

The NICHD Connection

February 2013

INSIDE THIS ISSUE

Hot Off the Press: Breaking the Circuit	1
Letter from the Editor	2
NICHD Fellows Shine at the 2013 GSR Symposium	3
Recapping the NICHD's Panel Discussion on Medical School Interviews	8
Career Planning with myIDP	9
February Announcements	10
February Events	14
PhD Comics	14

EDITOR IN CHIEF

Shana R. Spindler, PhD
Shana.Spindler@gmail.com

LAYOUT & DESIGN

Nichole Swan

CONTRIBUTORS

Rocky Ferrandino
Sisi Liu
Yvette Pittman, PhD
Kel L. Sheldon
Christopher Wassif
Xuefeng Yin

PHOTOGRAPHY

Jeremy Swan
Stock.XCHNG
Morguefile

Hot Off the Press: Breaking the Circuit

By Shana R. Spindler, PhD

Think of a simple circuit diagram. Straight lines represent wire connections, which are riddled with symbols for resistors, inductors, capacitors, and other devices meant to alter the flow of electricity. A graphical representation of the brain, complete with wired neurons and regulatory mechanisms, would parallel the engineer's circuit diagram in many ways. This begs the question: is there a way to control the circuitry of the brain, one line or symbol at a time, to decode how the brain controls behavior?

Dr. Harold Burgess of the NICHD is actively answering this question. Dr. Burgess and his team use a process they dub "circuit breaking" to study neural control of behavior in the larval zebrafish. Circuit breaking, as the name implies, involves manipulating the neural circuit in only one or a few places followed by screening for changes in behavior. "Circuit breaking is really getting at the root of what we want to do to understand how very specific parts of the brain control behavior," said Dr. Sadie Bergeron, postdoctoral fellow in the Burgess lab.



A major challenge to circuit breaking is the need to restrict cellular manipulation to the nervous system. The team uses hundreds of transgenic zebrafish lines to express destructive proteins in a cell-specific manner, but rarely do these transgenic lines restrict expression to the brain. Given that tissues such as heart and muscle are frequently affected in these transgenic fish, destroying these vital tissues can severely impact the interpretation of live behavioral studies in the zebrafish larva.

Dr. Burgess and his team have now described a new method to selectively affect nervous system tissue in transgenic zebrafish experiments, according to their recent report in the December 2012 edition of *Frontiers in Neural Circuits*. The group incorporated a set of **n**euron-**r**estrictive **s**ilencer **e**lements (NRSE) into the regulatory region of the DNA construct used to make the transgenic fish. NRSEs are short pieces of DNA that suppress

(continued on page 3)

Letter from the Editor

As promised in last month's issue, I'm sticking with my New Year's resolution to highlight more effectively the scientific findings of the NICHD Intramural program. So the theme this month is simply science, with a few recaps of last month's events of course.

The first "**Hot Off the Press**" column of 2013 highlights an elegant method to limit transgene expression in zebrafish larva to the nervous system, work done in the Burgess lab. We also highlight award-winning research presented by NICHD graduate students at the **9th annual Graduate Student Research Symposium**.

If you missed **last month's panel on interviewing for medical school** or if you couldn't catch the **workshop on Individual Development Plans (IDPs)**, we've got your recaps here. In fact, the IDP workshop was so successful that we will begin a regular "Career

Planning with myIDP" column next month to cover the heaps of information from the workshop and new **myIDP website**.

Please don't forget to check out the **February announcements** and **events** on pages **10** and **14**. There are a few great funding opportunities to consider, including the Postdoctoral Research Associate Program and Intramural Research AIDS Fellowship.

With that, I'll leave you to your reading. Enjoy!

Your Editor in Chief,
Shana R. Spindler, PhD

Please send questions, comments, announcements, pictures, suggestions, and anything else you'd like to see in this newsletter to **Shana.Spindler@gmail.com**.



Hot Off the Press: Breaking the Circuit

(continued from page 1)

neural gene expression in non-neural tissue. The inclusion of NRSE sites increased the recovery of transgenic fish with brain-specific expression patterns by five-fold.

The team then showed that proteins endogenous to zebrafish were likely binding the NRSE sites and inhibiting transgene expression in non-nervous system tissue. “You have to go through step by step, but it’s kind of like anything in science,” said Dr. Bergeron, co-first author of the report. “It’s just always a process until you reach what works best.”

Dr. Bergeron plans to use the NRSE-containing circuit breaking approach to screen the large collection of transgenic lines for neurons involved in modulating the startle response, a characterized set

of larval movements after an acoustic pulse. Thanks to marked technological progress, what once seemed an impossible feat—making hundreds of stable transgenic lines in a vertebrate model—has become rather routine in Zebrafish, explains Dr. Bergeron. “Given the simpler nervous system of the larval Zebrafish, we can use [them] as a model to understand the circuitry and genetic components that may be conserved in higher vertebrates.”

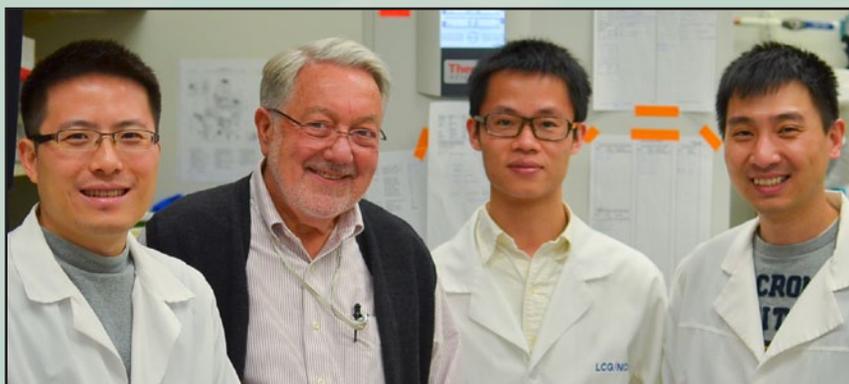
REFERENCE:

Bergeron SA, Hannan MC, Codore H, Fero K, Li GH, Moak Z, Yokogawa T, Burgess HA. (2012). Brain Selective Transgene Expression in Zebrafish Using an NRSE Derived Motif. *Frontiers in Neural Circuits*: 6(article 110), 1-11.

NICHD Fellows Shine at the 2013 GSR Symposium

NIH graduate students, mentors, renowned scientists, and members of the greater NIH community assembled on January 15, 2013 for the 9th annual Graduate Student Research Symposium. This event is the premier forum for NIH graduate students to exhibit their research.

We are proud to note that NICHD graduate students presented 18 out of 116 posters at the symposium, with students **Chris Wassif** of the Porter lab and **Sisi Liu** of the Stratakis lab receiving two of the 12 best poster awards, which entitles them to a generous travel award. We are also happy to recognize that NICHD graduate student **Xuefeng Yin** of the Storz lab was one of only four student oral presenters.



Albert Cheung, Owen Rennert, Dalton Liu, and Alan Pang

Two of the three mentoring awards were given to NICHD investigators, highlighting the tremendous dedication of NICHD mentors to younger trainees. Drs. **Tatiana (Tanya) Rostovtseva** and **Owen Rennert** received mentorship awards upon nomination by students **Kel Sheldon** and **Xiaozhuo (Dalton) Liu**, respectively.

The NICHD Connection would like to recognize the wonderful accomplishments of our graduate students and mentors this year. Chris, Sisi, and Xuefeng summarize their award-winning research below, and Kel shares his thoughts on what makes a good mentor. A big pat on the back to our graduate students for a widely successful year!

(continued on page 4)

NICHD Fellows Shine at the 2013 GSR Symposium

(continued from page 3)

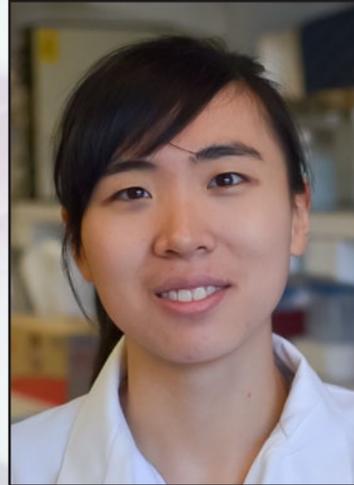
SMALL PROTEINS CAN PLAY A LARGE ROLE

By Xuefeng Yin

NICHD Mentor: Dr. Gisela Storz

Proteins of less than 50 amino acids have been largely ignored in many model systems. They were excluded from initial genome annotation and missed in conventional biochemical and genetic studies. A recent high-throughput study, however, identified over 60 conserved small proteins in *E. coli*, 39 of which localize to the membrane.

One such small membrane protein called AcrZ (formerly YbhT) binds to an AcrAB-TolC multidrug efflux pump—a transporter for extruding toxic substances—by interacting with the pump's inner membrane component AcrB. Cells



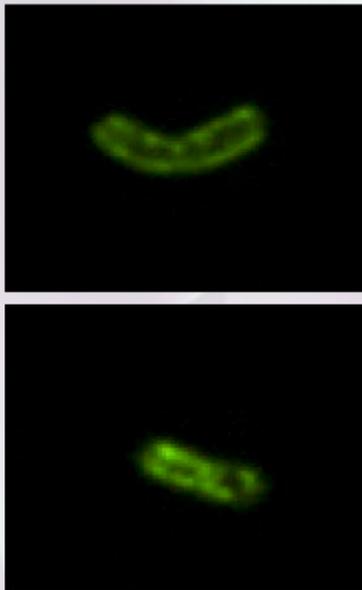
Xuefeng Yin

lacking AcrZ become hypersensitive to many different antibiotics, suggesting that AcrZ enhances the activity of the efflux pump upon binding.

Another small membrane protein, YneM, appears to regulate transport of magnesium (Mg), which is a metal critical for host cell infection of intracellular pathogens. YneM is highly expressed under Mg limiting condition and is required for cell survival during low Mg growth. Overproduction of YneM increases intracellular Mg concentration and substitutes the function of a major Mg transporter in *E. coli*.

Our findings with AcrZ and YneM echo the theme that small proteins can serve as active regulators of membrane proteins and complexes upon environmental stress conditions. By regulating the activity and/or stability of their partners, small proteins help to rapidly relieve environmental stress and enhance cell survival. These findings hold key implications for understanding antibiotic resistance and virulence of bacteria.

(continued on page 5)



Fluorescent microscopy shows that small protein AcrZ localizes to the cell membrane. Courtesy of Dr. Yue Hao.

NICHD Fellows Shine at the 2013 GSR Symposium (continued from page 4)

LEARNING FROM LESIONS IN CARNEY COMPLEX

By: *Sisi Liu*

NICHD Mentor: *Dr. Constantine A. Stratakis*

Carney Complex (CNC) is a multiple neoplasia syndrome inherited in an autosomal dominant manner. Those who develop CNC are at increased risk for noncancerous tumors and bone lesions. Mutations have been found in *PRKARIA*, the gene coding for the type I regulatory subunit of Protein Kinase A (PKA), in CNC patients. To understand how alternative PKA activities and subsequent cellular signaling lead to bone lesion formation, we utilize mouse models that are single or double heterozygous for different PKA subunits; these mice develop bone lesions, mostly in tail vertebrae.



Sisi Liu

According to transcriptome studies, the bone lesions occur when an unidentified population of adult bone stromal cells (aBSCs), a multipotent cell type found in the bone marrow, becomes activated by alternative PKA activity. We aim to isolate and identify these aBSCs, understand the function and origination of this particular set of cells, and find markers to better define this cell population. We also plan to investigate how different genotypes affect particular signaling pathways in the growth and malignant transformation of the lesion-initiating aBSCs in mice. Preliminary data suggests that different genotypes influence the percentage of lesion-initiating aBSCs, which can form colonies in culture conditions, in the mouse-tail vertebrae.

This project is a combination of clinical and basic research as the mutation found in CNC patients has influenced the study's design. We use relevant mouse models to understand how changes in PKA activity, due to subunit mutations, can lead to the recruitment of different lesion-initiating cells. This variability affects the frequency and malignancy of lesion formation. While this study stems from a neoplasia-associated syndrome, we hope these multipotent aBSCs have the potential to be used for bone regeneration and other clinical applications in the future.



Mouse models with Protein Kinase A mutations with tail bone tumors

(continued on page 6)

NICHD Fellows Shine at the 2013 GSR Symposium

(continued from page 5)

GENETIC MODIFIERS MAY EXPLAIN VARIABLE SYMPTOMS IN SLOS

By Christopher Wassif

NICHD Mentor: Dr. Forbes D. Porter

Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive cognitive impairment syndrome caused by mutations in *DHCR7*, a gene that codes for an enzyme (7-dehydrocholesterol reductase) used in cholesterol production. The *DHCR7* mutations cause elevated levels of the cholesterol precursor 7-dehydrocholesterol and decreased levels of cholesterol throughout all tissues.

Patients with SLOS have broad and variable symptoms. At the severe end of the spectrum, SLOS is a lethal disorder due to multiple major congenital anomalies. In contrast, SLOS patients can present minor physical findings with functional cognitive and behavioral deficits. It is likely that genetic modifiers may cause this degree of variation.

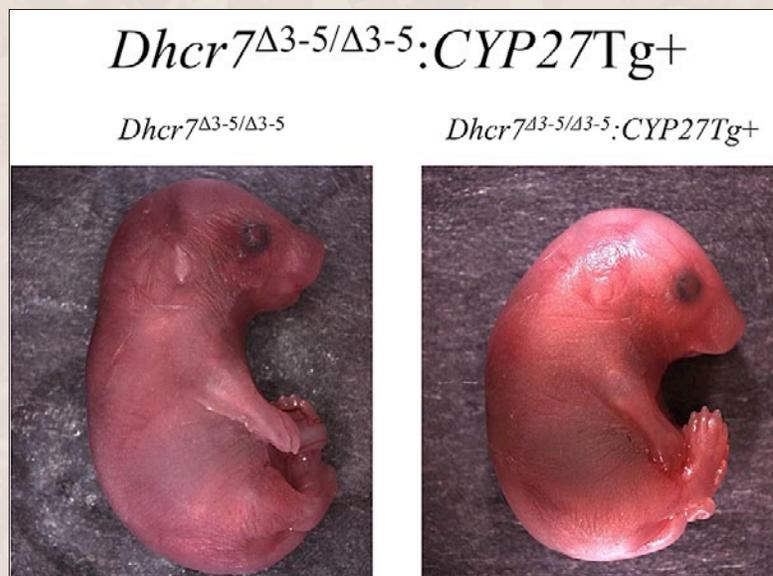
One such genetic modifier candidate is a gene known as *CYP27A1*. The protein product from this gene is responsible for the conversion of cholesterol to 27-hydroxycholesterol in the first step of the alternative bile acid pathway. We have identified two novel oxysterols (oxygenated derivatives of cholesterol): 27-hydroxy-7-dehydrocholesterol and 27-hydroxy-8-dehydrocholesterol, derived from 7-dehydrocholesterol and 8-dehydrocholesterol respectively. The presence of these oxysterols correlates well with serum cholesterol levels.

To test the hypothesis that 27-hydroxydehydrocholesterol suppresses total sterol synthesis during development—thus contributing to the SLOS phenotype—we generated mice harboring both the *DHCR7* mutation and increased levels of *CYP27* protein product.

This new mouse model better recapitulates the malformation spectrum found in SLOS patients and underscores the toxic role of 7-dehydrocholesterol in SLOS.

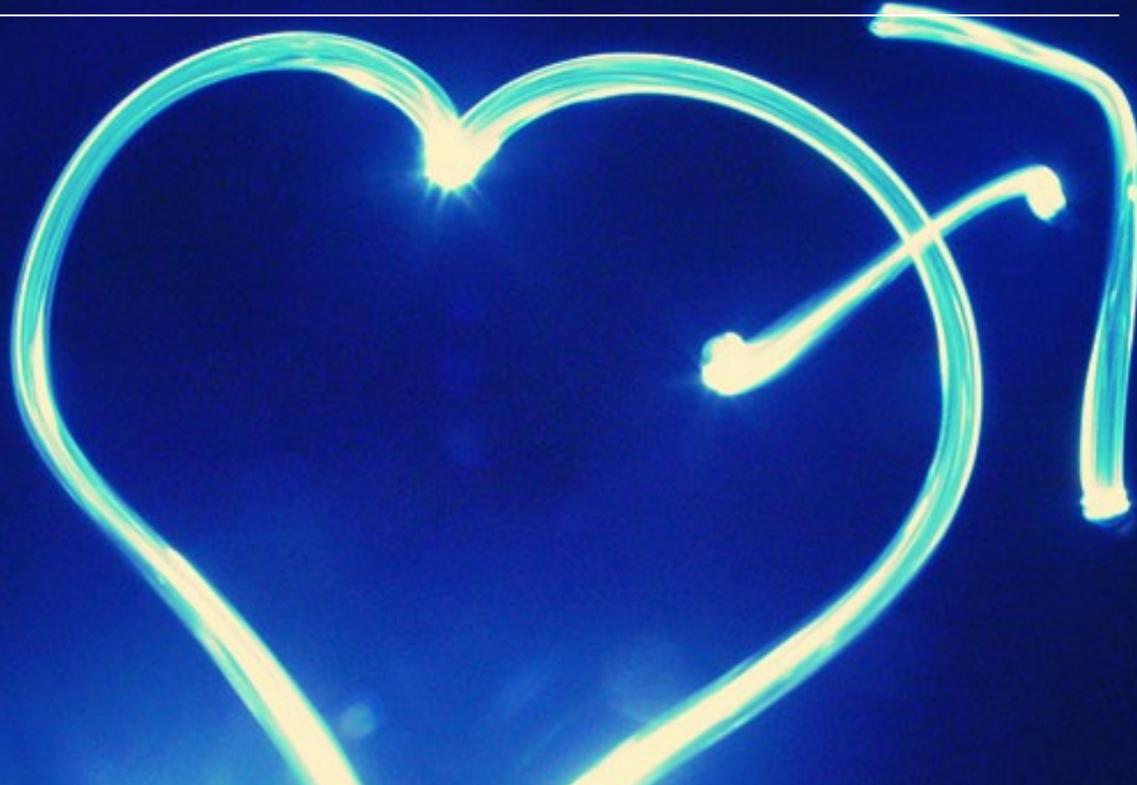


Chris Wassif



*The *Dhcr7* knockout mouse model of Smith-Lemli-Opitz syndrome is phenotypically normal (left), while the same model with increased expression of the gene *CYP27* (right) is significantly smaller, has craniofacial abnormalities, shows an umbilical hernia, exhibits limb defects, and has a curled tail.*

(continued on page 7)



NICHD Fellows Shine at the 2013 GSR Symposium

(continued from page 6)

“A GREAT MENTOR CHALLENGES YOU”

By Kel L. Sheldon

NICHD Mentor: Dr. Tatiana (Tanya) Rostovtseva

I think Tanya said it best, “Mentoring is treating your mentee as an equal, giving him enough room to make mistakes (albeit small ones) to learn from, and seeing him as someone with a new and fresh perspective.” Granted, I feel I am a bit spoiled by my mentor, but I truly feel that great mentors challenge you. They make you think in ways you might not have in the past. They question your reasoning, your understanding, and your motivation. They serve as a constant reminder of the scientist you aspire to become every day. They do not mind getting into passionate debates over results. They constantly question your next steps in life, where you will be conducting your postdoc research, or what scientific company you may be interested in joining. They are eager to promote you and your work. And every once and a while, they join you after work for a happy hour to discuss “you” as a person, not “you” as a scientist.



Kel Sheldon and Tanya Rostovtseva

To check out more from the 9th Annual Graduate Student Research Symposium, please visit <https://www.training.nih.gov/gsc/symposium/9th>

Recapping the NICHD's Panel Discussion on Medical School Interviews

By Rocky Ferrandino

For the postbac applying to medical school, the interview is the last obstacle that stands between you and your dream school. Naturally, this can be a pretty nerve-racking affair. The NICHD recently held a panel discussion for current trainees interested in hearing tips and personal experiences from those who have already been through the interview process.

The panelists, Aivi Nguyen (Jefferson Medical College), Juan Carlos Vera (Medical College of Wisconsin), and Julia Tse (Georgetown University School of Medicine) advised those in attendance that the best way to impress a medical school admissions committee is through solid preparation and knowledge of oneself. Prior to interviewing, applicants should research the school and become familiar with the mission statement, curriculum style, and special programs that they find interesting. An applicant can use this information to describe why he or she is a good match for the program and to ask questions at the end of the interview.

Additionally, interviewees should be ready to talk at length about items mentioned in their applications, particularly

research, community service, and clinical experiences. Interviewers may also ask about any weaknesses in an application. In these situations it is imperative that the interviewee discuss the issue without getting flustered or defensive. Maintaining composure through a stressful interview can demonstrate that you are well suited for the trials and tribulations of a career in medicine.

Our panelists recommended that the interview be treated as a conversation in which you answer honestly and avoid giving responses that you think the interviewer wants to hear. Applicants should realize that the admissions committee has invited you to interview because they already think you are qualified, so you just need to make a positive and memorable impression and accept that the rest is out of your hands.

Trainees looking for interview practice should visit www.interviewstream.com or schedule a mock interview through the OITE website, or with Brenda Hanning in the Office of Education, NICHD. For those with questions about the panel discussion, I can be reached at rocco.ferrandino@nih.gov.

Career Planning with myIDP

By Yvette Pittman, PhD

Dr. Philip Clifford, associate dean and professor at the Medical College of Wisconsin, led an interactive workshop titled “Put your PhD to Work: Planning for a Successful Career in Science” on January 16th. He conveyed an overall message to a group of postdoc fellows: an Individualized Development Plan (IDP) is a must-have item that can guide you into a fulfilling and productive career. Subsequently, you may ask yourself, “How can an IDP help me to identify and pursue my career objectives?”

To start, he shared attention-grabbing data on scientific careers. Interestingly, the population of talented doctoral recipients has grown, but the percentage of scientists employed in tenured or tenure-track positions has steadily decreased since the 1990's. This, of course, has made the competition for academic jobs much tougher for postdocs. Thinking about these facts—as many of us are interested in becoming a faculty member—causes us to wonder: “then what is the next move for me?” Thankfully, with enthusiasm, Dr. Clifford assured the audience that a basket full of career options exists for PhD scientists. Whether it is in academia or away from the bench, he encouraged us to take time to identify the careers that best suit us, even if they are unfamiliar.

Dr. Clifford suggested that there are two types of people in the world—people who plan and people who take life as it comes. In order to succeed in science, he advised us that we need a game plan to prepare

for our desired career paths. Supporting his advice, research has shown that people with a structured plan achieve greater career success as measured by salary, promotions, and job satisfaction.

To help identify career aspirations that are the right fit and develop a step-by-step plan to reach them, Dr. Clifford, one of the authors of myIDP.sciencecareers.org, shared with us this new interactive, Internet-based career-planning tool tailored to meet the needs of postdocs and graduate students in the sciences. There is no charge to use the site and your information is kept private.

Over the next few months, we will feature the amazing myIDP features in a regular “Career Planning with myIDP” column in this newsletter. The next myIDP column will discuss the four-step process to create your own Individualized Development Plan using the myIDP website. It’s waiting for you, visit the website and begin your own career planning process!

February Announcements

POSTDOCTORAL RESEARCH ASSOCIATE (PRAT) PROGRAM

Application Deadline (for positions starting in Fall 2013): February 27

The longstanding NIGMS PRAT Program is a competitive postdoctoral fellowship program to fund research in one of NIH's or FDA's laboratories. NIGMS oversees and funds the PRAT fellows. The program was initiated to address a national need for well-trained pharmacologists and continues to train fellows in emerging research areas. For the next three years (2013-2015), these areas are quantitative and systems pharmacology (QSP) and computational biology. **Fellows must be within five years of receiving a professional degree and within their first year of postdoctoral work at the NIH to be eligible for the award.**

The overall theme of the postdoctoral research project proposed by a PRAT candidate may be in a variety of subject areas, but the focus of the research conducted during the PRAT fellowship should fall within the definition of QSP and/or computational biology. QSP is an approach to translational medicine that combines computational and experimental methods to elucidate, validate, and apply new pharmacological concepts to the development and use of small-molecule and biologic drugs. Computational biology is the development and application of data-analysis and theoretical methods, mathematical modeling, and computational simulation techniques to the study of biological, behavioral, and social systems.

For more information or application materials, visit <http://www.nigms.nih.gov/Training/PRAT.htm> or contact the PRAT program assistant (301-594-3583 or prat@nigms.nih.gov).



Remember, if you apply for and receive a PRAT fellowship, the Fellows Intramural Grants Supplement (FIGS) entitles you to an award (or a stipend boost, for other grants you may compete for successfully). Please note that in the case of a PRAT fellowship, FIGS awards are only granted if the application is funded, not for unfunded applications.

(continued on page 11)

February Announcements

(continued from page 10)

INTRAMURAL AIDS RESEARCH FELLOWSHIP (IARF) APPLICATION OPEN

Note: No citizenship requirements for award eligibility

Are you looking for an opportunity to gain experience in grant writing while competing for an intramural funding award? The Intramural AIDS Research Fellowship (IARF) program is a collaborative effort of the Office of AIDS Research, the Office of Intramural Training & Education, and the Office of Intramural Research, designed to further cross-disciplinary research into HIV and AIDS at the NIH.

The aim of the program is to recruit graduate students and postdoctoral researchers from all scientific disciplines to the broad field of AIDS research and to provide a grant-writing opportunity for intramural fellows whose work can be directly related to HIV and AIDS. The fellowship is open to all GPP students and postdoctoral fellows who are part of the intramural research program at NIH. **THERE ARE NO CITIZENSHIP REQUIREMENTS.** Awardees will be individuals who show outstanding scientific potential through both an imaginative and thoughtful research plan and a well-thought-out career development plan. You can read more about the program at https://www.training.nih.gov/aids_fellowship_home.

Application deadline is **March 1, 2013**. Please address questions directly to Phil Ryan and Shauna Clark at IARF@mail.nih.gov.

NIH BACK-UP CARE PROGRAM AVAILABLE TO FELLOWS

According to the NIH Office of Research Services website:

The National Institutes of Health has contracted with Bright Horizons to offer the NIH community access to back-up care when they need to be at work and their regular child or adult/elder care is unavailable.

The NIH Back-up Care Program is available to the entire NIH community. All NIH Federal Employees, Fellows, Contractors and Tenants are eligible to use the program within the United States. A valid NIH email address is required. For more information, please visit <http://www.ors.od.nih.gov/pes/dats/childcare/pages/nihback-upcareprogram.aspx>

DO YOU FOLLOW NICHD ON FACEBOOK?

A recent NICHD Facebook post may be helpful to intramural fellows:

A range of training and career development programs for postdoctoral and clinical fellows and graduate students are available within the NICHD and across the NIH community.

Links to these programs are available on the NICHD Web site:

<http://www.nichd.nih.gov/training/intramural/Pages/resources.aspx>

(continued on page 12)

February Announcements

(continued from page 11)

NICHD FELLOWS' MEETING AGENDA ANNOUNCED

"An Open Forum to Maximize Your Training Experience in NIH"

February 12, 12:30-1:30PM, Building 31, Room 2A48

Agenda

1. Career Development Tools:
 - a. myIDP website
 - b. *NICHD Connection*: Fellows' Newsletter
2. Upcoming talk in February on 21st Century Science: The role of bioinformatics
 - a. Announcement coming soon
3. NICHD fellows' orientation (separate from OITE)—anyone interested in being a part of the planning?
 - a. Training Grid/Plan
 - b. Let incoming fellows know what is available to them at the beginning of their training
 - c. Information on the Core facilities
4. Ideas for upcoming workshops for spring?
 - a. Cover letter and CV session
5. One-on-One public speaking/interview coaching is available to you with expert Scott Morgan
6. FARE submission is coming up
 - a. Feedback on the usefulness of last year's workshop with previous FARE winners. Do we hold another one?
 - b. The "tips on writing an FARE abstract" document will be sent out to all fellows
7. NICHD Fellows Retreat
 - a. One-day event this year on May 21, 2013
 - b. At the Smithsonian National Museum of the American Indian
 - c. Confirmed keynotes: Drs. John Bahannon and Shirley Tilghman
 - d. Poster, career session, fellows' and Pls' talks
8. Informal discussions on:
 - a. Ways to enhance mentorship in the institute
 - b. A forum we can use to share job searching websites
9. Ideas for "Peer Networking" Event in the spring:
 - a. International potluck
 - b. Bowling (Navy)

(continued on page 13)

February Announcements

(continued from page 12)

CALLING ALL FELLOWS OF NICHD—IT'S IMAGE COMPETITION TIME!

The **9th Annual NICHD Fellows Retreat** will be held in May 2013, and we would like our fellows to supply us with an image that represents some of the work done by us here at NICHD.

Do you have an image of your science that you would like us to use as the image for this year's retreat? The winning image, chosen by the Retreat Steering Committee, will be showcased on the retreat website, on posters, and used as the front cover of the event program.

All submissions that we receive will be used to produce a gallery of our varied imaging talents on the retreat website, so even if yours isn't chosen as the main image, your work will be displayed. Have a look at last year's submissions here (<http://retreat.nichd.nih.gov>) and if you think that you have something interesting, then send it over (at the highest possible resolution) to Nicki Swan (jonasnic@mail.nih.gov).

The deadline for submissions is **February 22nd**. Best of luck!



*Last year's image competition winner,
Takaaki Miyazaki (Mark Stopfer Lab)*

February Events

MONDAY, FEBRUARY 11, 3-5 PM

FELCOM event: Careers in Industry

A panel of industry scientists will discuss their biotechnology careers and how to be successful in a non-academic science position.

Building 50, Room 1227

TUESDAY, FEBRUARY 12, 12:30-1:30 PM

NICHD Fellows' meeting

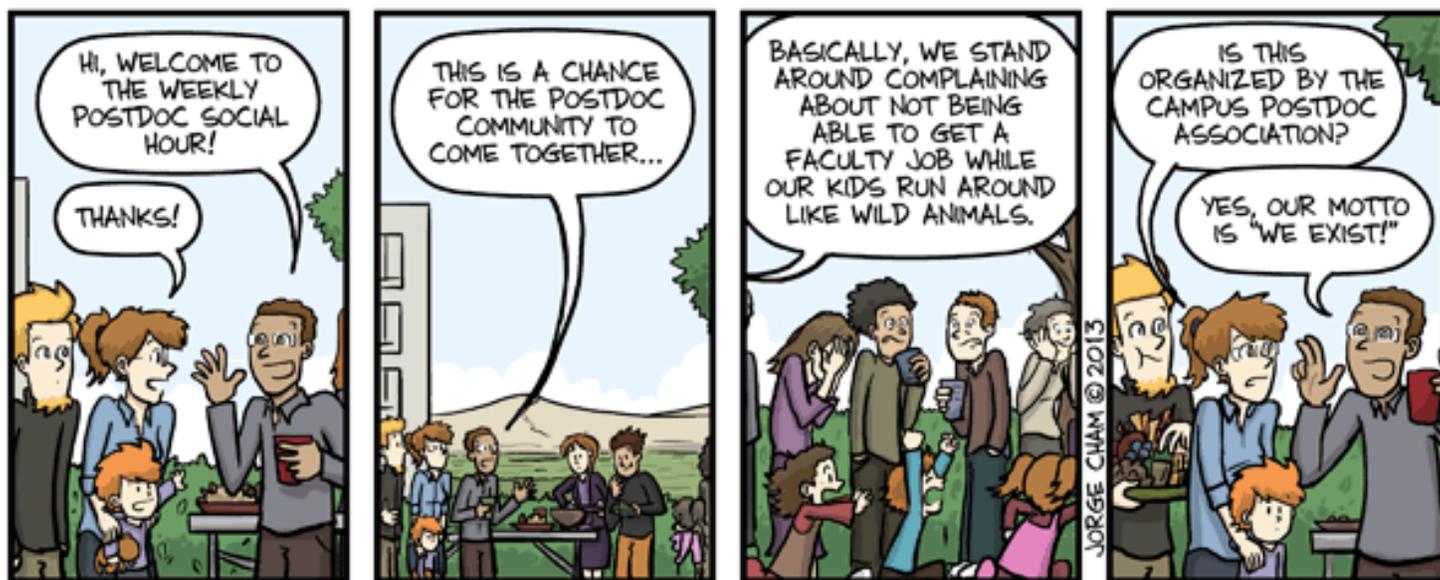
Open forum discussing ways to maximize postdoctoral training here at NIH. We will share valuable career development tools and opportunities, and upcoming events—the fellows' retreat in May and a bioinformatics presentation next month. In addition to your ideas of creating other activities in support of your professional interests and needs, please feel free to bring your lunch.

Bldg. 31, Conference Room 2A48

For the agenda see [page 12](#), and to RSVP, please contact Stephanie Cologna at stephanie.cologna@nih.hhs.gov

COMING SOON

Role of Bioinformatics in the 21st Century
with Dr. Andy Baxevanis, NHGRI



WWW.PHDCOMICS.COM