Stories in Molecular Medicine April 2021

Kavelaars, Annemieke; Claesson-Welsh, Lena; Culp-Hill, Rachel; Lothstein, Katherine; Rao, Rajesh C.; Boehmer, Verena I.; Dvela-Levitt, Moran

Published in:
TRENDS IN MOLECULAR MEDICINE

DOI:
10.1016/j.molmed.2021.02.002

Publication date:
2021

Trends in
Molecular Medicine

CellPress

TrendsTalk

Stories in Molecular Medicine April 2021

Life experiences influence our research and motivate us to ask scientific questions and shape research goals. Here, *Trends in Molecular Medicine* authors share their journey in science. Their portraits highlight the diversity of scientists and that there is no standard career in science. We hope that these inspiring stories will help to build bridges of understanding between science and society, and motivate others to join the melting pot of scientific disciplines united in *Trends in Molecular Medicine*.

Annemieke Kavelaars, PhD
University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Back to the Beginning

I started my career as a graduate student at the University Medical Center Utrecht, The Netherlands, where I stayed for most of my career. Mentors and colleagues frequently told me that I 'needed' to move on, go abroad, have new experiences. I did not listen, and never regretted it. That does not mean I never changed. The stable foundation gave me the opportunity to explore many avenues in this collaborative, scientifically rich, and stimulating environment.

I had the privilege of growing up as a scientist in the newly emerging multidisciplinary field of psychoneuroimmunology. When I started as a graduate student, my mentor and lifelong collaborator, Cobi J. Heijnen, changed from basic immunology to investigating the interactions between the immune and nervous system. Being part of this new adventure was highly stimulating and exciting. It was also tough at times; we encountered a lot of 'nonbelievers' ridiculing us and suggesting that we should use our skills to address a 'relevant' question.

To give just one example, my PhD thesis focused on leukocytes as a novel source of the opioid peptide beta-endorphin. This very novel idea, launched by Ed Blalock, was met with a lot of reluctance and skepticism and labs across the street tried to show we were wrong (and failed). After graduating, I moved on to other studies on neuro-immune interactions. In 2012, I finally did go abroad to the M.D. Anderson Cancer Center, another great institution. I now study neuro-immune interactions in chronic pain, for example, after chemotherapy. It is cool to see that I am back where I started; nowadays, it is completely accepted that leukocytes make opioid peptides, which have a role in controlling pain.

If I can give young scientists one piece of advice, it would be trust your instincts: do what you love, and love what you do.

Lena Claesson-Welsh, PhD
Uppsala University, Uppsala, Sweden

How I Have Learnt to Better Accept Criticisms

One of many rewards in science is the opportunity to discuss one's research with colleagues. My interest is in vascular biology, and I frequently interact with colleagues in academia, clinical medicine, or industry. This diversity of interests and perspectives among the colleagues opens the possibility of insightful advice, but also sometimes results in uncomfortable criticisms.

To receive feedback and advice is crucial for most of us. However, feedback can sometimes be perceived as destructive criticism, as is often the case in the publication review process. For conflict-shy, consensus-seeking Scandinavians, such as myself, even mild criticism can be difficult to accept. However, thinking back on my years in science, I can now appreciate that criticisms that at the time felt hurtful in fact have

been very important and resulted in considerable changes in the way I conduct my research.

I remember especially once when I was on a sabbatical period at Harvard Medical School during the 1990s and participated in a celebration together with the entire research program. Someone came up to me as I was standing there with a glass of wine in my hand, and said: 'I don't care much for what you do with your transformed cell lines. Why don't you use more relevant models?' At first, I was shocked by his candor, and it was difficult for me to finish my wine. However, it also forced me to think hard about what I actually wanted to achieve with my work. This triggered my decision to widen the scope of my research. I still occasionally use the transformed cell lines, but with care. Without those words, I would not have changed gears so decisively. In fact, it made me less hesitant to share my work with others. To receive sincere criticism is tough, but it may improve your research!

Rachel Culp-Hill, PhD Candidate
University of Colorado Anschutz Medical Campus, Aurora, CO, USA

Small Actions Create Big Impacts

My favorite science comic is from *Twisted Doodles*, which says: 'A lot of scientific research isn't about groundbreaking discoveries. It's performing a lot of experiments to find out a piece of information. Then you write a paper about what you did and what you found, and you put it where other scientists can read it, with all the science gone before. And it may just be a speck on the great mountain of understanding, but every piece pushes us further into the unknown… so that we may know it.' I have it pinned to my lab desk, so I am reminded every day why I chose to be a scientist: it is about the process and the joy of discovering something that no one else has before. In the grand scheme of things, that piece of information is infinitesimally small. However, there are ~8 million researchers worldwide and, together, those specks amount to the breakthroughs we hear about, whether it is finding water on Mars, completing the human genome project, or creating a vaccine in record time. However, this viewpoint does not come naturally: it is taught by others who share it. Similar to many other scientists, I have some fantastic mentors who push me beyond traditional ways of learning and thinking. I am not someone who experienced a life-changing event that led to a sudden career epiphany. Instead, I have been continually encouraged and inspired by people around me who, even with a mountain of work before them, chose to make time to support a young scientist. Mentorship is an under-rated facet of science, but is crucial to recruit and retain researchers. So, if you are in a position to be a mentor, I urge you to do so: that scientist might find the speck we need for the next big breakthrough.

Katherine Lothstein, PhD Candidate
Rutgers New Jersey Medical School, Newark, NJ, USA

Small Steps toward a Global Goal

Scientific research has been a part of my life from an early age due to my parents' involvement in medical science. Research lab positions and college courses further developed the focus of my interest. I was intrigued by the host immune response to various disease states, both extrinsic and intrinsic. This interest in infectious disease, cancer biology, and immunology directed me toward obtaining a Master's in public health in epidemiology and, subsequently, joining Rutgers to conduct my doctoral research. The combined study of molecular medicine and immunology highlights the dynamics of our immune system and the myriad, still unidentified response pathways to pathogens and/or diseases. These unanswered questions in this research area have motivated me to pursue my current area of study, where I am looking at molecular

interventions for specific disease pathologies. This past year, our global pandemic has introduced numerous hurdles that have been disruptive to my laboratory work. Yet, it has allowed me to recognize the inherent flexibility in scientific pursuits, where time spent on investigating and planning the stages of any project, and subsequent data analysis before further investigations, is as important as bench time. This insight allowed me to remain successful in this 'new normal'. Additionally, during periods when my research appeared stalled, I found new ways to focus my studies and renew my interest in my field, as well as increasing my knowledge of related fields. The current health crisis has demonstrated the need for disease prevention, as well as intervention. With my background in epidemiology, I recognize the intersection of research at both the molecular and global levels. Connecting primary research to world health is an area that I look forward to pursuing in my future endeavors recognizing that research in molecular medicine has a key role in medical innovation and global health.

Rajesh C. Rao, MD
University of Michigan, Ann Arbor, MI, USA

More Than Meets the Eye

Born and raised in the Midwest US, I was a first-year undergraduate at the University of Wisconsin-Madison when I learned that across campus, human pluripotent stem cells (PSCs) were first cultured. As I saw the news headlines, I realized that the capacity to grow virtually limitless amounts of hard-to-isolate cell types, such as many CNS neurons, could one day transform how we understand development and disease, and revolutionize regenerative medicine, especially in diseases which rob individuals of their most important sense, vision. It was this moment that sparked my interest as a physician-scientist.

Years later, as a retina surgeon-scientist, I've realized ophthalmology and the research laboratory have a lot in common. One spends lots of time at a microscope, seemingly engrossed in the birth, life, and death of the retina. At the lab microscope, I see how pluripotent stem cells form the rudimentary embryonic eye cup, as retinal organoids. In the clinic, I diagnose retinal disease in children, teens, adults, and elderly—many of whom I see every month for years—through the slit-lamp microscope. I use the operating room microscope to improve vision in these individuals through retinal surgery. The many facets of CNS disease, including bleeding, fibrosis, atrophy, edema, tumor require MRI or CT scans to visualize. Yet one can see the retina with one's own eyes using a couple of handheld lenses or a low-tech microscope. Yet as ophthalmologists, we are faced with blinding diseases, like macular degeneration and diabetic retinopathy, that are, each, nearly as common as all cancers put together. Yet the most frustrating dimension of this field is we cannot restore when retinal cells are lost to these pathologies. This unmet need drives me not only to better understand how mechanisms of gene expression governed by epigenetics contribute to vision loss but also how best to weaponize this knowledge against blindness through regenerative medicine approaches using stem cells, organoids, and chromatin-modifying drugs.

Verena I. Böhmer, PhD
University Medical Center Groningen, Groningen, The Netherlands.
Current affiliation: University Hospital Heidelberg, Heidelberg, Germany

Working at the Interfaces of Natural Sciences

Molecular biology is based on chemistry, which is based on physics. We are alive due to several thousands of chemical reactions that are all based on the physicochemical properties of molecules. I was always curious about Nature, for example how a tadpole turns into a little frog in only a few weeks' time. Since all natural sciences are intricately connected, I could not decide which one to study. Choosing biomedical engineering enabled me to appreciate interactions between all natural sciences to improve current healthcare.

During my studies, I received training on the interface of chemistry and biology, in particular in drug and gene delivery systems and medical imaging. Working in this interdisciplinary context enables me to be involved at different levels of projects, from the design and synthesis of molecules to their application *in vitro* and *in vivo*. To see a molecule that I synthesized showing an effect at a cellular level or even in animals motivates me every time to continue my research.

Knowing the fundamentals of different disciplines also taught me to work outside my comfort zone, a quality that involves a lot of work, persistence, and resilience. One has to strive to constantly improve oneself, being regularly confronted with lack of knowledge in certain areas. However, medical imaging is a unique field that requires an understanding of not only the molecular interactions between the medical imaging agent and its target, but also its biological function and participation in diseases, to be able to evaluate its potential as biomarker for a specific imaging technique. Doing my PhD on medical imaging at the University Medical Center Groningen enabled me to work on diverse interfaces of natural sciences. I hope that one day my (future) research in this field can contribute to improve current diagnosis and/or therapy approaches.

Moran Dvela-Levitt, PhD
Bar-Ilan University, Ramat-Gan, Israel

Feed the Flames

My interest in biology dates back to my high school days. While learning about the process of DNA replication, my assignment was to design an experiment to prove which of the three replication hypotheses is correct, based upon the legendry Meselson–Stahl experiment. Designing this experiment, predicting the possible outcomes, and for one second stepping into the shoes of the great scientists witnessing the results that are about to influence tremendously science and humanity, sparked a great light in me.

In an attempt to feed the flames and pursue my own scientific adventure, I enrolled in graduate biology studies. My scientific curiosity was nourished greatly by my doctoral mentor, who taught me much about research and beyond, but most of all, I grew to appreciate his great talent for storytelling. Strengthened by my own experiences, I learned that my passion includes the desire to tell the science story, engage, educate, and light a spark in the next generation of scientists. I truly believe that one's philosophy of science should be intertwined with education.

Moving on to my postdoctoral fellowship, while exposed to giant scientific leaders, innovative technologies, and transformative science, a crucial lesson learned from my mentor was the importance of bedside to bench work. I learned to appreciate the power of integrating the patient community to collaboratively impact translational research.

While establishing my own independent lab now, I reflect upon my experiences during the early stages of my career and the morals and lessons I would like to convey to the young and motivated scientists joining my group. I am grateful to the mentors and colleagues that paved my way. My vision is to conduct collaborative translational science, to educate and inspire the next generation of scientists, and hopefully be a source to light their spark in science.

https://doi.org/10.1016/j.molmed.2021.02.002