The Impact Factor Blame Game

By Damian Dalle Nogare, PhD

“...Science must break the tyranny of the luxury journals. The result will be better research that better serves science and society.” So concludes Dr. Randy Schekman, joint winner of the 2013 Nobel Prize in Physiology or Medicine, in a December op-ed in the British newspaper The Guardian. High profile journals like Nature, Science, and Cell, Schekman argues, undermine the scientific process by emphasizing “the flashiest work, not the best” and lead to a distorted incentive structure. They do this, in part, by aggressively curating their brand, limiting the number of papers published, and instituting a strict policy whereby professional editors accept only the papers most likely to make a splash. The subtext is clear: scientific journals select publications that further their own interests, which are not necessarily aligned with science’s broader goal of serving the public, who ultimately pay the bill.

All due credit to Schekman, who has put his money where his mouth is. He refuses to publish future work in such high profile journals and prefers to publish in open access journals, including eLife, which he edits. A cynic might note that Schekman himself, Nobel Prize in hand, has no further need to publish high profile papers and wonder how his postdocs, when faced with their own job search, feel about this policy. Setting that aside, for postdocs and other early career scientists, this debate is hardly academic. We will all face the decision of where to publish what we consider our best work. Do we send our papers to Nature or Science knowing that we are perpetuating a problem that in the long run may be detrimental to our careers or do we, as Schekman

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Letter from the Editor

Occasionally you come across a scientific publication that catches you by surprise. It may be the novelty of the data or the sheer difficulty of the methods. But sometimes, it’s the story behind the finding that jumps from the page. In this month’s “Hot Off the Press” column, we cover one such story from the Buonanno lab. Their recent Proceedings of the National Academy of Sciences (PNAS) publication reminds us to keep an open mind in research.

I’m now going to jump topics and ask you a question. When you saw PNAS—a well-respected, prestigious journal—in the preceding paragraph, did you automatically form an opinion about the paper? I’ll be honest; when I saw PNAS, I assumed it was probably quite good (and yes, it was!). But is it fair to judge a paper based on its host journal? Dr. Damian Dalle Nogare tackles this difficult question in a thought-provoking opinion piece, found on this issue’s front page. I urge each of you to think about this challenge and share your thoughts with the NICHD community. If you have a response, consider submitting a Letter to the Editor for publication in an upcoming issue (Shana.Spindler@gmail.com).

We round out the first issue of 2014 with graduate student research highlights, a look at the year ahead in the “Thoughts of a Postbac” column, new pictures in the “Life Outside Lab” column, some tips to build your network by Dr. Yvette Pittman, and January’s announcements and events.

Happy New Year!

Your Editor in Chief,
Shana R. Spindler, PhD

Please send your letters, questions, and comments to Shana.Spindler@gmail.com.
suggestions, send our papers to journals such as eLife, knowing that these papers will not carry as much cachet with job search committees?

In game theory, there is a solution wherein no players are incentivized to change their strategy unless the other players also do so. This position, called the Nash equilibrium, is where we find ourselves today. By not publishing in the highest profile journals—in essence, by changing our strategy unilaterally—we punish ourselves. This is unless, of course, we can convince everyone else that it is in their interests to do the same. Scientists have many admirable traits, but I’m not sure that martyrdom is among them. Ultimately, it will be the role of more established scientists to break this cycle, both by refusing to chase impact factors and, perhaps more importantly, by changing the conversation during grant review and job search panels.

When asked recently on the Internet forum Reddit about how to accurately assess publication quality, Schekman responded by saying “I believe the only way to judge the scholarly impact of published work is to read the paper!” This is an admirable sentiment, but the tyranny of the impact factor, which high profile journals exploit and perpetuate, is a very real response to a very real problem—how do we assess the worth of scientific publication? Within our own fields, we have a grasp on who is doing good work, through close reading of their publications, attending conferences, or informal discussions. However, to expect members of a grant review panel or job search committee to carefully read the dozens of papers that might constitute a scientific body of work for each one of potentially hundreds of applicants is unrealistic. Thus, we have to a large extent outsourced the development of the primary metric we use—publication quality—to journals and journal editors, thereby having our goals subsumed by theirs.

We are scientists. Part of our job is to measure things that are extraordinarily difficult to measure. That we continue—out of convenience or laziness—to rely on such poor metrics is a condemnation of ourselves. Before laying too much blame at the feet of journal editors, scientists might wish to take a good long look in the mirror. Perhaps Shakespeare would agree: the fault may not be in our stars, but in ourselves.

Opinions in this article are solely those of the author and do not represent the views of the NIH, federal government, NICHD labs, or anyone else.
As is often the case with discovery, you must neglect what you know to learn something new. Drs. Robert Mitchell and Megan Janssen could have mistaken novel data as an artifact if not for their persistence, passion, and ability to see beyond common knowledge. This is their story.

Mitchell joined the Buonanno lab on a brisk March day in 2011. As a protein biochemist, he enjoyed the challenge of deciphering protein interactions. Mitchell’s arrival was a welcome one. His skill set would enable the lab to utilize a newly created antibody aimed at the ErbB4 protein, an important player in neural activity, but whose protein interactions were not well understood.

He set to work. Within the year, he isolated ErbB4 and identified a peculiar binding partner: GABA receptor alpha 1 (GABARα1), a protein that enables inhibitory neurotransmission—the ability for one neuron to prevent signaling by another neuron. In the hippocampus, GABARα1 is localized to interneurons, short neurons that mediate the activity of long-range connections in the brain. Excited by this finding, Mitchell elicited the help of his labmate, Dr. Janssen, a practiced electrophysiologist with experience recording inhibitory currents.

Mitchell used his cell biology expertise to show that activation of ErbB4 triggered a decrease in GABARα1 from the surface of neurons, and Janssen found that ErbB4 activation reduced the amount of inhibitory currents in the cell, a beautiful correlation with Mitchell’s data. Their pilot study was blossoming into a quick-paced project.

ErbB4 is a special protein, called a receptor tyrosine kinase, whose recognized role is to modify the activity of other proteins via phosphorylation. Mitchell and Janssen reasoned that blocking ErbB4 kinase activity should restore inhibitory currents in these neurons, even upon ErbB4 activation. They exposed the neurons to a drug known to block kinase activity, but the drug seemed to have no effect at all.

“It was just trying to take what would seem to be negative data and figure out what was going on,” said Janssen. At this point, they had a decision to make. Accept the initial biochemistry and electrophysiology data linking ErbB4 and GABARα1 as an artifact, or throw out convention and test for kinase independent activities of ErbB4, something that had never been shown for this protein. While their labmates—and they themselves—were skeptical, their curiosity had been piqued.

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“I’m a protein biochemist, so I was really excited,” said Mitchell, with a chuckle. “Studying what proteins are doing is what I’m all about, so finding a new function for a protein was pretty exciting for me.”

It wouldn’t have been the first time a protein eschewed its kinase activity for a different function. Consider the EGF receptor tyrosine kinase (EGFR), for example. When EGFR is too abundant in cancer cells, the cancer is more aggressive. Researchers attempting to block the EGFR kinase activity found no effect on the cancer’s aggressive nature. To the researchers’ surprise, however, they found that EGFR stabilized a sodium glucose cotransporter. The cancer cells had a selective advantage due to the additional fuel. This novel role did not require the EGF receptor’s kinase activity, a finding with a significant implication: drug design.

For ErbB4 and GABARα1, drug design is a strong motivating factor. Both proteins are implicated in epilepsy and psychiatric disorders, such as schizophrenia. While the biology of these disorders is not completely understood, one explanation is that synchronization of excitatory neurons is impaired.

“Like when you’re reading a book, different parts of your brain communicate over large areas by excitatory neurons, but they’re kept in tune by these local inhibitory neurons,” explained Mitchell. If ErbB4 and GABARα1 are affecting interneuron function in a kinase-independent manner, then there is potential to target this pathway with drugs that avoid kinase inhibition, which is notorious for off-target effects.

Undaunted by their inability to alter neural currents with kinase-inhibiting drugs, Mitchell turned to a transgenic mouse lacking ErbB4 protein in the brain. With the help of labmates, Mitchell spent months isolating ErbB4-negative neurons to record inhibitory currents. At last, Mitchell obtained results showing that ErbB4 was required for inhibitory current regulation.

As more data rolled in, the entire lab got involved. In an elegant experiment, the (continued on page 6)
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lab’s molecular biologist generated a virally encoded ErbB4 protein that lacked kinase activity. Mitchell exposed the ErbB4-negative neurons to the virus and recorded inhibitory currents. The “kinase-dead” ErbB4, when activated, still reduced inhibitory currents.

“It’s really basic science. But it is a profound finding,” said Mitchell. They showed, for the first time, that the traditional receptor tyrosine kinase ErbB4 plays a vital role in inhibitory interneuron activity, and it does this completely independent of its canonical kinase activity.

Hypothesis-driven exploration is the cornerstone of research, but how many times has a “failed” experiment actually been an overlooked discovery? “When you’re figuring out a new mechanism, there are so many more questions than answers,” said Janssen. “That’s what research is doing, just generating questions that haven’t been asked before.”

REFERENCE:
Grad Student Anna Kane to Present at NIH Symposium

The tenth annual Graduate Student Research Symposium is quickly approaching. On January 14, students from the NIH Graduate Partnerships Program will gather to share their thesis work with the NIH community. Our very own graduate student, Anna Kane, was selected for an oral presentation based on her abstract submission. Read a sneak preview of her research below and be sure to mark your calendar to attend her talk! Student oral presentations will be held in the Nature Conference Center, room E1/E2, 9:30-11:00am.

**From Factory to Artisan Baker**
By Anna Kane
Advisor: Dr. Sohyun Ahn

I study how the mouse brain makes new neurons. Researchers formerly thought that neurogenesis, the process by which new neurons are made, ended at birth. In the late twentieth century, researchers demonstrated that new neurons are, in fact, produced into adulthood. This discovery provides hope that we can use these cells to replenish neurons that are lost in degenerative disease or traumatic brain injury.

New neurons are born of neural stem cells (NSCs). Little is known about how adult NSCs are controlled, as they differ greatly from embryonic NSCs. During development, embryonic NSCs are production machines, churning out neurons like a factory might make loaves of bread. At birth, this high rate of proliferation stops, and the NSCs resemble an artisan bakery, making just as many loaves of bread (or neurons) as needed. In order to make sure that new neuron production matches the demand, the adult NSCs must assess what is going on in the rest of the brain. They accomplish this by communicating with neighboring cells in the specialized regions in which they reside, called neurogenic niches. These neighboring support cells provide information about the rest of the brain through cell-cell contact and secreted signaling factors.

Since not much is known about the initial steps that assemble the neurogenic niche, my thesis work focuses on understanding the genetic and molecular mechanism of niche establishment. Specifically, I have shown that Gli3, a gene important in patterning and repression of the Sonic Hedgehog signaling pathway, plays a critical role in cell fate determination and organization of the adult neurogenic niche. By learning how the niche is formed, we can begin to understand how adult NSCs communicate with the niche—information that may allow us to manipulate neurogenesis in a living animal.
Thoughts of a Postbac: Planning for 2014
By Uma Srivastava

NICHD does an excellent job of creating activities that give IRTAs full exposure to many different opportunities. With so many events available, it is imperative to look ahead and make a plan.

At the postbac orientation last September, postbacs Jeffery Head and Amanda Krause discussed multiple activities for postbacs at the NIH. Grab your calendar and take note of the following ongoing activities:

» The Tuesday Genetics Clinic gives postbacs the opportunity to learn from NICHD’s experts in clinical genomics (recapped December 2012).
» ICU Rounds or ICU Simulator Rounds allow postbacs to observe fellows and members of a healthcare team react to patient scenarios using the “Sim Man” patient simulator (recapped November 2011).
» The NIH Children’s INN volunteer program needs postbacs and other fellows to perform science experiments with children staying at the NIH (recapped October 2013).
» Volunteering with Learning Ally is a program where postbacs can volunteer on the NIH campus to record medical and scientific textbooks for the blind and others with learning challenges (recapped April 2012).
» The NICHD Connection newsletter needs postbac volunteers to write for the “Thoughts of a Postbac” column. This is a great opportunity to share your thoughts, practice your writing skills, or even interview NIH scientists about their research and careers.
» The Becoming an Effective Scientist Class is where postbacs can learn how to analyze scientific articles over free pizza lunch (recapped September 2010). It runs every fall from September through December on Mondays.

In addition to these ongoing activities, keep an eye out for additional workshops and seminars. For example, there is an upcoming MD/PhD degree panel session on Monday, January 27, from 2 to 3 pm in Building 31, Conference Room 2A48. While planning your goals for 2014, keep these great opportunities in mind!
Life Outside Lab

On December 3, 2013, NICHD fellows attended the NICHD Fellows Fall Social Event at the Bethesda Naval Bowling Center. From left to right: Celine Cluzeau, Yoshii Hiroaki, Yasaman Ardeshirpour, Rui Kamada, Monica Gupta, Eric Cheng
Building Your Professional Brand and Networks
_by Yvette Pittman, PhD_

The first thing committees or hiring managers do after they’ve received your application is Google you! As a scientific professional who is preparing for this competitive job market, presenting yourself as effectively as possible is essential, and having a carefully thought-out LinkedIn® profile is a great start. I would like to share with you some tips to boost your profile and increase your chance of career opportunities:

» Connect with past colleagues and classmates
» Update your profile with new accomplishments
» Use the free LinkedIn application, and stay connected on the go
» Upload a professional photo
» Write a compelling, succinct summary about your expertise
» Don’t forget to add your work history, your education, and your skills
» Connect with groups related to your career interest and former academic institutions. For example, join the intramural NICHD alumni group before leaving NIH

Remember NICHD is launching the “three-minute talks—TmT” competition for intramural trainees at the graduate and postdoctoral level, to communicate in three minutes or less the substance of your research. Up to ten finalists will receive a “TmT” video clip of their research talk, which can be featured on your LinkedIn profiles. Competition details and submission forms are found at http://fellows.nichd.nih.gov. Sign up quickly, our first workshop is scheduled for January 30, 2014.
January Announcements

CALLING ALL NICHD FELLOWS WHO ARE APPLYING FOR A K99/R00 AWARD IN 2014!

The Office of Education is here to guide you and offer our support as you go through the K99/R00 application process. Give yourself six months of lead-time, and we highly recommend that you first meet with your mentor to discuss your interest in applying. Then, assuming you have the full support of your mentor to apply for this career development award, you should arrange a meeting with Brenda Hanning and Dr. Yvette Pittman. We will provide you with some helpful documents full of grant-writing advice, including a detailed checklist of items that you will need to complete—starting from several months before the deadline up to the in-person electronic submission date. As an NICHD intramural fellow, be aware that you are required to have approval from the Scientific Director (SD) to apply for a K99/R00 award. Your mentor must write a letter of intent to the SD to request authorization to proceed with your application. Note: New applications and resubmissions can ONLY be submitted up to the end of your fourth year; the application deadlines are February 12, June 12, and October 12.

SAVE THE DATE: NICHD EXCHANGE, FEBRUARY 12, 3-5 PM

The next NICHD exchange will be held Wednesday, February 12 from 3-5PM in the 5th floor conference room of 6100 Executive Blvd.

Title: Healthy Lifestyles: Eat Well, Exercise Well, Drive Well, Be Well

Speakers to include:
» Gilman Grave, M.D. (PGNB): “Obesity: From Cosmetic Concern to Medical Alert”
» Tiina Urv, Ph.D. (IDDB): TBA

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10TH ANNUAL GRAD STUDENT RESEARCH SYMPOSIUM THIS MONTH
Join NIH graduate students at this year’s annual Graduate Student Research Symposium. The event features dissertation research posters, a keynote address from Dr. Chris Austin, director of the National Center for Advancing Translational Sciences, oral presentations by NIH graduate students (including our own Anna Kane, see pg 7), granting of NIH Graduate Student Research Awards, presentation of the annual Outstanding Mentor Awards, and a graduation ceremony to honor those who have recently defended. Read more at https://www.training.nih.gov/gsc/symposium/10th. See you there!

CALLING ALL NICHD FELLOWS—IT’S IMAGE COMPETITION TIME!
The 10th Annual NICHD Fellows Meeting will be held in April 2014 and we would like one of you 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. You can take a look at the image submissions from previous years at retreat.nichd.nih.gov. In addition to image resolution and quality, selection criteria include the relevance to our institute’s mission and aesthetics of the image.

If you have something interesting, then send it over (at the highest possible resolution) to Nicki Swan (jonasnic@mail.nih.gov) with a brief caption for the image. The deadline for submissions is January 13th. Best of luck!
January Events

TUESDAY, JANUARY 14, 8:30 AM-4:30 PM
10th Annual Grad Student Research Symposium
Natcher Conference Center

MONDAY, JANUARY 27, 2-3 PM
A SESSION FOR POSTBACS: “A Day in the Life of an MD/PhD”
Building 31, Conference Room 2A48

If you are interested in pursuing an MD/PhD degree or incorporating research into your medical career, this year’s NICHD postbac representatives are hosting a session for you!

A panel of physician-scientists and MD/PhD students will provide insights into the pursuit of their dual degrees and answer questions about the career path. Followed by a 20-minute Q & A, each panelist will speak five to ten minutes—discussing their academic background, why they decided to pursue an MD/PhD, and how they balance clinical and research obligations.

If you would like to attend, please email Dr. Yvette Pittman at yvette.pittman@nih.gov.
Light refreshments will be served.

TUESDAY, JANUARY 28, 12-1 PM
LUNCHTIME SESSION: “Resume Writing Workshop”
Lori Conlan, PhD, Director, OITE’s Postdoctoral Services

Are you looking for ways to improve the overall appearance and effectiveness of your resume? It is often the first impression an employer has of you!

Join us for an interactive workshop that can offer you helpful resume tips and strategies. This is a great forum to gain valuable information you can use to enhance your resume. As a practical approach, Dr. Conlan will provide samples of resumes for attendees to see, using some poor examples to invite input, and highlight how you can convey the best aspects of your work experience, education, and skills as a trained scientist.

If interested in attending, please email Dr. Yvette Pittman at yvette.pittman@nih.gov.
There are only 25 slots available.