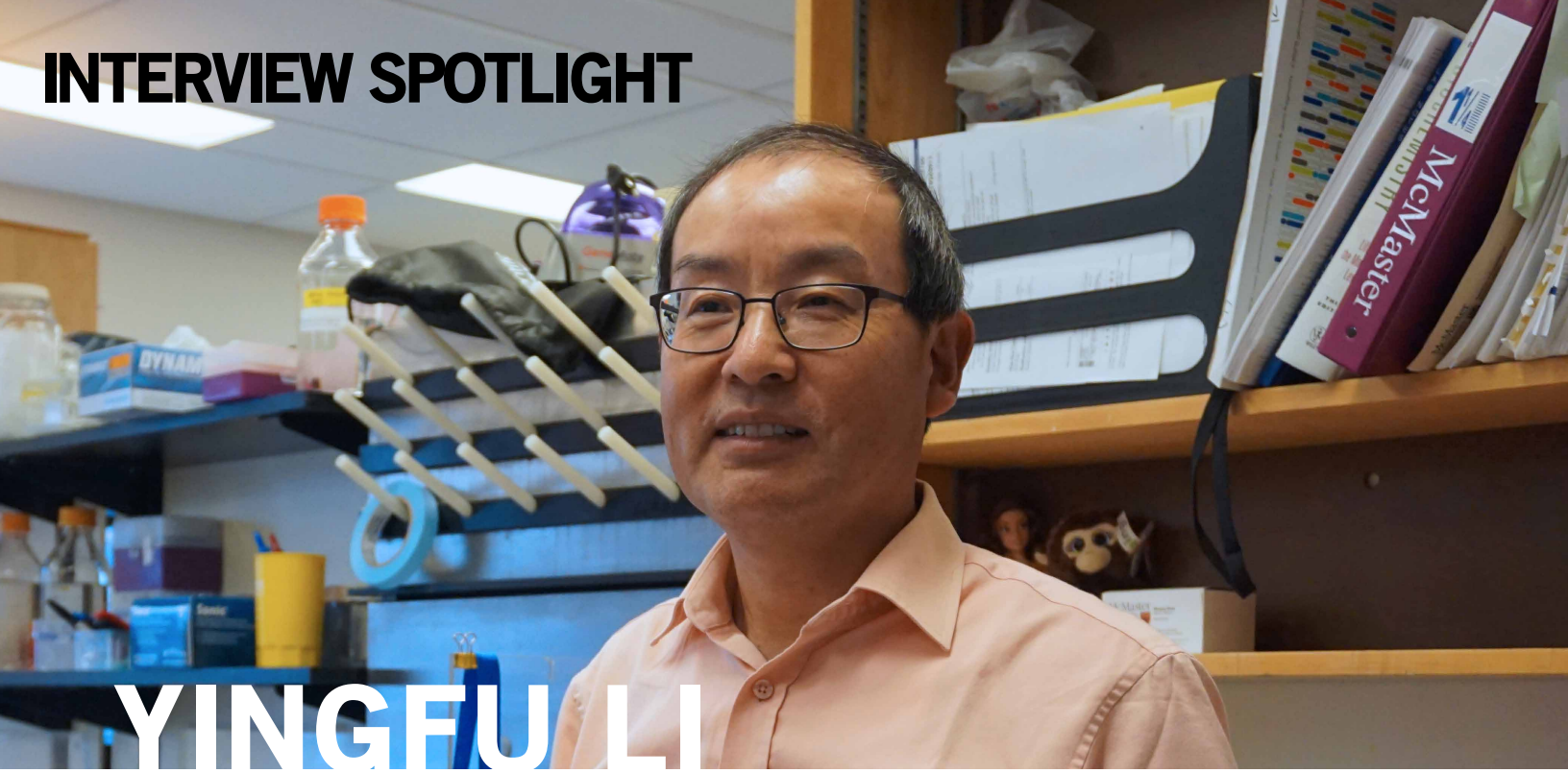

YINGFU LI

A FORERUNNER IN DNA DIAGNOSTICS

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DR. YINGFU LI IS A PROFESSOR OF BIOCHEMISTRY AND BIOMEDICAL SCIENCES AT MCMASTER UNIVERSITY, AN ASSOCIATE EDITOR OF THE JOURNAL OF MOLECULAR EVOLUTION, AND IS A CANADA RESEARCH CHAIR IN NUCLEIC ACIDS RESEARCH. HIS WORK EXPLORES DNAZYMES AS POTENTIAL THERAPEUTIC AGENTS AND PROTEIN BIOSENSORS. A LEADING RESEARCHER IN HEALTH AND BIO-INNOVATION, DR. LI FOSTERS CREATIVITY IN HIS STUDENTS, TEACHING BIOMEDICAL DISCOVERY AND COMMERCIALIZATION COURSES, AND PROVIDING MENTORSHIP TO THE YOUNG SCIENTISTS OF LI LAB.

CAN YOU TELL US A LITTLE ABOUT YOURSELF, YOUR LAB, AND HOW YOU GOT STARTED IN BIOCHEMISTRY?

I came to [McMaster University] in October 1999. I was born and raised in China, where I did my Bachelor and Master of Science degrees. I worked in a couple of places there, but I knew that science at the time was much better outside [of China]. I wanted to receive the best training in science so I decided to apply to western universities and was fortunate to be admitted to Simon Fraser University in Vancouver. That's where I started my PhD degree and did my training in the biochemistry of nucleic acids. I then took a research position at Yale University for two years before returning to Canada to establish my own group. Since then, I've been motivated to establish a top research laboratory looking at interesting functions of nucleic acids. In the initial years, I looked at both DNA and RNA, but I found that there were not [too] many differences. [However], I realized that DNA can be easily produced through chemical ways. For the last few years, the lab has focused more on DNA molecules.

YOU'VE LEARNED MANY THINGS OVER THE YEARS. WHAT WOULD YOU SAY HAS BEEN THE MOST INSPIRATIONAL?

There are many people who have had a huge influence on me. In middle school, I had this amazing mathematics teacher. I think she really got me interested in science, because she kept on telling me that I had a special talent for the subject. When I was in college, I had one [professor] who had a huge influence on me. I felt that learning science with him was fun. It was not about merely memorizing the chemical reactions or mechanisms. Particularly for chemistry — which I loved even when I was in college — I found it really fascinating that you could build complicated molecules using simple reactions, and that you could predict what would happen.

Of course, when I came to North America, my PhD supervisor had an amazing influence on me as well. From him, I learned how to [justify] important scientific questions. He did not want me to just go after a question. He always asked, "Why are you doing this?"; he had to feel satisfied before he [proceeded with] anything. At Yale, I worked with a scientist named Ron Breaker and I learned different skills from him such as how to focus, how to write scientific stories, and [how to] treat science not as a profession, but as a passion with an engaging process.

DR. LI, YOU MENTIONED THAT YOU DO A LOT OF WORK ON NUCLEIC ACIDS. WHERE IS YOUR RESEARCH AT NOW AND WHERE DO YOU SEE YOUR RESEARCH HEADING IN THE FUTURE?

That's an open question! In the ideal world, I want to continue to make fantastic discoveries about the capability of DNA beyond genetic rules. There are many things we don't know and nature only provides us with a limited number of examples. This is why I decided to use artificial systems to create [DNA]; this will continue to be a big focus for us. Also, now that we know DNA can do amazing things, can we get it to do more? For example, can we get DNA molecules to see subtle differences between similar targets such as protein molecules? One of the things our lab has recently been working on is to see if a common protein from different bacterial species, with very small differences, can be identified using artificial evolutionary tricks which guide the DNA to recognize these differences. The reason we want to do this is because molecular recognition is very important. If we can find a simple way to generate the kind of DNA sequences that can fold into well-defined three-dimensional structures which detect subtle differences [between similar proteins], then we can turn these kinds of molecules into biomarkers. We can use [biomarkers] to track diseases and conditions, and potentially use them as therapeutic molecules. If the protein that we have is also a protein that bacteria has, then we can see the differences and design these sort of weapons which only attack bacterial targets, but don't interact with human targets. We then know that it can be developed into a very effective therapeutic molecule.

In the next three years, we really want to create an artificial DNA sequence for recognizing or targeting induced catalysis. This is on the fundamental side of my lab's research. We then want to turn around to target certain applications. We have always known about bacterial and viral infections for humans and also for animals, [as well as] horrible diseases like cancer. If we can perform early diagnosis for any kind of human disease, we can prevent [the disease] and find better cures to treat patients, or prevent a larger outbreak. Our goal is to use the DNA molecules that we are creating and apply them to practical applications like the ones just described.

LI LAB HAS MANY INCREDIBLE ACCOMPLISHMENTS. WHAT IS IT ABOUT THE LI LAB MENTALITY OR PHILOSOPHY THAT YOU HOPE TO CULTIVATE TO ALLOW THIS SORT OF GROWTH? WHAT DO YOU DO AS A PRINCIPAL INVESTIGATOR?

I think every lab is unique. I wouldn't necessarily see my lab as any more special than other labs. Obviously, as the head of the lab, I want to make sure that I am excited about the science we are doing. Also, I normally don't think of myself as a scientist. I see myself as a decent human being working on something. [I believe that] in order to be a scientist, you have to first be a great human being, and that's what I'm trying to teach in my group.

On the science side, we make sure that we are doing creative science and not just copying [what is already] known. Often for me, publishing a paper is just a way of telling the story [of our] scientific discoveries. Although sometimes we do have a need to publish, [we are so excited] when we actually come to this stage [we know that] it's time for us to get that piece out so other people can also get excited about it. I think that's what my lab has: we have this strong interest in what we are doing. Each of [my lab members find] DNA and nucleic acids interesting, and actually want to work together to try making more discoveries about them. For me, I really just want to provide directional guidance and let my students be creative on their own. I try to be on the sideline and [support them by] telling them how excited I am.

In science, maybe 99% of the time, we don't see the things we want to see. So then we have to figure out what we are seeing and what the data is trying to tell us. As scientists, we need to objectively look at the data and revise our hypothesis and try to make changes. I think my students are really receptive to that. We are not really looking for success, but rather trying to understand the class of molecules we are dealing with and trying to apply whatever we learned to challenging [real-world] problems. I think that lab culture is a big word and I don't know if we are necessarily set up to achieve a certain type of lab culture. [However], I do encourage students to get involved in science and other events such as local conferences or departmental activities. I encourage [my students] to be creative and be a part of the community. I think that's my favourite part about my lab. Essentially, we have a bunch of [creative] young people [working on a] project directed at understanding DNA molecules in artificial systems and applying the findings to practical applications.

YOU MENTIONED THAT SOMETIMES THE DATA ISN'T ALWAYS WHAT YOU WANT IT TO BE. WHAT DRIVES OR MOTIVATES YOU TO CONTINUE DOING RESEARCH?

Growing up, I was puzzled by the changing of nature. Seasonal changes, why insects can fly, why dogs can bark, things like that. I'm generally interested in finding out the reason behind this. When I was young, I was less patient and could get down quite easily. Like my grad students, in the beginning I came in [thinking], "Yes, I'm so excited, I'm going to change the world, I'm going to change the field," but then I realized that [there are many] challenges. In science, we publish by the peer review process, so getting rejections is normal. Of course, now we get fewer rejections. [However], when you start and nobody knows you, your skills are not great, your data may not be outstanding, and your writing skills are limited, [you] face these kinds of challenges and get rejected by better scientists. After [these rejections], we have a couple of days of [down time], but then we return and objectively look at the comments to identify what we need to do and what we have learned from [this experience]. So

each cycle when you publish a paper, you learn more and more. Now that I've published 170 papers, through all that cycling, I've really learned a lot. I'm an author. I'm [now] also a referee. I treat other people's papers as if I were the author. [Conversely], when I write my own papers, I look at them as a referee. I want to make sure I understand both sides.

The reason I have stayed persistent in working on projects, science, and challenges is because I honestly really love it. Everyday I go to my office, I feel quite excited because there are so many things waiting for me to do. Right now, I have about 10 manuscripts that I need to [complete]. There are so many exciting stories I want to tell!

[I feel] most happy about our work when we submit our paper to a journal and receive feedback. When our manuscripts get accepted right away, I know we've done something right because every manuscript is reviewed by several people. If everyone says this is a fantastic piece that needs to be published, then we know that we have done an amazing job in our research.

LI LAB IS NOTABLE FOR GIVING ITS MEMBERS RESOURCES. WHAT OTHER SOURCES OF RESEARCH, EDUCATION, OR MOTTOS DO YOU HOPE TO IMPLEMENT?

[Sometimes], we talk about predictions for what might be the biggest discovery made in a specific field. We also go to scientific meetings and invite the experts in our field to give talks and answer our students' questions about career development, skill development, or whatever they have in mind. We use these events to [expose] students and young scientists to all kinds of scenarios. We also have collaborations; my lab has accepted visiting scientists and I have also sent my students to other labs to learn techniques. Through these exchanges, students get to see the world outside of McMaster.

Every couple of years, we do a lab retreat. In the last six years, we did three retreats at Blue Mountain where we talked about science and interesting ideas not related to lab work. I'm [also] pretty big on exercise. I run and play golf, and this also encourages my students to do the same thing — not spending all their time in the lab. I think our effective time [in the lab] is 7 or 8 hours maximum, so spending too much time working might frustrate us. We might be better off if our mind is not on science. Go for a run or do whatever you choose to do. That's why I don't normally look over the shoulders of my students to see what they are doing. It's really trying to get them to engage in an activity that is important.

YOU HAVE A HUGE IMPACT ON MCMASTER IN TERMS OF RESEARCH AND EDUCATION. WHAT ADVICE WOULD YOU GIVE TO ASPIRING RESEARCHERS?

There are many, but maybe two [main] things for anyone who is willing to accept my advice. One, go with your heart — that's very important. You can only succeed and enjoy life if you decide what you want to do with your life. Whether you want to be a farmer, scientist, medical doctor, astronaut, or anything that you think would be exciting, I think this is what separates our human race from animals — we are capable of achieving things if our minds are set on something.

My second [piece of] advice is to dream. I think it's very important not to get frustrated by the things at the moment. Really look way beyond at what you want to achieve and have that in mind. Think bigger, not necessarily about things you can never achieve, but rather about something that you really want to do that is beyond what you can reach at this point. This is something that will really keep you motivated and also happy. Being yourself is also very important. If you have something that you want to pursue, even if you are not successful every time, you'll get back into it. If you're forced into a situation or you feel that you need to do something, it will be a completely different outcome. Many of my friends are unhappy because they did not [follow their interests]. [Thus], I think it's important to be yourself and go with your heart. Who knows what you can achieve? I have seen many talented scientists like that who have made huge discoveries because they are totally interested and driven in their field. If you decide to go down a road [you are interested in], you will really make a difference. No matter what, you can always reflect back, maybe when you're in your 70s, and honestly say that, "I have done absolutely the best I can."