Personal reflection (*RNA* journal 20th anniversary)

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I count myself among the fortunate. I get to do science for a living. I spend my days pouring over data, trying to understand what they mean, and testing ideas both reasonable and half-baked. I interact with amazing people every day. They come to my University from the far reaches of the planet. I write. I think. I brainstorm with students and colleagues. On the best days, I perform an experiment. More than anything, I enjoy creative problem solving—trying to find unique solutions to complicated problems with multiple unknown variables. This is my passion. This is my career.

I began my research path approximately one year after the first issue of the *RNA* journal was published. I started as graduate student in Molecular Biophysics and Biochemistry at Yale University in the Fall of 1996. I chose to go to Yale for a variety of reasons, but in essence it boils down to my fascination with RNA as a biological catalyst. I interviewed at Yale shortly after the structure of the P4-P6 domain of the Group I intron was solved by Doudna, Cech, and colleagues. The excitement in the department was palpable. This was the largest RNA structure to be determined since tRNA was published in the early 1970s by the Rich lab. It was immediately clear from the work that RNA could adopt complicated shapes; that two RNA helices could pack together tightly; and that much more work was necessary to understand how structure led to function.

For this reason, I chose to pursue graduate studies in Scott Strobel's lab. He had developed an approach called Nucleotide Analog Interference Mapping that enabled chemical group resolution insights into an RNA's activity. The approach, while relatively simple, was an extraordinarily useful tool to probe RNA structure-function questions. The challenge was interpretation in the absence of a structure, as the approach could not easily distinguish among groups involved in structure formation, ligand binding, and chemical mechanism. Luckily, I worked on the hairpin ribozyme, and my good friend and colleague Adrian Ferré-D'Amaré—whom I met when he was a post-doc in Jennifer Doudna's lab—solved the high-resolution crystal structure of this ribozyme shortly after setting up his own lab. His structure provided the platform I needed to interpret the data that I collected, ul-

timately enabling the completion of my PhD research and publication of my final research paper as a graduate student (in *RNA*). Thanks Adrian. I am sure that I still owe you beverage in payment for the timeliness of your discovery.

The RNA structure field exploded while I was a graduate student (1996–2001), with crystal structures of the hairpin, hammerhead, and hepatitis delta virus ribozymes, and, of course, the myriad structures of the ribosome in various states from a variety of labs around the world. It was an impressive expansion in our knowledge of RNA structure. This work spawned intensive studies into chemical mechanism of RNA catalysis that continue to this day. Metal ion-mediated mechanisms that had long been postulated were revealed in three dimensions. We learned that RNA could act as an acid-base catalyst. New ideas about the chemical mechanism of the ribosome were formulated and put to the test.

It was an exciting time to be a student. Watching the pace of new discoveries was a lesson in the value of an open collaborative environment. Not just among the faculty, but within the student and post-doc population as well. Coffee breaks turned into discussions about methods, tips and tricks, pitfalls to avoid. Lunchtime was practically an informal group meeting. What are you up to today? How'd your experiment turn out yesterday? Happy Hour on Friday was a celebration of the week's accomplishments (or failures, which in truth are really accomplishments if you keep an open mind). I benefited from numerous smart people thinking about my projects, and I did my best to provide insights to their work in kind. It was fun. We had an expectation of success and an eye towards the future. Many of my colleagues did go on to run successful independent research labs. I follow their work to this day.

Now it's 2015 and much has changed. I'm older, balder, and a little less wild than I was as a graduate student. I've come to appreciate the value of scientific discovery not just as a learner, but as a patient too. (Thank you Professor Vilcek and colleagues for Remicade.) As I monitor the literature, I see incredible discoveries continue to be published at an astonishing rate. Most notably, the field of non-coding RNA biology has rapidly advanced in the past 20 years. From the initial discovery of miRNAs, to RNAi technology, piRNAs,

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lncRNAs, and now RNA-guided Cas9 DNA endonucleases, there is hardly an aspect of biology or biotechnology that is not touched upon in some way by RNA. The field has moved so fast it is challenging to keep up with new discoveries. And of course this pace has been aided by new technology—like RNA-seq and ribosome profiling—that enable identification and quantitation of RNA contents of a cell at unthinkable resolution. This ability to generate large, high quality data sets has enabled new experiments that address long-standing issues in RNA biology. The insights continue to roll in with each new table of contents that winds up in my inbox. There has never been a better time to be engaged in RNA research. The tools and toys at our disposal are amazing!

But everything is not sunshine and roses. I worry about the students and post-docs I see around campus, when I'm traveling, and at meetings. I was fortunate enough to have trained during the time of the NIH budget "doubling." I was provided with all the resources I needed to do the experiments I had planned. I watched as universities expanded their research enterprises, as job opportunities grew, and I had a reasonable expectation of success when I went in search of a faculty job of my own. The doubling is over. Sequester inflicted painful cuts to the NIH budget. This is on top of a multi-year trend of flat funding, a de facto cut as salary, equipment, and material goods continue to increase in cost. The current group of students is just as skilled and talented as any that have come before, but many see this trend and rightly do not have the same hope for the future that I enjoyed when I was in their position. Their mentors are spending more time in the office trying to craft "perfect" grant proposals than in the lab. Many universities have slowed or halted hiring. Students are wisely seeking alternative careers.

So what can be done? Clearly, more resources and/or more thoughtful allocation of available resources are needed to

keep the pace of discovery moving. This requires lobbying budget makers to take advantage of the incredible advanced state of research technology. Big business derives from new insights made in basic research labs (Remicade sales in 2013 = \$4.1 billion), so funding basic research is not an altruistic pursuit. More, scientists should support the organizations that are actively working to improve resources and opportunities for their members. This includes scientific societies such as the American Society for Molecular Biology and Biochemistry (ASBMB), which lobbies congress directly to support research budget efforts, and our own RNA Society, which works tirelessly to provide opportunities to students and post-docs through travel fellowships, awards, networking opportunities, and similar.

The easy way to support such efforts is to join the society and publish your work in their journals, including our own—*RNA*. We have a choice in what journals we submit our best work, and we have a choice in how much value to place in each publication when it comes time to evaluate others for hiring, promotion, tenure, funding, etc. I would argue that value is an inherent quality of the work performed, and the best papers I read do an exceptional job of minimizing the "spin" needed to convince some journal editors that a paper has "impact." As editors, reviewers, authors, mentors, students, we must all do our best to ensure that the science that does get published doesn't fool the readership into thinking we've accomplished more than we actually have. Society at large must trust our product. But we must also pay attention to the secondary goal of scientific publishing—providing a record of accomplishment that our students and post-docs can use to move their own career forward. We must do our part to ensure that our students remain excited about their experiments and their future prospects. From what I have seen, the two go hand in hand.

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