JEM Journal of Experimental Medicine

PEOPLE & IDEAS

Golnaz Vahedi: My environment enables me to achieve impossible goals

Lucie Van Emmenis

Golnaz Vahedi is an associate professor of genetics at the Perelman School of Medicine, University of Pennsylvania. Golnaz runs a multidisciplinary lab that uses cutting-edge computational and experimental approaches to understand the molecular mechanisms by which genomic information in immune cells is interpreted in normal development and during immune-mediated diseases. We talked about her diverse scientific background, the benefits of integrating molecular biology and immunology, and the importance of staying positive in academia.

Please tell us a little about yourself and how you first became interested in science.

I was born and raised in Iran, a country rich in history and marred by complex political issues. As a high school student, I liked physics and math and thought I disliked biology, mostly because of the way it was taught to us at the time. In order to enter university, all high school students in Iran take the same ∼5-h exam (called "Konkoor"), which occurs only once a year. It is an excessively harsh method of student selection, as your performance in that grueling 5-h assessment determines your fate, and if you fail, you would need to wait another year to take the exam. It is not an exaggeration to say that the most critical day of my life was the day I took Konkoor, defining what came next in my career. I got a high ranking in that exam, which allowed me to go to Sharif University of Technology. One of my proudest achievements to date is being a Sharif alumnus. Sharif University is known for its large number of elite alumni who join the academic world. Almost everyone around me was smart, hard-working, and extremely ambitious. We didn't really have mentors as you define it here. We always challenged each other, and our peers were our role models. Although the competition was not fun at the time, now that I look back, many classmates influenced me by showing me that the sky is the limit. The university offered a great training for me, but spending 4 yr with Sharif students changed the trajectory of my life.

I'm very interested in how you went from training in electrical engineering to molecular biology; from the outside, the two disciplines seem completely different!

Following what top students in the entrance exams oftentimes did, I chose to become an electrical engineer, not knowing much about the profession and what one can do in Iran with that degree. I was a good student at Sharif but not an outstanding one. Outstanding students included the late Maryam Mirzakhani, the first female to be awarded a Fields Medal, and my brilliant friend Mona Jarrahi, professor and Northrop Grumman Endowed Chair at UCLA. Mostly due to the influence of these peers and following their lead, I applied for graduate school to continue my education outside Iran. I received a full scholarship for a master's degree in Canada. It was in the lab of Dr. Chris Backhouse, who was at the University of Alberta at the time, that I got exposed to "biology." His lab used nanotechnology, and he was extremely passionate to create lab-on-a-chip to perform molecular reactions for mutation detection. I wrote my first scientific paper in his lab, which was a lot of fun. Although my master's thesis was still an engineering work, I realized that biomedical problems are complex and would benefit from systemic views, which are engineers' strengths. I chose to do my PhD with Drs. Ed Dougherty and J.F. Chamberland at Texas A&M with a bit of a deeper dive into biology, trying to model gene–gene interactions. My PhD thesis was very theoretical; we assumed there are only four or five genes in our genome and focused on trying to mathematically model the network of their interactions. I received great mentorship

Golnaz Vahedi

Lucie Van Emmenis: lvanemmenis@rockefeller.edu.

from both Ed and J.F. and realized that in order to do impactful research in the biomedical field, I needed more education in biology. This is why I started my postdoctoral training in the lab of Dr. John O'Shea at the National Institutes of Health. My interview with him took less than an hour; I really didn't know him, his research, nor how accomplished he was, but he offered me a job in bioinformatics analysis (which I also didn't know how to do, although I knew computer programming). I accepted the offer because he was so enthusiastic about his research. Looking back, I was very fortunate to meet with him. He was (and still is) a great mentor, and his lab was an environment which allowed me to get new education in immunology and molecular biology. Yet again, I was in an environment full of high achievers, which made me dream bigger and set the bar higher.

Reading about the work that your lab does, it sounds fascinating! What are the benefits of having a lab that is able to cover so many disciplines simultaneously?

I discovered my strength in studying gene regulation work in the O'Shea lab. Maybe staring at electrical circuits for many years and trying to understand how resistors and capacitors worked prepared me for the complexity of genome and epigenome. The O'Shea lab was interested in $CD4^+$ T cells, and in my postdoc research, we used these cells to uncover the unappreciated role of cytokine signaling on the epigenome (Vahedi et al., 2012, 2015; Wei et al., 2010). My productivity during this time led to a faculty job at the University of Pennsylvania. The first few years of setting up my lab to do both wet and dry research were very challenging. On one hand, I had to figure out how to address my lab's computing needs, set up servers, and be a Linux administrator for my own lab. On the other hand, I had to learn how to set up a wet lab and do different genomics experiments. The hardest part was convincing immunologists (colleagues or reviewers of papers and grants) that molecular biology in immunology is an important research direction. I recall a colleague whose primary research focused on a transcription factor saying "I don't care what happens inside the nucleus" at a student thesis committee meeting, making me think deeply about biases towards molecular versus cellular immunology. Despite all of this, I am proud of my lab's contributions! We have been productive since the beginning, which is a challenge when a lab first begins (Johnson et al., 2018; Fasolino et al., 2020; Wang et al., 2020; Fasolino et al., 2022; Yoon et al., 2022; Wang et al., 2022; Michieletto et al., 2023; Chandra et al., 2023). Once again, my environment, in particular scientists on our floor including Jorge Henao-Mejia and John Wherry in addition to amazing trainees and staff, was critical in enabling me to achieve an impossible goal. Now that both wet and dry components of research are strong, our ability to comprehensively analyze complex data and prioritize many layers of measurements allows us to create new hypotheses which could be tested in the wet lab. This integrated infrastructure has also made us continuously explore new areas and less likely to be scooped.

What are you currently working on, and what projects are you most excited about?

We are obsessed with a new nuclear architecture called multi-enhancer hubs, which are spatial clusters of enhancers. Our first study, which was published in *Immunity* (Chandra et al., 2023), established a paradigm wherein multi-enhancer hubs control cellular competence to respond to an inductive cue through quantitative control of gene dosage. We are building many new tools which can enable us to better understand the importance of multi-enhancer hubs and transcription factor networks in quantitatively controlling gene expression in response to changes in cellular environment.

Please tell us about some work in your field that you are currently interested in.

Super-resolution microscopy. To better understand genome organization, we need to measure how individual chromosomes fold inside the nucleus at high resolution. We follow the microscopy scientists very closely and are trying to integrate microscopy with genomics as a standard way to interrogate genome organization in immune cells.

What are some of the qualities that you learned during your graduate studies or postdoc that you maintain and foster in your own lab?

The most critical quality is to stay optimistic. When an experiment doesn't work or a grant gets rejected, I ask myself, "Where is the silver lining?" Maybe we learned something from reviewers' concerns that is valuable. Maybe a later start date for a grant would benefit the lab better. Sometimes it's hard to see the positives, especially for early career investigators with tight timelines. But often, looking ahead and planning for the next step is easier if one looks at everything with a positive take. Another critical quality is to focus on what you can do and pay the least amount of attention to what you can't do. As an Iranian with so many visa-related issues, there were many critical moments that I couldn't control what came next. It is impossible not to worry, but reminding myself "what can YOU do" is empowering. In the lab, I try to foster this as well. If a paper gets rejected, especially if reviewers are not fair, we ask ourselves, "What can YOU do?" If we can address their concerns and the lab members agree to put in the time, we all roll up our sleeves and try to address reviewers' comments as a team. Sometimes that's not the best decision, but we always try to move forward and make the best out of every outcome.

There is still a lot that needs to be done to ensure gender parity in academia. Do you have any advice for women in science, particularly trainees, who are pursuing a career in research?

I've had great female scientists and engineers as role models. At every stage of my career, I looked up to them and asked myself, "Why not me?" This way of thinking motivates me, although I am not sure if it works for everyone. Creating a network of supportive mentors and peers is a step towards finding such role models. The University of Pennsylvania is a particularly special environment with many powerful women in leadership roles; we might have more female National Academy members than male members!

It has been heartbreaking to see what has been happening in Iran recently, and to see the ongoing protests. If you feel comfortable, I would really appreciate to hear how these events have affected you, particularly as an Iranian living in the U.S. And if you would like to share ways in which the academic research community can continue to shine a light

on these issues, that would be appreciated.

"Women, Life, Freedom" is perhaps the first movement in Iran's history that is led by women. It was impossible for me to get any work done in the fall of 2022. One very tough night was when we got video footage of a group of male and female students who were trapped inside Sharif University, the same institution which transformed my life. The security guards locked the students inside and chased some of them to the university parking lot. Even now, several months following last year's protests, the unwavering bravery of Iranian women and girls who defy the mandatory hijab on a daily basis continues to be astonishing. The Women, Life, Freedom movement showed the world that Iranian women are very tough. The academic research community can support Iranian students who come to U.S. institutions for graduate school and increase awareness of this movement whose success would mean a lot for all women.

While not in the lab, how do you like to spend your time, or alternatively, how *would* you like to spend your time?

Over the years and especially as a PI, I learned the value of workouts and intense physical activities such as running. Sometimes including a regular exercise routine in my weekly schedule remains a challenge, but it is what makes me happy and I like to do.

References

Chandra A., et al. 2023. *Immunity*. https://doi.org/10.1016/j.immuni.2023.05.004

Fasolino, M., et al. 2020. *Immunity*. https://doi.org/10.1016/j.immuni.2020.01.003

Fasolino, M., et al. 2022. *Nat. Metab.* https://doi.org/10.1038/s42255-022-00531-x

Johnson, J.L., et al. 2018. *Immunity*. https://doi.org/10.1016/j.immuni.2018.01.012

Michieletto, M.F., et al. 2023. *Nat. Immunol.* https://doi.org/10.1038/s41590-022-01295-y

Vahedi, G., et al. 2012. *Cell*. https://doi.org/10.1016/j.cell.2012.09.044

Vahedi, G., et al. 2015. *Nature*. https://doi.org/10.1038/nature14154

Wang, W., et al. 2020. *Proc. Natl. Acad. Sci. USA*. https://doi.org/10.1073/pnas.1919259117

Wang, W., et al. 2022. *Nat. Immunol.* https://doi.org/10.1038/s41590-022-01232-z

Wei, L., et al. 2010. *Immunity*. https://doi.org/10.1016/j.immuni.2010.06.003

Yoon, S., et al. 2022. *Nat. Commun.* https://doi.org/10.1038/s41467-022-29258-9