Career feature

https://doi.org/10.1038/s41587-024-02201-7

Five questions with César de la Fuente

A pioneer in the emerging fields of AI for antibiotic discovery and molecular de-extinction describes his transdisciplinary background and lifelong passion to understand biology.

César de la Fuente is a presidential assistant professor at the University of Pennsylvania. He has pioneered computational and AI approaches that have greatly accelerated antibiotic discovery, yielding numerous preclinical candidates. Recently, he launched the field of molecular de-extinction, demonstrating that useful molecules could be found in extinct organisms. He has received over 70 major awards, including the Princess of Girona Prize; has published over 150 papers; and is an elected fellow of the American Institute for Medical and Biological Engineering.

What sparked your interest in science?

I have always been curious about the world around me. We are born scientists, but we tend to lose that curiosity as we grow up. I try hard not to grow up too much to preserve my hunger for learning, for knowing, for understanding.

More specifically, my lifelong passion has been to understand biology at a fundamental level. I thought early on that if this was achieved, we would then be able to use biological principles to improve the world. However, this is not easy. Biology is complex, challenging and playful and can appear to be chaotic. It cannot be understood as a single discipline and instead necessitates the connection of patterns and concepts from across domains, including chemistry, physics, engineering and so on. I was drawn to that chaos and have been trying to understand and engineer biology ever since.

What motivates you?

I love working on difficult problems and challenging myself. My brother has Down syndrome, and I have learned a lot from him. He faces daily challenges greater than my own. This taught me the importance of striving for excellence and discerning what truly matters. Being an immigrant has also meant being apart from my family, and seven years ago my father passed away. He was just 57, and I was

30 years old. This incredibly difficult moment taught me about the shortness of it all. I try to honor my brother and father in my daily life.

What has been the most rewarding aspect of starting your lab so far?

Big problems require many minds with different kinds of expertise working together, so working with bright people coming from different parts of the world, different backgrounds and different ideas has been most rewarding. My group is a collaborative team of postdoctoral researchers, students and staff members. We have chemists, computer scientists, bioengineers and microbiologists all working to solve the major issue of antibiotic resistance. We are also fortunate to be working with numerous collaborators across the globe.

What impact do you hope your research will have in the real world?

My dream is to translate our scientific discoveries from the lab into the world in ways that touch people and save lives. I get letters all the time from patients in the hospital or their family members who have infections that can't be treated with contemporary antibiotics, and I respond to every single one of them. I think it's a very important reminder that we're working on real problems, such as severe bacterial infections that are killing millions of people around the world. Without new, effective treatments, drug-resistant infections are predicted to kill 10 million people each year by 2050. I think it's important for me to keep that in mind every single day – that's what fuels me.

And as a scientific community, we need to get more young people thinking about being scientists and engineers – especially women and underrepresented minorities – and support them through mentorship. It's important to have role models to see a path forward. Some science and engineering departments still don't have women on the faculty, and it's time to change that. Without role models, it may be difficult to envision yourself getting there, so we all have to work together to change this landscape and make the sciences more accessible and equitable.

What new technologies do you find exciting, in your field or elsewhere?

I find the application of AI to the field of antibiotic discovery incredibly exciting. Our work has greatly accelerated antibiotic discovery, reducing the time and cost needed to discover preclinical candidates. What used to take years now can be done in hours. Also, our finding that, by using computers, useful molecules can be discovered in extinct organisms (molecular de-extinction) has been exhilarating. We have already discovered numerous preclinical candidates, including mammuthusin and neanderthalin, from the woolly mammoth and Neanderthals, respectively. I think we can learn a lot by studying and comparing molecules that have evolved over time. The future is exciting!

Michael Francisco
Senior Editor, Nature Biotechnology.

Published online: 17 April 2024