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Interview with Dr. Marietta Lee

Sherry Liou
New York Medical College

Margaret Nguyen
New York Medical College

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Q&S Managing Editors

Dr. Marietta Lee is the winner of the 2013 Dean's Research Award. We chose to interview her for this volume of* Quill & Scope *because she is a successful female scientist in a profession that is largely male-dominated. Dr. Lee proves to be a force outside of the NYMC lecture halls as an important contributor to the research behind the structure of DNA polymerase delta. Through the years, she has managed to be devoted to her family and to the graduate and medical students that she has mentored. What follows is an account of the events and turning points that have allowed Dr. Lee to become the prominent researcher she is today.

Managing Editors (ME): *Congratulations on receiving the Dean's Research Award this year. Could you please tell us a little about your work?*

Dr. Lee (L): My laboratory studies the protein machinery required for DNA synthesis. In particular, we are studying DNA polymerase delta, a key enzyme that has to replicate DNA with the utmost fidelity to avoid mutations. My group is focused on the study of human proteins—ours is one of the few laboratories in the world that studies polymerases that replicate the human genome. Our goal is to understand their role in maintaining the integrity of the genome through the avoidance and repair of mutations. We use a wide range of biochemical, molecular, and cell biology approaches.

ME: *You began your career as a researcher studying polymerase delta. Do you expect to continue in the same direction, or has the direction of your research changed?*

L: My early research was focused on the biochemistry of DNA polymerase delta. When I was a postdoctoral fellow at the University of Miami, I purified DNA polymerase delta to homogeneity from calf thymuses and identified the two-subunit core. I also demonstrated that DNA polymerase delta has an intrinsic proofreading 3' to 5' exonuclease activity and is a different enzyme from DNA polymerase alpha. When I moved to New York Medical College, I found the two additional DNA polymerase subunits and reconstituted the polymerase delta holoenzyme in baculovirus-infected insect cells. Over the years, my research has continued to focus on polymerase delta, but has evolved to include studies of the role of polymerase delta in DNA repair, its regulation in response to DNA damage, and its regulation during the cell cycle. Right now, I am collaborating with Dr. Zhongtao Zhang (NYMC Department of Biochemistry and Molecular Biology) to solve the structures of the polymerase delta proteins.

ME: *Who has played an indispensable role in shaping who you are today?*

L: The first person is Dr. Erminio Costa. After I graduated from college in Kentucky, I was offered a scholarship with a professor in parasitology at St. John's University in New York, but I was not interested in parasitology. Soon after, Columbia University offered me an interview for a research position, and I ended up interviewing because I was curious to see the work of other scientists. Dr. Costa, who was then starting a laboratory as an Associate Professor of Pharmacology at Columbia, offered me a position as a laboratory technician. I went back and declined the position at St. John's University and joined him. Once I started working with him, he told me that I had the potential to be a good scientist.

Eventually, he decided to move back to Washington, DC and arranged for me to go to Georgetown University for my Ph.D. and be an investigator in his group. He was so charismatic—I was always enthralled during his talks. I really liked him, and he helped me gain a lot of confidence.

The second person who has played an indispensable role in shaping my career is my husband. I don't think that I would do him justice if I did not mention him here. He is 10 years ahead of me, not in age, but in terms of academics, and he is very, very supportive. His input is always invaluable.

Finally, I would say that my high school teachers also had a very influential role in shaping me as a person. I went to an all-girls high school, and the teachers really instilled in us that if we fall down, we should get back up. I remember a skit I had to do in my senior year: they had us say over and over to the younger students, "If at first you do not succeed, try, try, try again." That stayed with me.

ME: *How did you first come to teach at NYMC?*

L: We came because they had two offers for both my husband and me. Before I received NYMC's offer, I was headed for the Pacific Northwest Laboratories in Richland, Washington. It was more of an administrative position, which would have made it difficult to interact with students. I had even bought a condo on the top floor of a building that I was going to renovate, and I was going to fly back to Miami every month. In the end, I got cold feet. My husband and I came to the decision

that we should not live separately and that commuting from the East coast to the Pacific Northwest would be too difficult.

When I first came to NYMC, I was so intimidated. I often sat in the back of the lecture halls trying to learn from the professors who students said were good teachers. I was attending a lecture by Dr. Susan Olson, and she asked me, "You know this material already; why are you here?" I told her that I wanted to learn how to improve my lectures. One of the students that I sat next to in a few of the lectures, told me that he was quite impressed that I was making an effort. When Dr. David Frick left, I volunteered to teach his lectures because I had the background for it. I had already been teaching the masters students and so the transition from teaching the masters students to the medical students was simple. That is how I came to teach medical students about DNA replication and repair.

ME: *At what point did you decide to prioritize both research and teaching? Many people choose either or. Why are both important endeavors to you?*

"In order to do research, you need drive and passion."

L: I started teaching around 1996, one year after I was admitted to the graduate faculty at the University of Miami. Prior to this, I worked with only postdocs and undergraduate honors students. I was sent to the main campus to teach the undergraduates, which was a new and exciting experience for me.

At NYMC, research and teaching became my career goals. I really think teaching was my next calling. In teaching, you have to explain known material as clearly as possible. In research, you discover new material. It opened my eyes to how fulfilling it could be to teach as well as to conduct research.

Research is fulfilling when you get a grant or when your papers are accepted, but when you receive critiques from students saying they really liked your lectures, or when students become managers in the industry, postdocs at Harvard or Cornell, professors, and doctors—it is rewarding on a different scale. As an educator, you are building the next generation of scientists and doctors.

ME: *That leads us into our next question. Do you think you are where you envisioned yourself to be when you started out in the field?*

L: My career could have been better, but it could have been worse. I am pretty happy with where I am, but of course, being an ambitious soul, I could have been better.

I was lucky that I never had to look for a position after my Ph.D. I always had different options available to me, and I am glad I made the choice to balance work and family.

ME: *What is the most rewarding aspect of your job? What are the most challenging ones?*

L: It is very rewarding when students tell you that they appreciate your efforts. One of my critiques said that my lectures were "crystal-clear". I don't know how many times I re-read that critique. It is also rewarding when the students keep in touch with me. I love hearing about what they are doing now and seeing the pictures they send.

In my work as a researcher, it is very, very gratifying when a paper is accepted or when a grant application is approved. Our laboratory tries to explore new technologies as they become available, and it's rewarding to see students master these technologies. When they ask intelligent questions, take on challenges, and attempt to explore new directions, they are maturing as scientists and I know they are ready to go. I feel proud when they are accepted to good postdoctoral positions and later succeed in their professions.

It's challenging when papers get rejected. But sometimes, rejection can be good. We submitted a paper on p12 degradation in response to DNA damage, and the reviewer said that there was no evidence that it was targeted for proteasomal degradation by ubiquitination. We went back and developed an assay to prove that it was. This work in turn led to the identification of the E3 ligases that are involved.

Another challenge is when grant applications are denied, especially when I know that a grant has been improperly reviewed. For instance, one of the reviewers mentioned 12 times that I was working with polymerase gamma, a mitochondrial enzyme. It's the wrong enzyme—I work with polymerase delta, a nuclear enzyme.

ME: *As an educator of medical students, what is one piece of advice you would give to medical students?*

L: If you don't know something, ask. Do not pretend, especially when you are a resident.

Additionally, know your oath, you really must adhere to it and try your best to save lives. Whether your patients are poor or wealthy, insured or uninsured, treat everyone regardless of their status.

ME: *And for Ph.D. students, what advice do you have for them?*

L: Graduate students are undergoing a very hard time because of funding issues. The pot of money is just too small. Ph.D. students really must be the best in order to succeed.

In a paper from the April 2014 *Proceedings of the National Academy of Sciences*, "Rescuing US biomedical research from its systematic flaws", Dr. Bruce Alberts et al. discuss how the growth of the field is reaching its limits:

> *There is now a severe imbalance between the dollars available for research and the still-growing scientific community in the United States. This imbalance has created a hyper-competitive atmosphere in which scientific productivity is reduced and promising careers are threatened.*

The US research community cannot continue to ignore the warning signs of a system under great stress and at risk for incipient decline.

In this funding climate, it is important for institutions and the government to help young scientists, both men and women, for the good of the next generation of science. When I began my career in science, it was easier for young scientists to get started with an R01 research grant and make it. Now there is more competition and this rarely occurs. But don't be discouraged because most of the time you can turn negative things around. Persevere, find mentors, and network.

ME: *Are you involved in other activities at NYMC, and how are you able to balance those responsibilities with teaching and research?*

L: I am on the Advisory Committee for new Ph.D. students and the Graduate school Curriculum Committee to help evaluate new courses to see if they are appropriate for students. I am also on the Graduate Faculty Council, the Intramural Research Grants Committee and Radiation Safety Committee. Previously, I was on the Research Support Services Committee.

"...know your oath. Whether your patients are poor or wealthy, insured or uninsured, treat everyone regardless of status."

I balance my research, teaching, and committees by delegating. I learned how to delegate from a very successful scientist at the University of Miami, Dr. Mary Ann Fletcher. She once asked me, "Are you still spending all of your time splitting hybridomas? Do you want to get tenure?" She explained, "Look, you have to have time to read and think. The best way to do that is to delegate and have people help. You're the one who is supposed to look at the big picture. If you're splitting cells, you cannot think globally." Don't be afraid to admit that you can't handle it all and to let someone else take a bigger portion of the pie.

ME: *Do you think that attitudes toward women have changed since you started in the field, and if so, how have they changed?*

L: When I started, there were far fewer women in science. But I was lucky, I never felt that I was in the minority as far as those who were working in the area of DNA replication were concerned. In actuality, several of the well-established scientists that studied DNA polymerases were women.

I had some lucky breaks in my career. One of them was meeting Dr. Bruce Alberts, who came to the University of Miami to be an external examiner. He was a reviewer for a paper I submitted—a paper that was initially rejected. When I met him, I discussed my work with him and made sure all of his questions were answered. Afterward, Dr. Alberts talked to Dr. Antero So, the principal investigator of my lab at the time, and told him that he had the right person working on polymerase delta. Before he left, he told me, "Marietta, you're going to purify polymerase delta to homogeneity. I know it."

When the time came for me to apply for an Established Investigatorship Award from the American Heart Association, I needed someone whose name carried weight in the scientific community to write me a letter. Dr. So suggested that I ask Dr. Alberts, and he agreed to help. He was and is an outstanding, honest, and well-respected scientist, so his letter meant a lot to the reviewing committee.

The award helped me gain a tenure track position, and the chairman in the Department of Medicine at the University of Miami, Dr. John McKenzie, switched me from Research Assistant Professor to the tenure-earning track. This was very unusual in a clinical department. Dr. Fletcher, the scientist who taught me to delegate, spoke to the chairman and helped get me that position.

However, when it was time for the committee to decide on my tenure, I had a hard time. The tenure committee was critical of my maternity leave. They did not think that I was a serious researcher because I took time off. Fortunately, Dr. McKenzie spoke up for me. Our offices were on the same floor, and he saw me working during evenings and on weekends. I think it also had to do with a seminar I gave that he happened to like, so he vouched for me.

Dr. Bernie Fogel, the Dean of the School of Medicine at Miami, was also very supportive. He realized that I needed to teach graduate students and initiated my switch to the Department of Biochemistry and Molecular Biology. When I became a full professor and joined the Department of Biochemistry, I was one of only two women in a department of over 20 faculty members.

ME: *What do you think still needs to be improved for women in science?*

L: Things have changed greatly since I first started, but there is still room for improvement. Women faculty are still underrepresented. I was surprised to read in a Nature paper from 2013 that "in the United States and Europe, around half of those who gain doctoral degrees in science and engineering are female—but barely one-fifth of full professors are women." Furthermore, there are still disparities in salaries for women in science. The Nature article cited that on average, women earn just 82% of what male scientists make in the United States.

At NYMC, our department is unusual in that we are almost balanced in the number of female versus male faculty members. The general increase in the number of women faculty is an improvement from what it was when I started out.

ME: *How do you think women scientists can better support other women in science?*

L: There are societies with workshops for women in science.

Actually, I was on the committee for Equal Opportunity for Women in the American Society of Biological Chemists. I was also a panelist in the discussion of Women in Science in a program for young women scientists at the 16th International Congress of Biochemistry and Molecular Biology in New Delhi, India, in 1994. This past May, I attended the 2014 Women in Science meeting in San Diego. I was pleased to see more women scientists networking and helping each other. Female scientists should mentor younger female scientists.

These meetings can be helpful because everyone talks about the problems they experience and how to handle situations. I remember that there were discussions about maternity leave. I think we should be more accepting of women taking maternity leave. If she is a good scientist, she will be able to catch up.

ME: *If you could give one piece of advice to your students who are interested in pursuing research, what would it be?*

L: In order to do research, you need drive and passion. You need to have a desire to succeed. The rest will come. Try your best and be persistent. If you don't love your work, it shows. In the present climate, it might be more difficult, but if you have the drive to reach your full potential, it might unlock doors.

Set high standards.

Always think positively. "Pessimism never won any battles."

Don't hesitate. Start, and the tools you might need to overcome obstacles will be found along the way.

Try to collaborate. The world of research has expanded so much that you cannot sit in a corner and conduct research alone. Before, I was struggling on my own, but now I feel very happy that I am collaborating with Dr. Zhang. We are going to solve the structure of polymerase delta—it's something that I couldn't even dream of before.

Throughout my career, I followed my instincts for what I thought was right, and I'm very happy with where I have ended up.

ME: *Thank you Dr. Lee for sharing your journey on becoming the accomplished academic you are today.*