What Does a Scientific Career Look Like?
By Swagata Roychowdhury, PhD

With the increased numbers of biomedical Ph.D. graduates in the last decade, competition for academic positions has become fierce. On average, there is a 3.4 percent annual growth in the number of doctoral degrees awarded in the United States.¹ Last year, a staggering 211,900 doctoral degrees were awarded in the life sciences, with 12,100 postdoctoral scientists already appointed in postdoctoral positions for at least five years.¹ Coupled with this, research funding opportunities from the NIH continue to wane, and the availability of academic positions hasn’t been able to keep up with demand. This has led to a gradual shift in the traditional academic career path for qualified doctoral students and postdoctoral researchers.

The introduction of diverse career opportunities requiring advanced science degrees has created a need to evaluate the end-goal of doctoral and postdoctoral training. What was once considered “falling off the bandwagon” of academic research has transformed into rich careers in science policy, communication, industry, and the list goes on. Take the recent statistics for the career paths adopted by NICHD alumni. Only 20 percent continued into an academic research position (See Fig 1). So where do the bulk of the alumni go, and what career choices do trainees have after years of developing fine-tuned skills at the bench?

![Career Paths of NICHD Alumni (331, 2008-14)](image)

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¹ Data from National Center for Education Statistics (2013).
Letter from the Editor

_Nature_ recently published two pieces on “life after academia.”¹ ² They reawaken the reality that not all graduate and postdoctoral scientists will land a tenure-track position, partly—maybe mostly—due to limited academic positions and funding. What makes the articles unique, though, is their emphasis that entering a non-academic field is not always failing at academia. They follow the lives of several successful scientists who find fulfillment in non-academic positions, by choice. The articles combat the assumption that anyone with a Ph.D. who is not in academia simply failed to make it. They also highlight a point that seems to be spreading in conversations around the country: if not everyone is going to become a principal investigator (PI), why aren’t we being trained for other career options too?

NICHD postdoctoral fellow Dr. Swagata Roychowdhury reflects on this question, and others like it, in the first of a series of articles about the changing definition of a science career. We hope all fellows and PIs will join the discussion as we explore the transition from “alternative” careers in science to “all” careers in science.

As you consider your future career options, please visit the Bio Careers website, covered here by Dr. Yvette Pittman. NICHD fellows have access to the multitude of Bio Careers resources, thanks to a subscription provided by the NICHD Office of Education. Our new basic science postdoctoral representative, Dr. Megan Sampley, also is available to field ideas about postdoctoral training opportunities. Her bio and contact information can be found on page 4.

But let us not forget our ultimate goal as NICHD fellows: contributing to a rich body of research on child health and human development. Even if you choose not to continue into academic research, the work you complete here will provide a strong foundation for the next line of questioning. Several of our NICHD 2015 Fellows Award for Research Excellence (FARE) recipients have graciously agreed to share their award-winning research projects with _The NICHD Connection_. Check out their contributions on page 6.

Enjoy the cooler weather, and don’t forget to mark your calendars with important October announcements and events!

Your Editor in Chief,
Shana R. Spindler, PhD


Please send all questions and comments to Shana.Spindler@gmail.com.
What Does a Scientific Career Look Like?  
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But before delving into a world outside the lab, let’s look into how prepared we are to accept this transition. Postdoctoral years have traditionally served to jump-start a young scientist into his or her own independent research. But given the increasing length of postdoctoral tenures and the decreasing number of academic positions available, many top scientists are venturing into careers that have very little to do with pipetting microliter solutions or running Western blots. This transition creates new questions: Who is a scientist? What is the purpose of postdoctoral training if not to develop an independent line of study? How can advisors mentor and support students who will enter a career track different from their own?

Ultimately, we all want to find a career that allows us to use our high level of scientific training in a way that is both meaningful and satisfying. There is much to learn and what better place to start than within our own NICHD community, whose alumni represent a collection of diverse career fields.

In the forthcoming editions of the newsletter, we will talk about this topic from the perspective of our alumni, current postdocs and graduate students, as well as our principal investigators. It is a matter that has taken center stage and hence requires our attention and scrutiny. How we are trained and informed will help us shape our future, be it inside or outside academia. Join us as we explore what a scientific career looks like. I have a hunch that no two look the same.

REFERENCES:
Meet Your New IC Postdoc Rep, Dr. Megan Sampley

I grew up in Murfreesboro, Tennessee and graduated from Middle Tennessee State University, also located in Murfreesboro, with a degree in biology. Having developed a strong interest in studying gene expression mechanisms, I headed to Lexington, Kentucky, a gorgeous town surrounded by beautiful rolling hills and horse farms, to attend graduate school at the University of Kentucky College of Medicine. After joining the Department of Molecular and Cellular Biochemistry, I conducted my dissertation research in Dr. Sabire Ozcan’s laboratory where we studied gene transcription mechanisms for the Ins2 gene in mice. I came to the NIH in 2011 to work in Dr. Karl Pfeifer’s group to research transcription mechanisms of the Igf2/H19 imprinted gene cluster.

While progressing through my professional training, I’ve become passionate about reforming and improving science education and training at all levels ranging from primary school to the postdoctoral level. I worked as adjunct faculty at Bluegrass Community and Technical College in Lexington, and I’m a teaching fellow at the University of Maryland in the Integrated Life Sciences program, where I work with other talented NICHD postdocs to develop more effective active learning teaching methods for an honors cell biology course.

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Meet Your New IC Postdoc Rep, Dr. Megan Sampley
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I’m very excited to serve as the basic science representative for the NICHD, and I’ve recently begun working with Dr. Yvette Pittman on a professional development workshop that we are planning to offer in the coming months. I would very much like to hear from the community of trainees in the NICHD about further developing and creating professional development opportunities as well as concerns about training here in the NICHD. Please feel free to contact me at megan.sampley@nih.gov.

An Institutes and Centers (IC) representative is a postdoctoral-level fellow who serves on the NICHD Fellows Committee on behalf of the institute’s fellow population. In general, most institutes have one basic science representative and one clinical representative. Representative appointments last for 12 months and can be renewed for an additional year. The rep also serves on the NIH-wide FelCom on our behalf.

Responsibilities of the IC representative include attending all scheduled FelCom meetings, participating on a subcommittee, disseminating information to the fellows in the IC, communicating concerns to the committee from the IC’s fellows, and coordinating the distribution of information via subcommittees. In NICHD our representatives also work closely with the Director of the Office of Education to plan events specific to our trainees.

If you would like more information about serving on the NIH Fellows Committee, please contact Brenda Hanning at hanningb@mail.nih.gov.
Presenting NICHD Award-Winning Research

Since 1995, the Scientific Directors and the Office of Research on Women's Health have funded the Fellows Award for Research Excellence (FARE), a competition to recognize intramural fellows’ noteworthy research. Each winner of the FARE competition receives a $1000 travel stipend to present his or her work at an upcoming scientific meeting, the chance to display a poster at the FARE awards presentation ceremony, and the opportunity to serve as a judge for the following year's FARE competition.

Congratulations to all of our NICHD FARE winners. Check out some of their projects here!

CHROMOSOMAL NEIGHBORHOOD MATTERS IN POLYCOMB GROUP REPRESSION

By Sandip De, PhD (Kassis lab)

DNA sequence alone is not enough to govern the complex growth and development of multi-cellular organisms. Epigenetics, the chemical modification to some DNA base pairs and associated proteins, is an important factor too. The Polycomb group proteins (PcGs) are critical players in epigenetic regulation. PcGs, first identified in fruit flies, help remodel chromatin to enable epigenetic silencing of several hundred genes where required. In Drosophila, cis-regulatory DNA elements known as Polycomb response elements (PREs) recruit PcG proteins. Two developmental genes that utilize the chromatin remodeling effects of PcGs and PREs are engrailed (en) and invected (inv). Given that epigenetic regulation influences development, stem cell regeneration, and even disease, we hope to use this model system to better understand PcG regulation.

The genes en and inv form a co-regulated gene complex containing four strong PREs in the region—two at inv and two at en. Fruit flies lacking en do not survive. Surprisingly, deletion of either the inv or en PREs fails to cause over expression of inv or en. Even more surprisingly, flies that have a deletion of all four PREs survive and are fertile. Genome-wide experiments uncovered six potential weak PREs present in the en/inv domain and strong PREs in the Enhancer of Polycomb [e(Pc)] and toutatis (tou) flanking genes. Further analysis using a high-throughput technique to analyze chromosome organization in the cell shows that these weak PREs, along with PREs in the neighboring regions, interact with each other to maintain the repression and three-dimensional structure of the en/inv domain in the absence of major PREs. These data show that chromosomal neighborhood is important for PcG repression and that PREs from flanking genes can regulate en and inv expression.

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Huntington’s disease (HD) is a neurodegenerative disorder characterized by the build-up of toxic mutant huntingtin protein aggregates in neurons. The huntingtin aggregates cause neuronal cellular dysfunction and eventual cell death. Loss of neurons in HD patients leads to the patient suffering from cognitive, behavioral, and motor difficulties, contributing to a poor quality of life and shortened life expectancy. There is a dire need for therapeutics for HD patients, for there is no cure, and current therapies only attempt to control clinical symptoms.

A prevailing goal in HD therapy is to keep toxic mutant huntingtin protein aggregates to a minimum, allowing the neurons to survive. The DePamphilis laboratory has recently identified a family of small molecule therapeutics that promote autophagy, a biological process in which cells digest intracellular components, such as proteins, organelles, and pathogens. Initiating autophagy has been shown to promote the digestion and clearance of protein aggregates. These new small molecule therapeutics are more effective at inducing autophagy than the gold standard drug, rapamycin. In our studies, we have shown this family of novel small molecules to be effective at reducing mutant huntingtin protein aggregates and improving the survival of cells in an HD cell model system. Given that rapamycin is too toxic for long-term treatment in HD patients, the discovery of new autophagy-inducing therapies is of the upmost importance.
PRESENTING NICHD AWARD-WINNING RESEARCH

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EXPLOITING DUAL HOST MACHINERIES
By Yi-Han Lin, PhD (Machner lab)

Intracellular bacterial pathogens utilize various strategies to infect and replicate within their host. These pathogens can alter specific host cell processes, such as signaling pathways and innate immune response, by translocating effector proteins into the host cell during the course of infection. These effector proteins target different cellular pathways and execute their function by mimicking eukaryotic host proteins.

Legionella pneumophila, the causative agent of Legionnaire’s disease, translocates over 300 effector proteins into its host during infection. We used bioinformatics to search for effector proteins that mimic E3 ubiquitin ligase, the enzyme that mediates the last step of protein ubiquitination and controls protein degradation in eukaryotic cells. After experimental verification, we found that the Legionella effector protein GobX exhibited robust E3 ligase activity, and in transfected fibroblast-like cells, displayed exclusive localization to the Golgi compartment. Truncation and mutagenesis studies revealed that a single cysteine residue at position 175 localizes GobX to the Golgi. We further demonstrated that a host-mediated lipid modification to the cysteine residue (called S-palmitoylation) is required for GobX’s subcellular localization and E3 ligase activity in host cells.

Taken together, we have identified a novel bacterial effector protein that can exploit both host ubiquitination and lipidation machineries. Such findings broaden our understanding of the strategies bacterial organisms evolved to interfere with their host and also provide insight into future designs for drug targets.

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Biomarkers are an increasingly valuable source of information, particularly as technology to measure biomarkers has improved. This increased capacity, however, conjures new challenges. The potentially high cost of analyzing biomarkers, along with corresponding measurement error from the lab assay, may prevent researchers from utilizing specimens to their full advantage. One method to simultaneously reduce lab costs and improve measurement precision is to pool specimens prior to performing lab tests. The subsequent measurement is representative of the average biomarker concentration from each of the individual specimens in the pool. Researchers may be hesitant to adopt a pooling strategy, however, since analysis of pools often requires specialized techniques. Statistical analysis can be particularly complicated when the distribution of a biomarker is skewed (i.e., not symmetric), as many measured biomarkers naturally are, since standard analyses may no longer apply.

In our study, we propose an analytical strategy to calculate the association between an observed exposure and a skewed biomarker that is measured in pools. We develop a straightforward and accessible method that is applicable to pools containing specimens from participants with identical predictor values, such as demographic information (e.g., age, BMI, socio-economic status). When pools are heterogeneous, i.e., specimens have different predictors, we propose an effective but more computationally complex alternative. By applying these estimation techniques to strategically formed pools, valid and efficient estimates of the association between an exposure and a biomarker of interest can be obtained at a fraction of the cost required to analyze all individual specimens. Our methodological contribution to the base of available statistical methods to analyze pooled specimens will empower researchers to more confidently consider pooling as a potential study design.

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ADDITIVE EFFECTS OF CHROMATIN REMODELING COMPLEXES ON GLOBAL CHROMATIN STRUCTURE

By Josefina Ocampo, PhD (Clark lab)

One of the most challenging aspects of eukaryotic cells is to understand how DNA is packaged into chromatin to fit the topological constraints imposed by the nucleus. The nucleosome is the basic subunit of chromatin structure and has inhibitory effects on transcription, DNA replication, and DNA repair. Thus, a balance between DNA packing and access must be achieved. Chromatin remodeling complexes are major actors in this dynamic process. They use the free energy obtained from ATP hydrolysis to assemble, eject, or slide nucleosomes. Mutations in components of human remodeling complexes were recently detected at high frequencies in human cancers.

We have addressed the roles of four different chromatin remodeling complexes in nucleosome organization in vivo in the yeast Saccharomyces cerevisiae, including ISW1, ISW2, CHD1, and the essential RSC complex. In yeast, nucleosomes are regularly spaced and show a global phasing (nucleosomes are bound to a particular DNA sequence that keeps them at a regular distance relative to the transcription start site).

We constructed strains with the essential RSC8 subunit under the control of the GAL promoter and isw1, isw2 or chd1 null mutations in all possible combinations in the same genetic background. In the absence of RSC, nucleosomes shift towards the transcription start site with consequent narrowing of the nucleosome-depleted region typically found at most promoters. Nucleosome spacing remained unchanged at every 165 base pairs (bp). In the mutants, the spacing in isw1 mutants reduced by 6 bp to about 159 bp. While the chd1 mutant showed loss of phasing with little change in spacing, the isw2 mutant did not show any obvious changes in global chromatin structure. The chromatin structures of the double, triple, and quadruple mutants represent the sum of the effects observed in the individual mutants, indicating that these remodeling complexes have distinct functions in chromatin organization.

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Income inequality is the unequal distribution of income in a population. It is an issue of increasing concern in the United States (U.S.) where the current income gap between the wealthiest and the poorest Americans is the largest it has been since 1928. Income inequality is thought to have a harmful effect on population health. One metric of population health is the preterm birth rate, defined as birth of a baby before 37 weeks gestation. Preterm birth is a leading cause of infant illness and death in the U.S., and these births more often occur to poorer women compared to wealthier women.

We used statistical models to determine if rates of preterm birth were greater in states where income inequality was increasing compared to where it was decreasing using electronic medical records from 19 hospitals in 11 states and the District of Columbia from 2002 to 2008. We found that women living in states where inequality increased over the year leading up to delivery were about seven percent more likely to have a preterm birth. This was true regardless of the degree of initial inequality, and the amount of increase in inequality was less important than the increase itself. Our findings were not explained by differences in maternal characteristics including race, age, insurance status, smoking or alcohol use during pregnancy, chronic medical conditions, or state-level poverty or unemployment rates. Understanding the mechanisms through which increasing income inequality increases the risk of preterm birth and identifying modifiable risk factors should be priorities for future reproductive health research.
STUDYING BLOOD VESSEL BUILDING BLOCKS—ONE AT A TIME

By Jianxin Alex Yu, PhD (Weinstein lab)

Angiogenesis, a process through which blood vessels sprout from existing vessels, is critical for vertebrate organogenesis and plays an essential role in pathological conditions such as cancer. Although vessel formation has been studied at the tissue level, limited in vivo imaging and a lack of genetic tools have hampered the study of individual cellular architecture and behaviors during angiogenesis. Basic questions, such as how individual endothelial cells (ECs, the building blocks of blood vessels) coordinate movements and shape changes during sprouting and lumenized tube formation still remain poorly understood.

We have developed endothelium-specific transgenic zebrafish and high-speed two-photon confocal imaging methods to examine in vivo endothelial morphological changes at single cell resolution. New fluorescent transgene tools simultaneously mark both EC nuclei and plasma membranes, or cell-cell junctions, to monitor the morphology and dynamic behaviors of individual ECs. Single cell analysis and three-dimensional reconstruction reveal the heterogeneity of EC morphology hinting at multiple cellular mechanisms governing endothelial tube formation.

These newly developed transgenic tools and imaging methods allow us to visualize complex cellular and subcellular dynamics during angiogenesis with an unprecedented level of resolution. Application of this approach with emerging single cell transcriptome sequencing technologies will help us understand not only the concerted EC behaviors during normal vessel development but also the underlying cellular mechanisms of abnormal endothelial formations in zebrafish models of human vascular disease.

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Every human life derives from a single fertilized egg that eventually divides to around 40 trillion cells in a normal adult body. The majority of these cells have identical genetic materials enclosed in chromosomes. Failure to maintain the integrity of chromosomes may cause severe disorders and diseases, including birth defects and cancer. We are trying to understand how normal cells manage to maintain chromosome integrity during the numerous cell divisions that occur during a lifetime.

When a cell is about to divide, each chromosome replicates itself. The next major task is to equally distribute the two copies of chromosomes into two daughter cells. A protein structure called spindles is responsible for chromosome allocation. It works like two Spidermen sitting on opposite sides of a mother cell. They are shooting webs (spindles) to catch one copy of each chromosome and then pull the chromosomes to either side.

Real spindles are not as magical as Spiderman’s webs. They require signals to find their chromosomes. A protein named RCC1 on chromosomes generates the required signals, but RCC1 also exists in other places. How do spindles know which RCC1 is the correct target? In our study, we demonstrate that an RCC1 inhibitor named RanBP1 specifically blocks signals from RCC1 proteins not located on chromosomes. When we removed RanBP1 from the system, spindles were unable to find their targets. We hypothesize that in the absence of RanBP1, spindles are puzzled by RCC1 signals from both on and off chromosomes. RanBP1 may help spindles target chromosomes by blocking non-chromosomal RCC1 signals.

Our study not only reveals a novel cellular function of RanBP1, but also suggests a potential therapeutic target to correct abnormal cell divisions.
Bio Careers®: An Online Career Resource for Life Scientists

JOB POSTINGS AND CAREER BLOGS, ARTICLES, AND WEBINARS

By Yvette Pittman, PhD

As you prepare for your next career move, I recommend that you regularly browse the Bio Careers webpage. It is specifically tailored for life science PhDs and MDs, and as a fellow in our institute, you can register for a free account by selecting NICHD from the member’s list.

First and foremost, the site will allow you to search and apply for over 1500 jobs in academia, industry, consulting, and government. Bio Careers provides many excellent, online, career development resources. It is categorized by career paths and includes hot topics from improving your skill sets to ample career guidance. There are numerous blogs to choose from, which give you an opportunity to ask your own career questions and read other scientists’ job searching stories. For example, the blog titled “The Power of Positive Thinking in the Job Search” caught my eye since many fellows may feel overwhelmed and anxious before even starting their search.

They also have a new “Career Paths” page that is filled with many relevant articles and videos for most, if not all, careers available to life scientists. Additionally, Bio Careers offers a series of monthly webinars presented by speakers who are familiar with the job search process. Some of the recent webinars were on J-1 visas, biotech startups, and industry and medical writing careers. You can also access past webinars, and as a reminder, I circulate their monthly newsletter, which announces the new blogs, upcoming webinars, and latest job postings.

Whether you are researching a new career path or wanting to develop professional skills to become a more attractive candidate, I encourage you to frequently visit Bio Careers at http://biocareers.com.

This is a great resource for all of your career needs!
October Announcements

SAVE THE DATE: NICHD WORKSHOP FOR FELLOWS, NOV 7, 12 – 1PM
“Applying to Teaching-based Academic Jobs”
Friday, November 7, from 12 noon to 1 p.m.
Led by Sydella Blatch, Ph.D., assistant professor of biology,
Stevenson University

For those are you who are considering an academic career, this workshop will provide an overview of what the teaching-based professorship is like on a daily basis, and how it differs from being at a research-intensive institution. It will go beyond introducing you to the components required for an academic application and focus on ways to stand out to various search committees. Dr. Blatch will share some of her helpful tips on writing a teaching philosophy and interpreting job ads to identify what key elements to include in an application. She will be available for individual consultations following the workshop to answer your specific questions on how to prepare a competitive packet.

Please note there are 25 slots available. If you are interested, sign up soon by sending an email to Yvette Pittman, at yvette.pittman@nih.gov.

2015 FELLOWS ANNUAL MEETING / RETREAT PLANNING: JOIN THE TEAM

The annual fellows retreat each spring allows you to step outside of your specialty, present your research, and connect with colleagues across the institute. All NICHD fellows and graduate students are invited to serve on the Steering Committee, which will plan our 2015 event for postdoctoral fellows, clinical fellows, and graduate students. This is a great opportunity to use your organizational skills and gain new transferrable skills while working in a team.

Please send a note to Amber Stratman, chair of the Steering Committee, at amber.stratman@nih.gov to express your interest. The group builds the program for the meeting, invites speakers, reviews abstracts, selects fellow/graduate student presenters, moderates sessions, and plans a social outing, among other responsibilities. We held our first monthly meeting in September, welcome new members and new ideas as we move forward to plan for May 1, 2015 (save the date!).
October Events

WEDNESDAY, OCTOBER 8, 2 – 3PM
NICHD Welcome and Social Event for ALL POSTBACS!
Building 31, room 2A48

Our institute has about 45 postbacs conducting both clinical and basic science research and planning to continue on to graduate or professional schools. We would like to bring you all together over the coming year for career development and outreach activities that will enrich your NIH experience.

On Wednesday, October 8, we will have our annual welcoming event for you to get to know other postbacs and learn about exciting programs such as ICU simulator rounds, shadowing at our Genetics Clinic, and volunteering at the Children’s Inn. This is also an opportunity for you to share your interests with us as we plan future events.

Please RSVP to Yvette Pittman at yvette.pittman@nih.gov. We hope to see you all there!

FRIDAY, OCTOBER 24, 12 – 1PM
Lunchtime Career Session: Science Policy
Building 31, Room 2A48

Are you thinking of a career in science policy after you complete your postdoctoral training?

The Office of Education is offering a brown bag lunchtime session with Katherine Donigan, PhD, a congressional health policy fellow in Washington D.C. This is a great chance, in a small-group setting, for you to learn about this career path and its various opportunities. Dr. Donigan was an NICHD postdoctoral fellow and completed the Genetics and Public Policy Fellowship at NHRGI in January.

Given her recent experiences with a career away from the bench, you’ll get a sense of what you can do throughout training to be ready for this competitive job market, some job searching strategies, and of course, hear how her skills at the bench and other professional activities prepared her for a career in science policy.

If you would like to attend, please send Yvette Pittman (yvette.pittman@nih.gov) an email.

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October Events
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TUESDAY, OCTOBER 28, 3 – 5PM
NICHD Exchange
6100 Executive Boulevard, 5th floor conference room

"Translating Animal Model Studies into Human Health Advances"

Animal models have proven vital to the advancement of scientific knowledge, accelerating the pace of research and in many instances providing a window into biological processes which is not possible in humans. Any given model will offer particular advantages for the process being studied, but ultimately relevance to humans must be demonstrated. Join us for a discussion of some specific examples of animal models as we explore their value as well as the limitations and challenges of translating insights gained from them into humans.
For more photos from the relay, please visit http://newsletter.nichd.nih.gov