

The NICHD Connection

October 2010

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Image After

Lost and Taken

Interesting Opportunities

By Kris Langlais

Opportunities abound at NIH to use your scientific training away from the bench and gain valuable perspective and experience in program management, policy, communication, and other aspects of what drives and guides science at a federal agency. For example, fellows have the opportunity to be “detailed,” with the support of your advisor, in a policy or program office almost anywhere at NIH, or even at other HHS agencies. I sought out such an experience and am currently serving in a detail at the Office of Global Health Affairs (OGHA), at HHS headquarters in downtown DC. I started on September 1st, and even though I have been there full-time for only a few weeks, serving as an International Health Analyst, I’ve learned an enormous amount about global health policy, science diplomacy, and foreign relations. My work, which focuses on Southeast Asia, includes writing meeting briefs and memos for the OGHA director; developing strategies to use HHS resources in developing countries to support and build health capacity, and communicating with overseas HHS staff to provide program support and coordination. The position has been very challenging, and of course moving from the bench to the office takes some getting used to, but I now know what life is like in a policy office and that this is the direction that I would like to take my career.

If you seek such an experience, I recommend speaking with Brenda Hanning, our fantastic training director, who knew of my interest in global health, helped me to find my detail office, and facilitated the paperwork and other important details. She can also provide advice on how to approach your advisor with a request for a detail. Finally, to help you explore the possibilities, you should contact and set up informational interviews with office directors to see what places and types of detail might be a good fit for you. Whether you are early or late in your postdoctoral career, the best time to start thinking about the future is now.

Editor’s note: A detail is a short-term rotation in another area of the organization, either part-time (e.g., two days per week) or for a one- to three-month period, typically.

Letter from the Editor

As the Editor for *The NICHD Connection*, I have had a wonderful time meeting and interviewing amazing fellows and staff at our institute, and it has been my privilege to share their stories with you. I sincerely thank everyone who has helped get this newsletter up and running!

On to the important stuff! The October issue is packed with fun, popular science-style articles written by the NICHD FARE winners about their own research, and Kris Langlais gives a great description of his “Interesting Opportunity”—a new column discussing unique programs that can broaden a fellow’s experience while at the NIH. As always, don’t forget to check out the

upcoming events in October, including The NIH Research Festival, informative seminars, and a not-to-be-missed fellow lunch outing to Rock Bottom Brewery.

On a final note, we are still looking for a replacement Editor for *The NICHD Connection*. If you are interested in trading a small amount of time for a very rewarding experience, please contact **Brenda Hanning** at hanningb@mail.nih.gov.

Signing out!
Your Editor-in-Chief,
Shana Spindler, PhD

Event Announcements

OCTOBER 5-8, 2010

NIH Research Festival
Natcher Building

Head over to hear great talks, including those by our own NICHD FARE winners!

TUESDAY, OCTOBER 19, 12-1 P.M.

Research Ethics Series: #1

“What’s in a Picture? The Temptation of Image Manipulation”

Dr. Kenneth Yamada, NIDCR.

Please register with **Brenda Hanning**, hanningb@mail.nih.gov, to attend. If anyone would like to submit an image for review by Dr. Yamada, to contribute to the discussion, please send it to Brenda.

TUESDAY, OCTOBER 26, 12PM

October Fellows Lunch Outing at Rock Bottom Brewery

Meet in front of Building 50

Please see [page 3](#) for more information

WEDNESDAY, OCTOBER 27, 3-5 P.M.

Job Interviewing, with Scott Morgan

For fellows who are applying for permanent positions this year, an interactive session to perfect your presentation skills (job talks, chalk talks, the interview itself).

Register with **Brenda Hanning**, hanningb@mail.nih.gov

October Lunch Outing

TUESDAY, OCTOBER 26TH

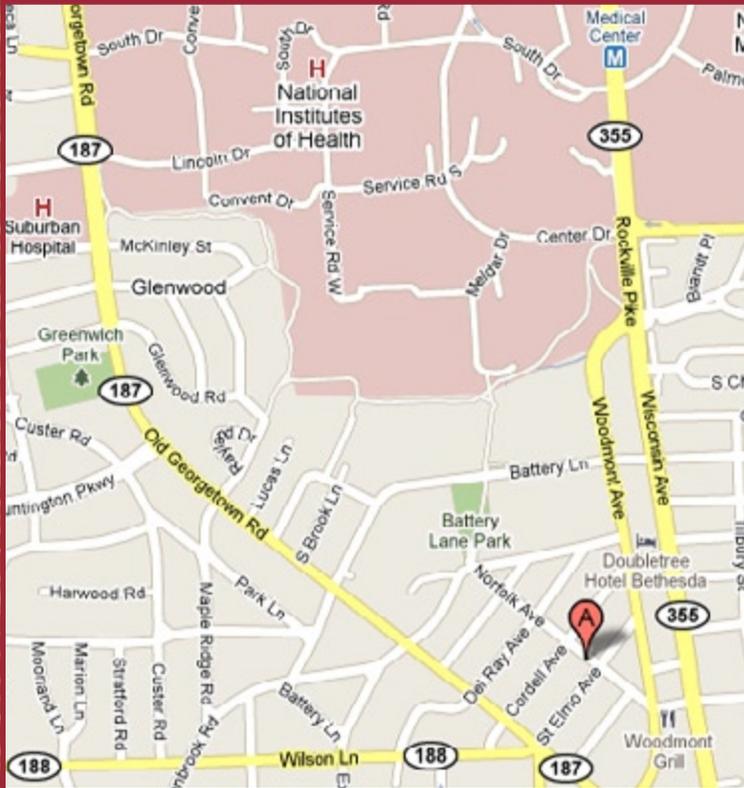
Meet at 12 pm in front of Bldg 50

Join us for an NICHD Fellow lunch outing to a local favorite: **ROCK BOTTOM BREWERY** in Bethesda! They have plenty of salads, pizzas, burgers, and brewery classics for anyone's tastes!

WHERE AND WHEN TO MEET:

On OCTOBER 26th, we will meet in front of BUILDING 50 at 12PM. To reach Rock Bottom Brewery, we will use the employee pedestrian exit that is just south of building 38A. We will then walk along the trolley trail to Norfolk Ave (see map at left). This will give us a short scenic walk to the restaurant (about 10-15 minutes walk time). If your building is already near the south side of campus, feel free to meet us at the pedestrian exit. Hope to see you there!!!

Rock Bottom Brewery
7900 Norfolk Avenue
Bethesda, MD 20814



Thank you for the Pizza, PIs!

The September 21st pizza party hosted by the NICHD PIs—*A Pizza PI* as it was called—in appreciation of hardworking postdocs was a hit! On behalf of the postdoc community, *The NICHD Connection* would like to thank the PIs for a much-needed pizza break. And come on, who doesn't like free food???

Please take a moment to view our gallery of photos from this fun event, located on [page 9](#).

Congratulations to the NIH Research Festival FARE Winners for 2011

The 2010 NIH Research Festival is just around the corner, from October 5-8, and we're excited to announce so many NICHD FARE winners! Many of our FARE winners have contributed a popular-science style article to this month's newsletter (pages 5-8). If something piques your curiosity, check out their talk at the festival! A full schedule for the Research Festival can be found at <http://researchfestival.nih.gov/index.php>.

INTRODUCING THE 2011 NICHD FARE WINNERS:

FELLOW / MENTOR

Chase Beisel / Storz
Naveen Bojjireddy / Balla
Katherine Bowers / Zhang (DESPR)
Charu Chaudhry / Mayer
Yang Chen / Machner
Marko Jovic / Balla
Jana Kainerstorfer* / Gandjbakhche
Hisatsugu Koshimizu* / Loh
Janesh Kumar / Mayer
Julian Lui* / Baron

Elena Makareeva* / Leikin
Attiq Muhammad / Hinnebusch
Weijun Pan / Weinstein
Yogikala Prabhu / Bonifacino
Arjun Saha / Mukherjee
Chinmoy Sarkar / Mukherjee
Zakir Ullah* / DePamphilis
Joaquin Villar / Dufau
Hong Ye* / Rouault

Repeat winners noted with *

Curious what your fellow Fellows are up to? Check it out here—popular-science style!

Maybe the Hulk had abnormal histone modifications

By Julian C. Lui

Have you ever wondered why children grow while adults do not? How body growth slows as an individual reaches adult size and how growth of the different organs is coordinated to maintain body proportions are largely unknown. We have recently found evidence that body growth deceleration is regulated by a multi-organ genetic program. This program involves the down-regulation of hundreds of growth-stimulatory genes. When comparing 1-week-old rapidly growing mice with 4-week-old slowly growing mice, we find that these genes are being “turned off” simultaneously in multiple organs with age. As a result, we observe a reduction of cell division within the organs.

How might hundreds of genes get switched off with age? One possibility involves modification of histones, proteins that act as spools around which DNA is wound. Histones can be chemically modified by cells to make nearby DNA more or less accessible to factors needed for gene expression, thereby turning genes on or off. We found two histone modifications (trimethyl-H3K4 and trimethyl-H3K27) changed in many genes from 1 to 4 weeks of age in mice. These changes may help switch off the growth-promoting genes and thus play a previously unsuspected role in limiting body growth.

“Compartment matters” in Alzheimer’s Disease

By Yogikala Prabhu

Alzheimer’s disease (AD), characterized by impairment in learning, memory, decision-making, language, emotion, and orientation, is the most common form of dementia affecting the elderly. A key pathological hallmark of AD is deposition of plaques in the brain. The building block of these plaques is the very small protein amyloid-beta, which is generated by a sequence of cleavage events by specialized enzymes, one of which is known as beta-secretase (BACE). BACE is the rate-limiting enzyme in the generation of the amyloid beta product. Increased amyloid-beta levels are observed in the post-mortem brain sections of AD patients as a result of increased BACE levels/activity. It is therefore essential to un-

derstand the intracellular sorting and transport mechanisms that govern the levels of BACE.

In our current study, we have found that a specific complex of proteins, called the adapter protein complex-2, is required to internalize BACE from the cell surface. Our data implies that this internalization is to keep BACE levels in check by targeting BACE to degradation compartments in the cell. We hypothesize that elevated levels of BACE at the cell surface result in amyloid-beta overproduction and amyloid plaque formation. This study offers novel insight into the molecular mechanism leading to the pathogenesis of Alzheimer’s Disease.

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FARE Winners *(continued from page 5)*

Modulating neurotransmitter receptor activity *By Charu Chaudhry*

Rapid communication between nerve cells involves the interconversion of electrical and chemical signals. At the junction between nerve cells, electrical impulses promote the release of a chemical neurotransmitter, such as glutamate, from one nerve cell. Glutamate diffuses across a small space—the synaptic cleft—and binds to glutamate receptors on adjacent nerve cells, causing them to open their transmembrane pore and in turn generate an electrical signal. Glutamate receptors are fascinating molecular machines that mediate neurotransmission at about sixty percent of synapses in the brain and play crucial roles in central nervous system function, learning, memory, and disease. The region where glutamate binds to its receptor forms a clamshell shape with two domains. Binding of glutamate in the cleft between the domains promotes clamshell closure and formation of a critical “active” interface that places a torque on the ion channel pores, causing them to open. For a subset of receptors, binding of small ions is also required for receptor activity. What is the molecular basis for this? Using x-ray crystallography, a method to determine the three-dimensional atomic structure of proteins, and biophysical measurements, we found that ions bind at this interface and contribute substantial free energy to stabilizing the active state in these receptors, which is required for function. In the future, I hope to expand my studies to understand the interactions between glutamate receptors and auxiliary proteins that form signaling complexes in neurons.

Partnering-up to make glutamate receptor ion channels *By Janesh Kumar*

Ion channels activated by the small molecule glutamate are known as glutamate receptor ion channels, and they mediate the majority of communication between neurons in the brain. Dysfunction of these ion channels has been associated with several neurodegenerative disorders, such as Alzheimer’s and Parkinson’s Disease. In eukaryotes, a family of 18 glutamate receptor ion channel genes code for proteins that can assemble in different combinations to form the varying subtypes of receptors that are required for neuron communication. The assembly of proteins in each receptor subtype is controlled by a large amino terminal domain (ATD) at the beginning of each protein that resides on the outer surface of the cell. The molecular mechanisms that regulate this specific assembly are not well understood. We have revealed these molecular mechanisms and the role of the ATD in the assembly of glutamate receptor ion channels using crystallography, biochemical and biophysical methods. Our research shows that the ATDs provide the primary signal for receptor association and have identified key elements that determine subtype selectivity and assembly.

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FARE Winners

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Ribosomes...Where to begin?

By Attiq Rehman Muhammad

To make new proteins in all eukaryotic (nucleus-containing) cells, dedicated protein complexes known as ribosomes must recognize and bind to specific start sites on mRNA. Previous studies have implicated a number of initiation factors in the stringent selection of the start site, but the involvement of ribosomal proteins in this step is virtually unknown. I am studying a subunit of the ribosomal proteins, known as Rps2, to uncover its possible function in correct start site selection using budding yeast as a model system. I have identified novel mutations in Rps2 that reduce the accuracy of start site selection. These results provide the first evidence directly implicating a ribosomal protein in scanning and start site selection in a living system, and we hope that further analysis will provide us with insights to explore the Rps2 mechanism of action. Our findings greatly increase our understanding of the molecular function of ribosomal proteins during the beginning of protein production.

Risk factors for gestational diabetes during pregnancy

By Katherine Bowers

I am a perinatal epidemiologist with a focus on pregnancy complications and the subsequent childhood outcomes. With a background in public health, I am particularly interested in modifiable exposures and how they interact with genetic susceptibility. My thesis research focused on genetic and environmental determinants of autism spectrum disorders. Currently, I am involved in studies evaluating the long-term effects of exposures during pregnancy (for example, excess fetal growth and risk of childhood hypertension) and risk factors for gestational diabetes, one of the most common adverse pregnancy outcomes. Part of my research includes evaluating the effect of pre-pregnancy dietary iron intake as well as dietary intake of total and specific fats and risk for gestational diabetes. In the future I hope to evaluate whether diabetes during pregnancy may be associated with mental health and neurodevelopmental health outcomes in the child.

The fate of a stem cell--Just how are the decisions made?

By Zakir Ullah

Stem cells have the unique ability to turn into other types of cells, and they carry significant therapeutic potential. But how a cell switches from one type to another is not well understood. The focus of my research is to determine the mechanism used by stem cells to turn into other cell types. I am particularly interested in studying trophoblast stem (TS) cells, which give rise to the placenta and are essential for fetal development. Working together with other members of the group, I have identified key genes that regulate TS cell differentiation and have deciphered the mechanism by which these genes control the differentiation process. Deregulation of these genes has been linked to diseases such as cancer, pre-eclampsia, and Beckwith-Wiedemann syndrome. Our results, therefore, also have implications in developing therapies for these devastating diseases. We are in the process of identifying additional regulatory controls that govern the fate of stem cells and are discovering more pieces of this complex puzzle as we move on.

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FARE Winners

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A hereditary GLRX5 mutation causes Sideroblastic Anemia

By Hong Ye

Sideroblastic anemia (SA) is a human anemia characterized by abnormal erythroblasts, the precursor cell to red blood cells. A key feature of SA includes iron deposits in the erythroblast's mitochondria—the cell's powerhouse. Various gene mutations and DNA deletions are known to cause hereditary SA. In Europe, an SA patient was recently identified with a novel mutation in the gene glutaredoxin 5 (GLRX5). We have studied the function of GLRX5 and the pathogenesis of its mutation. We find that GLRX5 is involved in iron metabolism and biosynthesis of the oxygen-carrying molecule heme in mitochondria—a process particularly important for erythroblasts. Knockdown of this protein disrupts activities of iron-containing enzymes, induces iron deposits in mitochondria, and impairs heme synthesis, resulting in anemia. By reintroducing the healthy GLRX5 gene into the patient's cultured cells using a virus, we can successfully restore the patient's erythroblast cells to normal. Our results suggest that gene therapy is a potential treatment option for patients with SA.

Small RNAs make bacteria picky eaters

By Chase Beisel

I study how bacteria sense and respond to changes in their environment. This decision-making process helps bacteria survive under harsh and varying conditions and is a critical part of bacterial infection and antibiotic resistance. My research focuses on how RNA regulators, called small RNAs, aid in bacterial response to changes in the environment. While small RNAs are known to mediate a bacterium's reaction to environmental changes ranging from a decrease in temperature to the presence of antibiotics, little is known about how small RNAs contribute to each response.

Currently, I am investigating how the small RNA "Spot 42" helps *Escherichia coli* decide which type of sugar to consume as a source of carbon and energy. Sugars come in many different shapes and sizes, and even though *E. coli* can consume various types, this bacterium can more easily consume some sugars, such as glucose. My results suggest that Spot 42 works together with its own regulator, known as CRP, to help *E. coli* focus its resources on glucose consumption over other types of sugars. To do this, Spot 42 and CRP silence genes required for the consumption of less-appealing sugars and keep *E. coli* primed to consume glucose even when this sugar is no longer available. In the future, I hope to design synthetic small RNAs that mirror the function of Spot 42 and apply the designs toward applications in biotechnology and medicine.



A
Pizza P1
SEPTEMBER 21ST



VISIT US ONLINE: <http://science.nichd.nih.gov/confluence/display/newsletter>



