Former Fellow Follow-up with Dr. Maya Lodish

Dr. Maya Lodish is a Staff Clinician and Deputy Director for the Pediatric Endocrinology Fellowship at the NICHD. Prior to transitioning to staff clinician, Dr. Lodish served as an Assistant Clinical Investigator for three years mentored by Dr. Constantine Stratakis. She completed her fellowship in Pediatric Endocrinology at the NICHD in 2006, during which she focused her clinical research on Cushing’s syndrome. Dr. Lodish has kindly shared her experiences as a staff clinician and deputy program director in a Q&A with The NICHD Connection:

1. What’s your typical day like as a Staff Clinician serving as Deputy Director for the Pediatric Endocrinology Fellowship?

It’s an amazing privilege to have this position because it allows me to have a diverse day. Two of my main responsibilities include mentoring the fellows and seeing patients in the Clinical Center.

I’m very involved in curriculum, faculty meetings, and shaping our fellowship program. Today I spent about an hour meeting with a candidate who we’re trying to recruit to our program. I also get to work closely with trainees. Yesterday, I met with an undergraduate student at the University of Maryland to go over her abstract that we’ll submit to the Endocrine Society on data from clinical work at the NIH.

Blended with that are administrative duties, trying to keep the fellowship in line with the Accreditation Council for Graduate Medical Education (ACGME) requirements. We continuously strive to improve our program and to meet the specifications that are required of our fellowship. Some of it is a bit of paperwork, evaluations, scheduling, etc. I am lucky to work with a very supportive team—especially our program specialist Ms. Fetima Worthington, who juggles all the administrative work to keep the fellowship running smoothly.

(continued on page 3)
Letter from the Editor

This February is quite a month. While you flex your mental muscles at the bench, Olympic athletes go for gold, and Super Bowl hopefuls battle it out on the field. In fact, NICHD fellows have a lot in common with professional athletes. Our careers are a culmination of small victories. Every experiment, just like every game, adds to our know-how and inches us toward an ultimate goal. We may not ski miles a day or skate with unmistakable grace, but at the end of the day, we all do what we do because we love it. Professional athletes strive to break world records and test the limits of the human body, while we strive to break through the boundaries of human knowledge and expand the limits of reality.

Inside this issue, you’ll read about NICHD graduate students’ own award-winning research and the career decisions of a former fellow, Dr. Maya Lodish, who first joined team NIH as a 16-year-old high school student. Jeremy Swan rounds out the issue with a graphic design article about drawing DNA, found in “The Arts” column. And as always, don’t forget to check out the announcement and events section—two fellowship applications are now available!

Go Team!

Your Editor in Chief,
Shana R. Spindler, PhD

Please send questions and comments to Shana.Spindler@gmail.com.
So, the typical day consists of seeing patients in clinic, seeing patients on the ward, rounding with the fellows, going to various teaching conferences, sitting down with fellows one-on-one to mentor them through their research projects, and fielding calls from prospective patients or following up with patients about their particular condition. And then I have two young kids that I’m running around like crazy to pick up on time.

2. Can you describe your decision process about what you wanted to do after your time in the Assistant Clinical Investigator program? Did you always know you wanted to remain at the NIH?

I’ve always loved the NIH. I came here as a volunteer, starting at age 16, in the NIDDK with Dr. Alan Schecter—I have a copy of my volunteer NIH ID from 1994 on my wall! It reminds me of the opportunities that can come to trainees after they have had an experience at the NIH even at a young age. I worked here as a summer student in high school and college, so I knew a lot about what this place offers. I came back when I was in medical school doing a rotation in pediatric oncology, which gave me a taste of how amazing NIH is at bridging the bench and the bedside, working with patients coming to the NIH to participate in clinical trials. The NIH is incredibly cutting edge, and there’s just so much interdisciplinary, exciting work that goes on here. It just seemed like a natural progression from my fellowship to be able to stay here and take advantage of the available opportunities.

In terms of being a deputy director of the fellowship, I get to further my experiences with medical education, which has always been a dream of mine. My parents are both educators. My mom is a high school librarian, and my dad is a retired elementary school principal. I think it’s part of who I am that I really like to teach. It challenges your knowledge to teach something to others. I’m constantly learning new things by being at the NIH every day. And that’s something that I would never want to give up. My fellows teach me new things. My patients teach me new things. Our knowledge is evolving, and I just can’t think of a more exciting place to be. It is also incredibly gratifying to help students in their medical careers, and giving them the tools they need to give back to others. It makes my day when a former IRTA is accepted to medical school, or a former fellow receives a grant or passes their board examinations—to have played a part in their education is incredible.

3. What activities or resources at the NICHD helped prepare you for your career transition?

Dr. Stratakis has served as an amazing mentor along the way, and I have learned from his example. In addition, I have learned from my colleagues on the Graduate Medical Education Committee, which is a group of other NIH program directors, and, in particular, the Designated Institutional Official to the ACGME, Dr. Bob Lembo. He oversees the different fellowships at NIH. He’s a pediatric rheumatologist who has a love of medical education, and he’s mentored me through a lot of the nitty-gritty in terms of how to be deputy program director of a clinical fellowship and how to prepare for a site visit (an official visit to determine if the

(continued on page 4)
fellowship program meets the requirements of the overseeing body, in this case the ACGME). Another thing that helped me was talking to my colleagues who are leaders of other training programs at the NIH.

4. Do you have any advice for fellows who are entering the clinical research career field?

I would say that having the opportunity to be a staff clinician is a wonderful bridge between fellowship and what you decide to do afterward, and being deputy program director is giving me a lot of experience in medical education.

It’s a really rewarding career choice. The opportunities are increasing in this field because positions at academic institutions in clinical research as a clinician-educator are growing.

A few words of advice: keep going to grand rounds and meetings with folks outside your direct area of research—there are opportunities to form many fascinating collaborative endeavors. Never stop being inquisitive, and take advantage of the many resources and mentors here at the NIH. Think about how you got to where you are and the people that helped you get there, and try to return the favor and remember the shoes you used to be in.

5. What are your thoughts about getting clinical fellows and basic science fellows to communicate/collaborate more often? What benefit do you think could come of this type of communication?

It’s integral to the way that research moves ahead to have great communication. In the example of Dr. Stratakis’ lab, a lot of the fellows who are doing basic science come to the clinical conferences. In addition, many of the clinical and basic science projects overlap. For example, we may look at the clinical course of a patient in concert with genetic changes that we find in the lab. A lot of the work we do is collaborative in terms of how patients’ specific genetic make-up affects their disease course. It’s all tied together. Also, many of the most fruitful and innovative projects I have been involved in at the NIH bridge institutes, for example collaborating with the NCI to treat children with thyroid cancer.

A lot of our fellows choose to do part of their research years in the lab and then also do a clinical project to get exposure to both. I highly encourage that option when I’m mentoring the fellows about what research projects to choose. It really helps to broaden your exposure to what’s out there because it’s changing so fast.

6. Is it ok if current NICHD fellows contact you with questions? If yes, what email address should they use?

Yes! My contact information is lodishma@mail.nih.gov.
The Arts: Illustrating DNA in a Cover Graphic
By Jeremy Swan

In September 2012, Dr. Karl Pfeifer reached out to me with a request. He needed a compelling graphic to summarize his research, in an attempt to get the cover for Nucleic Acids Research. I enlisted the help of Amy Ton, an NICHD IRTA and talented artist interested in working on science graphics. We met together with Dr. Megan Sampley, a fellow in Dr Pfeifer’s lab and a co-author on the paper.

The first thing to do when starting a graphic is to sketch a few ideas on paper. While digital tools can certainly help to flesh out ideas, using pencil and paper has a psychological effect of being more malleable and less finished. In my experience, people are more likely to share input and contribute their ideas before moving to a digital format, where changes can sometimes be more time-consuming to implement.

To start, we thought about the composition of the graphic as a whole, in addition to reducing the graphic to the minimal amount of technical information to be included. We concluded the following: we’d represent a set of genes and how they associate differently on nonrealistic, colorized DNA contributed from both the mother and the father (pink and blue) as a simple schematic. We needed to have the DNA appear close in perspective to cue the viewer in on the fact that it was DNA, but then reduce it to a simple line to depict the interactions among the various genes.

Rendering this graphic according to the sketch presented a couple of challenges. How could we easily create DNA in

(continued on page 6)
The Arts: Illustrating DNA in a Cover Graphic
(continued from page 5)

Illustrator? Once created, how could we portray the DNA with a sense of depth without losing the 3D appearance of the DNA? There are several plugins for the line tool in Illustrator, but these are meant to be used on a flat plane. The first iterations of the graphic failed to look realistic because of this, so we needed to find a workaround to add perspective.

We started by creating a strand of DNA in Illustrator to create a straight line that was larger on one end than the other (see figure A). We exported the image to Photoshop, where we “transformed” segments in stages, giving it the perspective we lacked earlier. To accomplish this, I selected everything, except for one “turn” of the DNA (see figure B). I then transformed by “grabbing” the left handle and “squishing” the DNA until the dimensions of the right segment looked proportional. I then deselected the rightmost segment and repeated the same process until the entire DNA strand had the correct proportions. Using this process, the first segment was transformed one time, and the smallest segment on the left would be transformed 27 times (see figure C). This created an image with the proper perspective, which we

(continued on page 7)
The Arts: Illustrating DNA in a Cover Graphic
(continued from page 6)

could then “bend” by using the “puppet-warp” tool in Photoshop (under the “edit” menu). We first “pinned” down the right side of the graphic (see figure D), before adding other points, which could then be moved to warp the image (see figure E). This worked well, except that it caused some segments of the graphic to disappear, so manual “painting” with the brush tool in Photoshop was required to touch up the graphic.

Once we had our DNA, we changed the color by adjusting the hue to produce pink and blue versions to represent DNA that was contributed by the mother and father. We connected a curved line to the end of the DNA, added the other elements, and exported at 300 DPI for submission to the journal. The rest is history!

Congrats to Our NICHD GSRA Recipients

NICHD graduate students swept the Biochemistry/Genetics/Cell & Molecular Biology Graduate Student Research Awards (GSRA), winning three of the coveted honors at the tenth annual NIH Graduate Student Research Symposium on January 14, 2014. Congratulations to Caitlin Younts (Chitnis lab), Bennett Waxse (Lippincott-Schwartz lab), and Alex Ritter*. To recognize this achievement, The NICHD Connection invited the fellows to discuss their research with the NICHD community:

*Alex Ritter’s research summary “How Single Shot Cytotoxic T-Cells Stay Fully Loaded” can be found in the December 2013 issue (Volume 4, Issue 43).

MYOSIN MOTORS MIND THE GAP
By Bennett Waxse
NICHD Mentor: Dr. Jennifer Lippincott-Schwartz

Gap junctions are channels that facilitate metabolic and electrical coupling between adjoining cells throughout the body. In the heart, gap junction localization to the intercalated disc, the specialized interface between two adjoining heart muscle cells, is critical for coordinated contraction. Indeed, in models of heart failure and disease, gap junctions that mistakenly localize to lateral membranes—a process known as lateralization—can cause arrhythmias and sudden cardiac death. To understand the pathogenesis of gap junction lateralization, it is critical to understand how gap junctions are removed from the plasma membrane and degraded.

Multiple studies have implicated clathrin-mediated endocytosis as the means for internalization of these large, double-membrane gap junction plaques. This internalization is reported to require myosin VI, a known motor for clathrin-mediated endocytosis. Once internalized, gap junction plaques cannot be recycled to the plasma membrane and must be degraded. Recent studies have shown that autophagy—an indispensable mechanism for the degradation of large protein complexes, damaged organelles, and protein aggregates—is required to degrade internalized gap junctions.

(continued on page 9)
Our lab has shown that myosin VI localizes to autophagosomes in addition to clathrin-coated pits at the plasma membrane. Without myosin VI, autophagosomes fail to mature and do not fuse with the lysosome. Considering this new role for myosin VI, we aim to determine whether myosin VI plays a role in the endocytosis of gap junction plaques or the degradation of internalized plaques by autophagy—or both. Our results indicate that myosin VI targets gap junctions at the plasma membrane in only a limited fashion. Instead, myosin VI is mainly found on fully internalized gap junction plaques that are also positive for LC3 (the canonical marker of autophagy). Currently, we are trying to determine how the loss of myosin VI impacts the autophagic degradation of internalized gap junctions.

FISHING FOR FACTORS IN SELF-ORGANIZATION OF BIOLOGICAL SYSTEMS
By Caitlin M. Younts
NICHD Mentor: Dr. Ajay B. Chitnis

Zebrafish use a specialized sensory system, called the posterior lateral line (pLL), to sense water movement. The pLL is akin to hair cells of the mammalian inner ear, and it plays an important role in a variety of behaviors, including mating and schooling. Due to its superficial location on the side of the fish, it is an extraordinarily tractable system in which to study cell migration and pattern formation.

The posterior lateral line primordium (pLLp), a small cluster of migrating cells, spearheads the early development of this system. Crawling from the developing ear to the tip of the tail, the pLLp deposits rosettes of cells that will develop into the organs of the pLL. These organs, known as neuromasts, contain mechanosensory hair cells. Displacement of these hair cells communicates the direction of water movement to the fish’s central nervous system.

Two signaling systems work in concert to organize neuromast formation in the pLLp: Wnt and fibroblast growth factor (FGF). The balance of Wnt and FGF...
signaling is a critical determinant of the rate of neuromast initiation and deposition. Many diffusible factors, including Wnt and FGF ligands, associate with heparan sulfate proteoglycans (HSPGs) found in the extracellular matrix and on the cell surface. Differential interactions with HSPGs can influence how far signaling factors diffuse, which cells respond, and how effectively they can activate cell surface receptors.

Our results indicate that 3-O-sulfation, a very rare and specific modification of the heparan sulfate chain, is activated by Wnt signaling and important for regulation of FGF-mediated neuromast formation and deposition. Meanwhile, a loss of heparan sulfate chains altogether results in expansion of Wnt signaling in the pLLp and a decrease in the migration speed of the pLLp. These results indicate that HSPGs are critical for balancing Wnt and FGF signaling within the pLLp, thereby regulating pLL morphogenesis.

Ultimately, this research will determine the mechanism of how interactions with HSPGs regulate signaling networks and morphogenesis in the pLLp. Understanding the regulatory network that coordinates morphogenesis of the zebrafish lateral line system will ultimately contribute to a deeper understanding of the self-organization and emergent behavior of biological systems.
Job Well Done, NICHD Grads

Congratulations to our fellows who recently defended their dissertations!

NAZANIN ASHOURIAN, PHD
Dissertation Title: Establishing the Fidelity of Start Codon Recognition: Role of Eukaryotic Initiation Factor 2
NICHD Mentor: Dr. Alan G. Hinnebusch
Partner School: Johns Hopkins University

ANDREA INTROIINI, PHD
Dissertation Title: Determinants of Human Immunodeficiency Virus-1 Transmission to the Female Genital Mucosa: Role of Co-infecting Pathogens and Cytokines in Semen
NICHD Mentor: Dr. Leonid Margolis
Partner School: Universita’ degli Studi di Milano
Partner Mentor: Dr. Luisa Ottobrini

KELY L. SHELDON, PHD
Dissertation Title: Cytosolic Protein Interaction with the Voltage Dependent Anion Channel (VDAC) of the Mitochondrial Outer Membrane Controls Cellular Respiration
NICHD Mentor: Dr. Sergey M. Bezrukov
Partner School: Johns Hopkins University
Partner Mentor: Dr. J. Marie Hardwick

MAUREEN K. THOMASON, PHD
Dissertation Title: Multiple, Unexpected Roles of the Antisense RNA McaS: Implications For the Prediction of sRNA Function
NICHD Mentor: Dr. Gisela Storz
Partner School: Georgetown University Medical School
Partner Mentor: Dr. Elliott Crooke
February Announcements

SAVE THE DATE! IT’S THE TENTH ANNUAL NICHD FELLOWS RETREAT, APRIL 21ST

The Tenth Annual Meeting for Postdoctoral, Clinical, and Visiting Fellows and Graduate Students is quickly approaching! The retreat will be held at the Smithsonian's National Museum of the American Indian in the heart of DC. It will allow you to step away from the lab for a day to network and participate in a career exploration session and, of course, to learn more about recent scientific developments in the institute.

This year’s speaker line-up is exciting! Dr. Eric Wieschaus of Princeton University, a Nobel Prize Winner, will open up the retreat with a morning keynote address. A few highlights for the events include two scientific perspectives by Drs. Lippincott-Schwartz and Marini of NICHD, and one of our most popular reasons to attend this year’s retreat is the chance to interact with professionals, who were once NICHD fellows, during the career round table session. The steering committee has invited representatives from academia, science writing, and government (FDA, US Patent and Trademark Office, and an NIH staff scientist). In line with our theme of “scientific careers and mentoring,” our afternoon keynote will be delivered by Dr. Sherri Bale, who co-founded GeneDx in 2000 after 16 years at the NIH.

Registration will go live on February 10th at http://retreat.nichd.nih.gov. Don’t forget to sign up for this not-to-be-missed event! For more information, contact Yvette Pittman at yvette.pittman@nih.gov.

IARF APPLICATIONS AVAILABLE—DEADLINE FEBRUARY 28, 2014, 5 PM

The Intramural AIDS Research Fellowship (IARF) 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. Please direct questions to Drs. Phil Ryan and Shauna Clark at IARF@mail.nih.gov.

For information about the application process and requirements, please download the call for applicants at https://www.training.nih.gov/assets/2014_IARF_Call_for_Applications.pdf

(continued on page 13)
February Announcements  
(continued from page 12)

**PRAT FELLOWSHIP APPLICATIONS AVAILABLE—DEADLINE MARCH 7, 2014**

The Postdoctoral Research Associate (PRAT) program is a competitive fellowship program providing up to three years of support for fellows conducting research within the NIH or FDA Intramural Research Programs. Fellows participate in an ongoing scientific seminar series tailored to the PRAT program, as well as receive additional training in a variety of career skills and mentoring.

Applicants should meet the following eligibility requirements:

» Be a citizen or permanent resident of the United States at the time of application.

» Possess a doctoral degree relevant to any biomedical research field and have less than 12 months postdoctoral research experience in the NIH or FDA intramural research program at time of application to the PRAT program.

» Have no more than five years total relevant postdoctoral experience at the time of application.

Research proposed by PRAT fellows encompasses a wide variety of emerging areas of science but a particular emphasis is placed on projects incorporating aspects of quantitative and systems pharmacology or computational biology. Additional information about eligibility, definition of research areas of emphasis, and the application process can be found at - http://www.nigms.nih.gov/Training/pages/PRAT.aspx

**Note:** Because a PRAT scholar moves from a trainee to a Full Time Equivalent (FTE) employee position, applicants for this grant do not qualify for the Fellows Intramural Grants Supplement (FIGS) at the time of application (the $250 award), but will be proposed for a $1000 FIGS award if their candidacy is successful.

**THE NICHD TWITTER IS ACTIVE!**

Want a quick, convenient way to stay up-to-date with NICHD achievements and recommendations? The NICHD Twitter feed is officially active, sign on now and follow @NICHD_NIH.
February Events

WEDNESDAY, FEBRUARY 12, 3-5 PM
Quarterly NICHD Exchange Meeting
Healthy Lifestyles: Eat Well, Exercise Well, Drive Well, Be Well
Fifth floor conference room, 6100 Executive Blvd
No registration required, just show up!

THURSDAY, FEBRUARY 27, 12-1PM
Lunchtime Career Session: Technology Transfer
Are you interested in a career in technology transfer, or have you considered pursuing an MBA after your postdoctoral training?

The Office of Education is offering a brown bag lunch session with Yolanda Mock Hawkins, PhD, MBA, a licensing and patenting manager at the NIH Office of Technology Transfer.

This is a great chance, in a small-group forum, for you to learn about this career path and its various job opportunities. Dr. Hawkins has served as an NIH postdoctoral fellow and the director of the NIH Academy. She completed the FAES Graduate School certificate program for technology transfer before receiving her MBA at Johns Hopkins University.

Given her experience with science careers away from the bench, you’ll get a sense of what fellows can do throughout their training to prepare for the competitive job market. Most importantly, you can hear firsthand why she decided to seek an MBA and how her scientific and business experiences led to a career in technology transfer.

If you would like to attend, please send Yvette Pittman (yvette.pittman@nih.gov) an email.
A Valentine’s Reading List

Give the gift of references.


The St. Valentine’s Day Frontal Passage. Sassen, K., (1980). American Meteorological Society, v. 61, p.122-122. At 1500 MST on 14 February 1979, a rapidly moving cold front entered the northwestern end of the Salt Lake Valley. Frontal passage accompanied by wind gusts in excess of 15 m/s occurred at 1530 at the field site.

Suicide and Homicide on St. Valentine’s Day. Lester, D. (1990). Perceptual and Motor Skills, v 71, p. 994-994. No unusual large numbers of either suicides or homicides on St. Valentine’s Day in the USA from 1972 to 1987 were observed.

GRB 000214 Valentine’s Day Burst. Antonelli, L. A. et al. (2000). GRB Coordinates Network, 561, 1. In the first 20,000 seconds the source had a 2-10 keV flux of 5E-13 erg/cm2E/s and faded by a factor of two in the last 20,000s. We conclude that 1SAX J185427-6627.5 is the X-ray afterglow of Gamma Ray Burst 000214.


Influence Of Valentine’s Day And Halloween On Birth Timing. Levy BR, Chung PH, Slade MD. (2011). Social Science and Medicine, v23, p. 1246-1248. On Valentine’s Day, which conveys positive symbolism, there was a 3.6% increase in spontaneous births and a 12.1% increase in cesarean births. Whereas, on Halloween, which conveys negative symbolism, there was a 5.3% decrease in spontaneous births and a 16.9% decrease in cesarean births.

