Dr. Miler Lee Interview Transcript

***Yogi*:** Hello there, nice to talk to you Dr. Lee! Thanks for giving me some of your time! I write for the Pitt Pulse, a University Of Pittsburgh undergraduate-run magazine. I exclusively write about the cutting-edge research and importance of computational biology in mainstream science. Usually it's seen as a niche field, as I'm sure you know. The purpose of this interview is to understand more about your research, to learn about the importance of computational biology to human health, and to gather advice for other undergraduates who may be interested in the field. With that context in mind, I will go ahead and begin with my first question.

Can you give me a sense of who you are, where you grew up, what your academic path was like and what your hobbies are?

Dr. Lee: I grew up in California. I started out at Stanford University intending to be a biology major, but early on I took a computer science class as an elective, mostly because a friend told me to, and I ended up really enjoying it. But I stuck with biology for another couple of years and did some research in behavioral ecology, but never really felt satisfied with the major. By the middle of my junior year, I decided to drop biology, and based on my happier experiences with computer science, declared Symbolic Systems as my major, which is an interdisciplinary program that combines computer science with cognitive science, philosophy, and linguistics. A lot of my subsequent coursework focused on artificial intelligence and natural language processing, and I ended up staying at Stanford for a Master's degree in computer science.

After I came out of my Masters, I was pretty sure I wanted to get a Ph.D. in computer science, but I also decided to apply to Google – I got through four rounds of interviews, and was scheduled to meet with [Google co-founder] Larry Page (this was back when everyone who made it that far interviewed with either Larry Page or Sergey Brin), but he cancelled, and I didn't end up getting an offer. Meanwhile, I was applying to Ph.D. programs, and was discovering some brand new programs in computational biology. I took a chance on some of them, really enjoyed my visits, and ended up attending the University of Pennsylvania as part of their Genomics and Computational Biology Program.

Around the middle of my graduate work, we started working with some of the new Next Generation Sequencing (NGS) technologies, which I can say without hyperbole revolutionized the way we did biology, and pretty much laid out my path forward in science. After I defended my dissertation, which explored the structural properties of regulatory RNA, I moved on to a postdoctoral research position at Yale to work on developmental genomics. A few years later, I applied for independent positions, and ended up here at Pitt in the Biological Sciences department.

When I'm not in lab, I like exploring Pittsburgh on foot, and I try to go to several concerts a year, mostly pretentious indie rock bands.

Yogi**: So now that we got an introduction out of the way, what is your research primarily about? Why is it important?**

Dr. Lee: I study gene regulation during animal development. We investigate the molecular mechanisms that induce eggs to become pluripotent embryonic stem cells, focusing on the model organism zebrafish (*Danio rerio*). Pluripotency is the capacity for a cell to differentiate into any adult cell type. This is a special property that most cells lack, and is the reason that, say, heart cells normally can't become brain cells. There's been a lot of biomedical interest recently in deciphering how pluripotency is achieved, because of the enormous impact it would have on our ability to model and develop therapies for human disorders. Imagine if we could make a new organ for a patient by taking some of their skin cells, inducing them to pluripotency in a petri dish, then growing them up as a new tissue type. Biomedicine is still pretty far from being able to do that, but the more we discover about what regulates pluripotency, the closer we can get to that eventual goal.

My lab relies heavily on high-throughput experimental methods and computational genomics, combined with some classical genetics and embryology approaches. Being able to draw from a large toolbox of different bioinformatics techniques gives us a lot of power to move the field forward.

Yogi: **If I remember right, you received a grant not too long ago from March of Dimes. Can you explain what it was about and how that research can hopefully impact human health?**

Dr. Lee: Yeah, I received a grant from the March of Dimes about two years ago. At the time, they were funding a lot of basic biology that could contribute to therapies for human birth defects. Although I happen to work on something that has direct parallels to human embryonic development, it's important to realize that almost all biological inquiry has the potential to impact human health. Many important discoveries were made by scientists who did not originally set out to cure diseases. CRISPR/Cas9 gene editing is a recent example – it's become a powerful technology for biomedicine, but it came from work investigating how bacteria defend against foreign genetic material.

Yogi: **What do you think is the future scope of the field of Bioinformatics/Computational Biology? Do you see it becoming more mainstream?**

Dr. Lee: I don't like to think of Computational Biology as a field, as opposed to just a way to address biological questions with a different set of tools, computational tools. A lot of it may seem like really specialized skill sets right now, but I would not be surprised if a decade from now, a lot of what we do today will be automated and contained in a piece of benchtop equipment. Think about how much we take thermocyclers for granted for doing PCRs: there was a time when poor scientists were manually moving tubes back and forth between water baths. Well, one day we'll have a genomics machine that sits next to the PCR machine. I don't mean to belittle what computational biologists do – it's precisely their innovation that is propelling the field forward. When the genomics machine becomes a thing, there will be other challenges to address with computational tools.

Yogi: **If someone is interested in the field but a novice, what are some good tips for growth/development and getting your feet wet keeping in mind that obviously the field is very broad and diverse?**

Dr. Lee: There are a lot of resources online, including courses and tutorials that will give you a taste for what computational biologists do. Start there, then pick something that looks interesting and do some further investigation. There is a ton of biological data freely available, thanks to resources like NCBI's Sequence Read Archive, and a great way to get experience is to play with some of this data. For example, you could find a journal article that reports some finding, look up the raw data it was based on, and attempt to replicate it. Of course, Pitt BioSci also offers a couple courses that are good starting points as well, including two versions of BIOSC 1540, Computational Biology, one of which I teach during the fall.

Yogi: **If you could go back and change mistakes you made in your academic path towards being a Bioinformatician, what would you change and how?**

Dr. Lee: Take more math! Even if you think you hate math! It’s more important than most people realize, and I regret not taking more of it. A lot of computational biology can be very elegantly framed in a mathematical framework, but many of us lack sufficient math for it to be intuitive.