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EDITORIAL

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Young Investigators in Toxicology: Is There a Crisis?

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PREPARING STUDENTS FOR GREATNESS IS A FAR BETTER STRATEGY THAN PREPARING THEM FOR FAILURE

Reduced investment in research, sequester uncertainty, and the ever-decreasing spending power of the NIH budget over the past several years have been extremely trying for the scientific enterprise, straining the infrastructure on which so many of us depend. Several have written on the topic and proposed solutions to deal with these challenges. Notably, Ron Daniels, President of Johns Hopkins University, outlined many of the problems in a recent Editorial (Daniels, 2015), and others have addressed some of the more systemic problems with our biomedical research structure (Alberts *et al.*, 2014). Indeed, we may need some fundamental changes in how we perform biomedical research. That said, I believe that toxicologists are better positioned than many of the other subdisciplines within biomedical sciences.

A perceived dearth of opportunities for budding toxicologists is one of the most toxic results of the current scientific environment. I am not suggesting that it is all perception, but rather that it may not be as bad as it seems. Senior scientists lament the current situation often in the presence of their trainees, so much so that many seem to think that quenching the fire inside developing scientists is part of their job description. Such negativity may reflect reality, but mentors must resist the temptation to extinguish the hopes and dreams of their trainees. Intelligent trainees with creativity and enthusiasm are going to eventually succeed in some endeavor. We need this endeavor to be toxicology. Thus, while the basic biomedical scientist certainly has fewer opportunities than in the past, the field of toxicology has had and continues to have much more to offer. We still have the basic research positions in academia, but there are also numerous opportunities in government and the private sector (even though these entities are also suffering from shrinking budgets and reduced investment in research). The need for toxicology is not shrinking. Even if we think the support for these needs is lagging, we must remain competitive for the scarce resources. Yes, the environment now is different than when many of us were in school, but all hope is not lost. We must equip our trainees to succeed in the evolving scientific landscape.

I have taken the Editorial liberty of offering some unsolicited advice to my captive audience designed to abate the crisis.

TO THE MENTORS

1. Support the *future* success of trainees

If programs are not convinced that their graduates will benefit from a graduate degree, either by finding a job or gaining knowledge that allows them to pursue their desires, then we need to stop admitting them. Reducing the number of incoming students may be a necessary step to strengthen the training we are providing. However, I am firmly of the belief that once we make a commitment to a new doctoral student we must back them 100%. Admitting students to a program and subsequently telling them that the future is bleak is not only disingenuous, it is unethical. If that is truly the belief of the faculty then the program should close and stop admitting students today. Certainly, most faculty members want their incoming students to not just succeed, but also to thrive. While it may seem trivial, the first critical step is to cultivate in the students a mindset that will allow for success. Students must see that there is a future for them. Preparing students for greatness is a far better strategy than preparing them for failure. While neither strategy may achieve the intended goal, both will succeed to some degree. It may only take a few of the properly prepared trainees to revolutionize the field, but if they aren't in the field it won't happen. Thus, it is necessary for us to inspire our trainees to envision a future in which toxicology is innovative, robust, and essential. After which, we give them the tools that they need to seize future opportunities. It is also crucial for the academic mentor to be able to provide or find guidance on careers outside of academia as these can be attractive career options for their trainees.

Again, we must train them in cutting-edge techniques and approaches, even if they are outside of our area of expertise. The world in which science is conducted is changing. Basic principles of cause and effect and hypothesis testing still remain,

but we must encourage our trainees to envision what will be needed in 30 or 40 years. We can provide the historical context of the field, but if we do not also include the modern approaches we are doing our trainees a disservice. Encourage your trainees to pursue emerging areas of research and to incorporate novel approaches into their research projects.

2. Recognize your limitations

Senior faculty members who attempt to replicate or clone themselves in their trainees are doomed to fail. As outlined by Daniels and others, biomedical science has changed and will continue to change. The field must adapt and incorporate the most innovative of techniques and approaches. If the field of toxicology continues to innovate, as it should, in 20 or 30 years from now the routine techniques learned in the 1990's will be woefully inadequate. Therefore, mentors must recognize that all of the tools that they have in their scientific toolbox will not be enough for a trainee to succeed in the future. We must train our trainees to innovate and learn even after they graduate. Faculty must be willing to send their trainees to other laboratories and workshops that provide them with training unavailable in the mentor's laboratory. Those that have sabbatical benefits or reduced summer loads should use these opportunities to expand their experimental repertoire to benefit themselves and their trainees. Those that don't should carve out time to attend intensive workshops to refresh their skillset.

Regarding limits, at what point should a senior scientist hang up the pipettes? I see no reason for outstanding scientists who are continuing to do outstanding science to retire due to age. However, those who have reached retirement age and are not willing to compete for grants and be actively engaged in the scientific enterprise need to start considering retirement and perhaps transitioning into adjunct teaching or mentoring positions. For those scientists who are actively engaged in research and of retirement age, it would be great for their institutions to provide them with a 50% position. This would allow the investigator to stay engaged, receive compensation, be available for mentoring, and also to pursue other interests. This could open up funds, space, and positions for a very large number of new investigators. Often 50% of a senior salary is equal to 100% of a junior investigator. NIH is starting to explore an emeritus style grant program that would achieve something similar from the grant award side. My hope would be that the majority of senior investigators recognize the need to strengthen the pipeline of the field and transition into positions that create opportunities for young investigators. I am not one who thinks that investigators over 65 should be forced to retire as many of them are doing stellar work, but they do need to be given opportunities that are mutually beneficial to themselves and the young investigators looking to begin their careers. For those scientists in government or industry, as you approach retirement age consider expanding your commitment as mentors and teachers through adjunct academic appointments. To those senior investigators who are dead set in working full-time until they are dead, I say for the sake of the future of toxicology, if you are not going to retire, at least stop complaining. Yes, science is very different than it was 40 years ago. We know.

3. Shelter your trainees from the assault of negativity

On the topic of complaining, it is not only coming from the curmudgeonly senior faculty member. Some days negativity comes from all directions. As a mentor it is essential to protect trainees from the barrage of negativity and it starts with you. As noted above, once you agree to take a trainee into your group it is imperative that you let them focus on developing as a creative scientist. When research funding is scarce it is easy to complain about the system, but doing so in front of trainees merely trains them to blame others. Young scientists must learn to take responsibility for their scientific actions. It is not the buffer's fault or the mouse's fault. Trainees must learn to be responsible for every facet of their experiment and research. Mentors do not like the trainees who blame others for their problems. Why then as faculty members or senior scientists suddenly are we allowed to blame our laboratory woes on external factors, such as the payline, study section, program officer, department chairs, and deans? Yes, the paylines have decreased, yes, the awards are smaller, but what good is complaining in front of trainees? Stop discouraging young investigators by wringing your hands over budgets and the minutia of academic life. It is your job as the mentor to insulate the trainee from the vagaries of science and let their scientific innocence shine through. When a grant or paper is rejected, allow yourself 1 day to vent, but not in front of trainees. Demonstrate the value of resilience by showing your trainees how one moves forward after rejection. When we teach people to blame others it fosters negativity. When we teach people to find solutions it fosters creativity.

TO THE TRAINEES

1. Take responsibility for your future

Nobody cares more about your future than you. Don't expect otherwise. It is your responsibility to devise a strategy for success. You will need the input of several advisors and mentors. Individualized development plans can be helpful in providing a framework, but they are no panacea. Reflect on your inherent strengths and weaknesses. Can you build upon your assets and overcome your limitations? Trainees should be very deliberate in what they are trying to get out of their education. What areas have not been covered in the curriculum? Are there workshops that can help you gain a certain skill? Are there other scientists on campus that can assist you? Don't expect your faculty mentor to be thinking about these questions all of the time like you do. It is your job to figure out what you need and then go out and get it. Professors have a dizzying number of responsibilities and challenge in their academic lives. It is unrealistic that your dissertation mentor can provide all levels of advice and guidance to you. Thus, it is important to expand your mentoring sphere. Often the most influential mentors are not people one would even refer to as a mentor. It could be a visitor at your poster, the author of a key piece of research, or a colleague in a different field. You need to figure out what type of mentoring and support that you need and then seek it out.

2. Don't ever stop learning new techniques and approaches

To trainees, your advisors have accomplished a great deal to get into the positions in which they reside. You should respect that effort, but that doesn't mean their laboratory skill set will give you everything that you need. You must continually be pushing your limits from a technique perspective and that usually requires going outside your mentor's expertise. Attending courses at the Society of Toxicology meeting, Cold Spring Harbor Laboratory, European Molecular Biology Laboratory, or Woods Hole Biological Laboratory is a great way to get introduced to

cutting-edge approaches. Look for those courses that expand your skill set. The word toxicology doesn't need to be in the title, in fact it is probably better if it isn't. Twenty years ago I attended a workshop on differential display. This was the cutting-edge way to measure the differences in mRNA expression between 2 samples. Within 6 months the technique was obsolete due to the invention of the microarray. I didn't feel as if I had wasted my time, in fact, I was acutely aware of how much better this new technique was than the one I had just learned.

One only needs to look at the Tox21 initiative to see how the field is changing. NIH is now using robotic screening of thousands of compounds to look for their toxic effects. How many trainees are being equipped to interface with these approaches of the future? Are your getting experience with developing assays and scaling them up to 384 or 1536? Are you looking at these results as you conduct appropriate mechanistic follow up in more complex systems? Are you learning about the computational and systems biology approaches to develop the models needed to interpret the data? For the most part, your mentors don't have this expertise. Many of us typed our dissertations on an actual typewriter, or for those slightly younger we may have printed using dot matrix printer. Big data are a relatively new concept and one that few mentors have the appropriate expertise. One must seek out opportunities to learn these new approaches and tools. Results from these approaches complement basic laboratory research as they have their foundation in biological mechanisms of toxicity.

3. Gather information on your field from scholarly sources

Don't ignore reality. Trainees should be cognizant of how the biomedical landscape is changing, but they should gain this information from accurate sources and not base their scientific mindset on conjecture or water cooler complaining. When you want to learn about a new protein you go to reliable sources that are focused on data. So to for learning about the challenges facing your field. President Daniels' article is an example of the thoughtful type of analysis that trainees should be reading. To the young investigator, my advice is simple. Learn about the changes that are occurring in science, but stop listening to the naysayers. They have experienced unwelcomed change during their career. It has jaded them. Refuse to participate in their negativity.

4. Nourish your scientific curiosity

Trainees are continually juggling their responsibilities set by their mentors and programs. From laboratory meetings, graduate program deadlines, committee meetings, comprehensive exams, to tedium in the laboratory the tasks can feel daunting. These day-to-day activities involved in research can lead to a myopic view of the process. Trainees must learn to take a step back to view the big picture of science. Watch the acceptance speeches of Nobel laureates (certainly more important that acceptance speeches at the Oscars). Read biographies of great scientists. Let yourself get caught up in the excitement of research. It is essential to continue to remember why you entered science in the first place. Science has been and will continue to be a noble pursuit. Once you forget this, it is nearly impossible to tolerate the often oppressive failure that you will face in your daily life as a scientist. Those that retain their enthusiasm for the science are much more resilient, and ultimately more successful. Many of your colleagues will be facing personal crises in the upcoming years. There are fewer jobs in all sectors, but that doesn't mean the entire field is in crisis mode. Science will likely experience some transformative change in the coming years, but we will always need scientists with expertise in toxicology. Be one of those scientists.

CLOSING THOUGHTS

While there may be an impending crisis facing young investigators in toxicology and science in general, I believe that it can be averted if the field and the trainees themselves take some deliberate steps to do so. Our training programs must proactively embrace big data and bioinformatics. We must close the gap between cutting-edge science and our research endeavors. Our trainees should be demanding this knowledge and our training programs should be delivering. If we give into the general pessimism in biomedical sciences and continue to discourage our trainees we will indeed have a full-blown crisis. I am afraid that we are creating a system that is discouraging the superstars who will be essential for our future survival as a discipline. Losing this type of investigator to other fields would be tragic. We need to emphasize that toxicology has more to offer than many other subdisciplines in biomedical sciences. Career options beyond the professorate have always been part of toxicology. Toxicology has roles in basic science, pharmaceutical science, regulatory affairs, environmental health, health care, consumer products, emerging technologies, and the list goes on. We can use the scientific and professional diversity of our field to our advantage. We can give our young investigators an immediate advantage by continuing to make toxicology relevant, but the trainees must be equipped for competition. We need to step up our recruitment and training of those trainees who we have identified as having the potential to lead toxicology into the future. Finally, to mentors and trainees- don't let toxicology be mediocre. Aiming for greatness is the best strategy to avert crisis in the field, young and old alike.

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