Frozen*, *Willy Wonka* and many others are among the lineup.

If you're not **Cont'd on page 5**

## RECENT PUBLICATIONS BY NHLBI FELLOWS

**Caviston, J. P., Cohen, L. A., & Donaldson, J. G. (2014).** Arf1 and Arf6 promote ventral actin structures formed by acute activation of protein kinase C and Src. *Cytoskeleton (Hoboken. )*. 10.

**Ehrlich, L. S., Medina, G. N., Photiadis, S., Whittredge, P. B., Watanabe, S., Taraska, J. W., & Carter, C. A. (2014).** Tsg101 regulates PI(4,5)P2/Ca(2+) signaling for HIV-1 Gag assembly. *Front Microbiol.* 5:234. doi:10.3389/fmicb.2014.00234. eCollection@2014., 234.

**Feng, X., Scheinberg, P., Biancotto, A., Rios, O., Donaldson, S., Wu, C., Zheng, H., Sato, K., Townsley, D. M., McCoy, J. P., & Young, N. S. (2014).** In vivo effects of horse and rabbit antithymocyte globulin in patients with severe aplastic anemia. *Haematologica*. haematol.

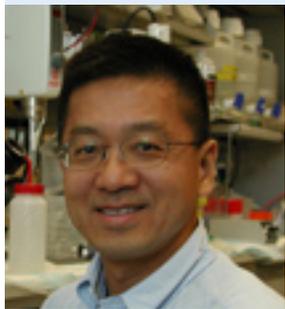
**Irvin, M. R., Zhi, D., Joehanes, R., Mendelson, M., Aslibekyan, S., Claas, S. A., Thibeault, K. S., Patel, N., Day, K., Waite, J. L., Liang, L., Chen, B. H., Yao, C., Tiwari, H. K., Ordovas, J. M., Levy, D., Absher, D., & Arnett, D. K. (2014).** Epigenome-Wide Association Study of Fasting Blood Lipids in the Genetics of Lipid Lowering Drugs and Diet Network Study. *Circulation*. CIRCULATIONAHA.

**McGlinchey, R. P., Jiang, Z., & Lee, J. C. (2014).** Molecular Origin of pH-Dependent Fibril Formation of a Functional Amyloid. *Chembiochem*. 10.

**Ueda, Y., Nishimura, J., Murakami, Y., Kajigaya, S., Kinoshita, T., Kanakura, Y., & Young, N. S. (2014).** Paroxysmal nocturnal hemoglobinuria with copy number-neutral 6pLOH in GPI (+) but not in GPI (-) granulocytes. *Eur. J. Haematol.* 92, 450-453.

## QUESTION & ANSWER WITH AN INVESTIGATOR

Postdoc Xiangbo Ruan interviews Dr. Paul Hwang, Investigator, Laboratory of Cardiovascular and Cancer Genetics, Center for Molecular Medicine .



Paul Hwang earned a B.A. in biochemistry and chemistry from the University of Kansas in 1985, after which he spent a year at the Swiss Federal Institute of Technology and the University of Zurich as a Fulbright Scholar. He graduated from the Johns Hopkins University School of Medicine with a M.D. and Ph.D in 1993. He did his internship and residency in internal medicine

at the UCSF School of Medicine in San Francisco, followed by a clinical fellowship in cardiology and postdoctoral research in molecular oncology at the Johns Hopkins University School of Medicine. Upon completion of his training in 2001, Dr. Hwang joined the NHLBI and in 2011 he became a Senior Investigator in the NHLBI's Center for Molecular Medicine. In 2006, he received an NIH Bench-to-Bedside Award.

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

I became interested in research when I was in college, conducting four years of undergraduate research with an excellent mentor. When I applied to medical school, I wanted to do both basic research and clinical work, so I entered a combined MD and PhD program.

Why did you choose to start your lab at NIH?

It was mainly the supportive research environment. It is helpful for a junior faculty to start their own research program based on some aspect of their post-doctoral research. The challenge for me was coming out of a cancer biology lab and attempting to make a transition to cardiovascular research. The NIH was willing to give me support without already having developed some sort of a cardiovascular research program. Another major reason I came to the NIH is that I knew Toren Finkel from his years at Hopkins. He was well established in the DIR as I was finishing up my fellowship. As many of you know he is an excellent scientist, and I realized that you need a good mentor at every level of your career. It has been great interacting with him and the many other investigators who have given me advice and support over the years.

As an M.D. and Ph.D., how does medical training benefit you when conducting scientific research?

A comprehensive understanding of human pathophysiology through pre-clinical and clinical training during medical school helps you appreciate the clinical implications of basic science in the laboratory. I feel very fortunate to be able to speak the medical language, and I try my very best to teach it at lab meetings as much as I can.

How do you communicate with your fellows?

We do most of our communicating during our weekly lab meetings. We have 3 fellows and 2 staff scientists in the lab, so everyone knows each other's projects. I like to have all lab members pool their thoughts into the presenting member's project, elicit and moderate the ideas from every member, and come up with the best plan forward during the meeting.

*Cont'd on page 5*

## QUESTION & ANSWER WITH A POST-DOC

Postdoc Xiangbo Ruan interviews Dr. Nazmul Haque, Laboratory of Ribonucleoprotein Biochemistry, Biochemistry and Biophysics Center.



How long have you been at the NIH?

I have been in NIH for almost 3 years.

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

The main reason I moved to NIH is quite diverse. There are labs studying different

areas of science. You can get more options for collaboration. If you have some special interest or difficulties in your experiments, you can always find some experts in that filed around you. NIH also has sufficient funding for basic research. Another reason is PI. J. Robert Hogg is an expert to develop the protocol for purifying RNA-protein complexes. This is a very powerful technique; I want to utilize this method to solve many questions with my interest.

What is your current research focused on?

I'm working on several projects. One of my projects is studying the proteins, which regulate protein translation of RNA with structured 5' UTR. You know that there are many RNAs those are regulated by their 5'UTR. My initial question is to find

novel protein factors involved in RNA stability or in translation regulation of mRNAs with structured 5' UTR. I have a few potential candidates that I have identified by mass-spectrometry. Currently I am studying whole transcriptome to regulate RNAs regulated by this protein.

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

I think it was quite early. When I was 9 years old I had my first project in our science festival in elementary school. At that time I went to all kinds of science activities where you made projects and present them. I'm not quite sure exactly at what time I decided to become a scientist, but I think it begins with the science projects in elementary school.

*Cont'd on page 5*

## Q&A WITH AN INVESTIGATOR

What characteristics of your personality have been most influential to your success thus far?

There are multiple factors involved but the ones that come to mind are creatively adapting to challenges, being happy with your work, and persistence. Not being deterred by negative results as long as the experiment is well designed and executed -- which sometimes can lead to even more interesting findings if you keep your eyes open. Appreciating the limitations of my ideas and letting nature show me how things really work.

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

It is pretty clear what you need to have before the end of your postdoctoral fellowship to land a good faculty position; they include high impact publications and a startup research grant of some type. It is important to select a supportive and collegial environment to sustain you through the challenges of establishing your lab. One last suggestion is being flexible in your career path/goals, capitalizing on your strengths. Going into pharmaceutical industry, technology transfer, patent law, or a host of other possibilities using your graduate degree and fellowship experiences could be even more rewarding than a traditional academic job depending on your personal strength and preferences.

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

I have two young children, so any non-work activity usually revolves around them. I need to make more of an effort to resume some of the types of activities that I used to enjoy when I was a postdoctoral fellow such as sailing and swimming.



National Heart, Lung,  
and Blood Institute



Do you have a *business card*?  
All NHLBI Fellows should!

A full template and helpful hints can be found on the intranet site, [available here](#).

## DON'T FORGET!

SUMMER STUDENT POSTER DAY IS  
THURSDAY, AUGUST 7TH!

THE REGISTRATION DEADLINE IS TUES-  
DAY, JULY 8TH AT 5:00PM.

POSTER DAY WILL BE HELD FROM 9AM - 3PM AT  
THE NATCHER CONFERENCE  
CENTER (BLDG 45).

SUMMER STUDENTS MUST HAVE PI APPROVAL  
TO REGISTER AND PARTICIPATE.  
REGISTRATION AND THE PROGRAM IS AVAIL-  
ABLE AT: [HTTPS://WWW.TRAINING.NIH.GOV/  
SUMMER\\_POSTER\\_DAY](https://www.training.nih.gov/summer_poster_day)

## Q&A WITH A POST-DOC

Can you briefly describe your postdoc experience so far?

Yes. NIH is a really nice place. My mentor is supportive and quite open to diverse questions. I can ask many different questions. I'm quite independent in my lab, which is very important for me. Based on my experience in different field, my questions are always diverse. We have more opportunities for cooperation in NHLBI. The core facility in NHLBI is great. For example, I'm now working with Proteomics Core, RNA Sequencing and Computational Biology core.

I also take advantage of using iPS cells from Induced Pluripotent Stem Cell and Genome Engineering/Transgenic Animal core. It's great for any post-doc.

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

Even though I don't have much time, I'm interested in photography and music.

sure where to start, Thrillist has compiled every summer outdoor screening into one calendar, [available online](#). Some highlights from the calendar include:

- "Bethesda Outdoor Movies" is also right next door and put on by the Bethesda Urban Partnership. The five nights of blockbusters takes place on Woodmont Triangle, at the corner of Norfolk and Auburn Avenues. Movies begin at 9pm from July 22 – 26.
- "Screen on the Green" is held on the National Mall on four Monday evenings throughout the summer and is an incredibly popular community event. This year will feature The Karate Kid on July 21st, Lover Come Back on July 28th, Key Largo on August 4th, and A Soldier's Story on August 11th.
- "Canal Park Thursday Movies: It's a Whole New Ballgame" takes place in Canal Park (by Nationals Stadium) every Thursday night at sundown through September 11th. The full schedule can be found on their website. Great for everyone who finds themselves down on the Capitol Riverfront!

There are many other regular movies and more live music events sprinkled throughout D.C. So grab a blanket, picnic basket, and some friends and head outdoors for the evening!

## ABOUT TOWN, CONT.