JEM Journal of Experimental Medicine

PEOPLE & IDEAS

Soyon Hong: My role is to empower

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Soyon Hong is a group leader at the UK Dementia Research Institute at UCL. Her lab is interested in investigating how multiple cell types work together to maintain brain function, and how these interactions are affected and altered in neurodegenerative disease states such as Alzheimer's disease. Here, Soyon talks about how she got interested in science, what she's currently working on, and the importance of good mentorship throughout your academic career.

Let's start out with a bit of an introduction; tell us about where you grew up and how you first got interested in science.

How much time do you have? Haha. I grew up in many different countries: South Korea, Indonesia, Brunei, and the United States. I'm Korean American, but I would have to say I'm very multicultural. When it comes to the Olympics or World Cup though, I support South Korea first, then the USA.

I became interested in science and biomedical research when I was an undergrad. My passion in science grew from both an emotional sense and an intellectual sense, and I'll explain what I mean by that. I didn't enjoy biology too much during school years because it was mostly about memorization, and I didn't like that at all. I really enjoyed chemistry and physics because I felt there was more of understanding what was going on and applying a structure to it. I then studied Mendelian genetics and biochemistry, and that is when biology became interesting to me. It was more than just learning what mitochondria looked like, it was now understanding the process and the mechanics of how our body and brain work or how our brain degenerates, which is what I'm doing now. I was always interested in the mechanics of how things work and what happens when they fail. I also read two books that inspired me to pursue neuroscience: one was a memoir called "Tuesdays with Morrie" by Mitch Albom, where he was writing about his college mentor who was dying of amyotrophic lateral sclerosis (ALS). I was completely emotionally blown away by the tragedy of it all, and I became very inspired to want to do something. I had this kind of 'savior complex' you might say. The second book was "The Man Who Mistook His Wife for a Hat," by Oliver Sacks. It's a book that you must read if you're interested in the brain, and for me it made me realize that the brain is fascinating! Together it meant that I became very curious to study the brain further.

Coincidentally, after I read "Tuesdays with Morrie," I came across a student newspaper where they described a new ALS research collaboration between Johns Hopkins and the University of Washington, and I decided I really wanted to be a part of it! I contacted the principal investigator (PI), Michel Kliot, and I told him I don't have any experience, but I really want to be part of your team, I want to learn, and I want to contribute; thankfully he said yes! That was my first step in biomedical research. I started working with rat models of ALS and really became intrigued with the scientific process of observation and trying to come up with a hypothesis and a question. I was very lucky because my postdoc supervisor, Patrick Weydt, was so patient and very involved in supervising me. At that time, one of our close collaborators was Thomas Möller, and so I became involved in microglia work within the context of ALS. Microglia are beautiful and fascinating cells, and that's when I fell in love with them!

Soyon Hong.

Tell us about your career progression, and how you got to where you are now.

I stayed on as a technician in Thomas's lab after I graduated from the University of Washington, and I was very lucky because he gave me independence as a technician and I was also able to publish co-first author papers before starting grad school. I was just very lucky from the beginning to get the kind of mentors I had, and I think my story is really about the power of mentors. Thomas was super supportive; he gave me ownership, gave me the ability to be somewhat independent, and I was very lucky to have this experience. When I went to grad school, I chose Harvard, and one of the reasons was because I was still very interested in neurological diseases and was really interested in understanding what makes the

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brain degenerate or dysfunctional. I chose my rotation projects based on this, and one of them was with Dennis Selkoe. I loved Dennis's style of mentorship; he was super critical and focused on what the key missing questions in the field were. I really wanted to hone my critical thinking, so I wanted a mentor who would help me to understand how to tease out the key questions and how to learn the scientific thinking process. Dennis was the best person who could help me with this; he's a very sharp and clear thinker, and hopefully I learned some of that thinking process from him.

When I started grad school, microglia were not very hot. At that time, I was one of the few students who was raising their hands and asking, "But what about microglia? What about astrocytes?" And so I always wanted to go back to studying microglia. I was really interested in Beth Stevens's lab, and after meeting with her I knew that I wanted her as my mentor. I learned a lot of things from Beth; her way of mentorship was different from Dennis, and I was extremely lucky because the mentors at each stage of my scientific career were able to provide the unique kind of mentorship needs that were necessary at the time. In Beth's lab, I started learning more about microglia and understanding microglia–synapse interactions in the context of early-stage Alzheimer's disease involving amyloidosis. Then 4 years ago, I started my lab at the UK Dementia Research Institute (DRI) at UCL. At the time, this was a new nationwide institute that was being established in the UK, and both Dennis and Beth strongly encouraged my husband and me to go there to be part of this momentum and this exciting time. UCL is one of the top institutions for neuroscience, and to be a part of the UK DRI at such a prestigious institution and surrounded by so many great scientists was a no-brainer. Also, one of the reasons I chose to come here is because of mentorship; we need strong mentorship at every stage of our lives. I am lucky to receive strong support here from multiple mentors, including Bart De Strooper, my director, who has been a cheerleader from the beginning, even when I felt like I was failing. Giampietro Schiavo is my mentor I am most indebted to, in almost all aspects but especially regarding mentorship about mentorship! He has provided me so much support, advice, and wisdom, particularly about how to be a better PI and mentor to my lab.

It's wonderful to hear you talk about the importance of mentorship, and to follow up on that point: What are the values or qualities that a person, particularly a grad student or a postdoc, should be looking for in a mentor? Or do you feel that's more of a personal choice?

I think it's both. First, one of the basics is that you want someone who really takes mentorship seriously. And more than a PI; you don't want just a manager, you want a leader, and someone who considers mentorship to be a big part of what they do and commits to being a mentor to you. I think when you're a grad student, more important than the exact scientific question is the kind of individualized mentoring the PI is willing and able to do, as every PI is different. As a grad student, seek out the mentorship that you need, and at this stage it is often learning how to ask a question, learning how to design experiments, learning about critical thinking, learning how to troubleshoot and being okay with failure. When I was a student, it was really important that I had someone to gently encourage me when my experiments were not going well, who cared about my growth as a scientist rather than how well my experiments were going. As a postdoc, I would encourage that person regardless of what career path they were on, to gain skills on grantsmanship and presentation. The ability to write, present, and network are really important skills to have, regardless of what career path you take. But we are all different, and so it is important to realize what your mentorship needs are so that you can identify whether the PI's mentorship style is ideal for your optimal growth (or if not, whether they are willing to adapt). Equally, I think it's very important that the PI themselves understand and are willing to adapt their mentorship styles to best facilitate the growth of their mentees. This is something that I am recognizing I should be doing more and more as I get older.

Now in the position of being a PI yourself, how would you define being a successful mentor to people in your lab? Do you have any defined metrics?

As mentoring can be so personal, I don't think you can say that one person's mentorship style is the most successful or the best. For me, I do have some generalized features I try to follow, but it's critical for me to also cater to the person's unique needs and personalities, as well my own personality. I can't say that someone should follow exactly what's most comfortable for me, as a leader I need to be more flexible and I need to understand how to make my team work together. What's really important to me as a mentor is that I really want to see growth. I try to recruit the people to my lab not based on their GPA or how successful they are, but on how hungry they are, how passionate they are, and also their growth potential—do they have a growth mindset? For me, a successful mentor is someone whose trainees feel empowered to make their own discoveries. Two things I try to instill in my lab are their sense of ownership and growing confidence in critical thinking. Regardless of what stage their project is at, it's really important to me that they are always thinking critically, for example about controls, and thinking deeply and thoughtfully about their results. And the reason is because I am not the one who is sitting at the microscope, it's my teammates; that is, the students, postdocs, and technicians in the lab, who are the ones seeing things for the first time. I also think one of my major roles as a PI is to help my students feel confident to drive their own projects. I want them to be not afraid of making mistakes and to be open eyed so that they're excited about what they are seeing, they're ambitious with their experiments, they're curiously looking at their specimens, and it's not just a box-ticking exercise. I see my role as helping to really empower their questions, empower their curiosity, and empower their motivation. Those are the general mentorship characteristics I try to follow.

It's great to hear somebody speak so openly about the importance of mentorship, and the focus on the growth of the people within their lab. It's clear that your own experiences have really shaped how you mentor your current team. Thinking about your lab, tell us about the projects that you've got going on at the moment, maybe some that you're particularly excited about.

I study microglia in neurodegeneration, and in particular what I'm interested in is to

understand what triggers microglia to eliminate synapses and what the functional consequences are. There is now a growing number of studies from both humans and animal models that implicate immune signalling to be critical in increasing risk for Alzheimer's disease. There are also amazing studies from basic neurobiologists who are dissecting neuroimmune mechanisms in the healthy brain, which is important because I think fundamentally if we want to understand what goes awry, we first have to understand or have some insight into what happens normally. Studying microglia–synapse interaction is also highly relevant in disease because region-specific synapse loss is a critical hallmark of neurodegeneration. When I started up my lab 4 years ago, our focus question was what regulates microglia to engulf synapses, which was a continuation of my postdoc, where we showed that microglia are engulfing synapses in disease models. What I was interested in now was what the region-specific triggers that reactivate this pathway in microglia are. Our most recent study (De Schepper et al., 2023) is investigating the role of perivascular macrophages (PVMs) in this process. What our lab found is that when PVMs get activated, osteopontin (SPP1) gets upregulated and secreted by PVMs in the hippocampus, which leads to an increase of microglial phagocytosis. What we observed is that SPP1 secretion by PVMs, and to a much lesser extent perivascular fibroblasts, is instructing microglia to induce a phagocytic cell state, including the upregulation of complement. If we genetically knock out SPP1, despite there being a continuous amyloid beta challenge, microglia are unable to eliminate synapses. These data suggest that SPP1 is a molecule that acts as a potential trigger for microglial engulfment pathway. Further, it suggests an intriguing crosstalk between two types of brain-resident macrophages, so I'm really excited about that. Our lab is beginning to investigate such cell–cell interactions in the context of how crosstalk between two cell types impacts microglia–synapse interaction. Besides PVMs, another cell type we are investigating to be involved in such crosstalk at the synapse are the astrocytes. If you look at electron microscopy images of the synapse, you almost always see beautiful astrocytic processes ensheathing synapses, and so for me, it makes sense that they play a role in helping to regulate microglia–synapse interaction. We are also seeing very exciting cell–cell communication involving PVMs and circulating adaptive immune cells in our models.

It's great to hear your enthusiasm for the projects in your lab; is there a particular direction that the field is heading in that you're excited about?

Crosstalk between immune cell populations within and across brain borders! There is now a growing body of data from many groups that altogether suggest a much closer link between adaptive and innate immune cells that impact brain function and homeostasis throughout the lifespan. I am really excited about that because it suggests a dynamic regulation at brain borders that is required for proper brain health and function. I still think that microglia within the brain parenchyma play central roles, because they're the ones that are sitting right next to the neurons, but it is also becoming increasingly clear that other brain-resident macrophages such as border-associated macrophages (such as PVMs) act as crucial immune sentinels and the meningeal adaptive immune cells can help coordinate tissue resolution and modulate neuronal homeostasis. The brain is not isolated. I am very excited about understanding this cell–cell crosstalk across borders of brain compartments.

I'm sure you're aware that there's a lot of discussion about brain drain within academia. As a researcher in the UK, how do you feel about the challenges that you're facing as a PI and the future of academic science?

I think that Gen Z are smart, they're trying to figure out what they don't want to be, and learning that perhaps they don't want to stay in a harsh bullying environment and asking, "What am I living for?" I think this goes back to the idea of mentorship, and for me, whilst I can't solve brain drain, what I can do now is to be a good example for the next generation. It also comes back to what motivates you, what kind of work you like to do, and where your passion lies. I think it is a good thing that young scientists are asking, "do I really want, and need, to do a postdoc?" And then as a mentor, you can help that person to find what the next suitable career step is for their own path rather than people thinking that becoming a postdoc or staying in academia is the default, and that if you don't become an academic PI you are a failure, which is wrong. I actually don't think brain drain is such a negative thing; I think people are beginning to think about what kind of career choice they want to have, what the options are, and where their passions lie. And if people are recognizing that, and really thinking about their paths, it doesn't have to be a negative thing.

It's also a call for us to be proactive about changing our environment to be more accepting and more fluid of what is required for success in academic science. In particular, women face challenges because in general, society can still be very traditional. I feel very strongly about this. Anne-Marie Slaughter wrote an article in *The Atlantic* called "Why Women Still Can't Have It All," and some people thought it was depressing, but I didn't think it was depressing at all; it's true! It's not depressing to think we (women AND men who share the responsibility of parenthood) cannot do it all; I think it's a very healthy approach to understanding the reality. In the article, Slaughter says the most important choice we can make is our choice of life partner, and I 100% agree with that. Ruth Bader Ginsburg said, "I had a life partner who thought my work was as important as his, and I think that made all the difference for me." For me, this remark is so powerful because it is not about whose career is more important, but it is about realizing that in a partnership, what I do (in my case, my career) is as important as my partner's, and this goes both ways. I'm extremely lucky and blessed because I have a husband who's like that, he's also a PI and he believes in me and thinks my career is as important as his. Together we support each other's careers and share parenthood duties. There are many times when we feel like we cannot do it all, but together we lessen the challenges and we become enablers for the other person. I'm so lucky to have that support at home and people who believe in my potential, sometimes more than me. I am also very grateful because I have such a supportive team also at my work: my lab is this amazing group of young people who are kind, gracious, and understanding of my need to be flexible. Finally, as mentioned above, mentorship is also super critical at helping to make our

environment more facilitating for young parents. It is really important that we are not losing young parents from pursuing further academic science because they feel overwhelmed or unsupported. We need to come with tangible ways to provide young parents with more time, flexibility, funding, and structural support. But of course, the reasons why people choose to stay or leave academia are very personal and diverse, and for people like me who stay in academia, we have to make sure that we represent the types of mentors that will support and encourage, and to not be discouraged if someone feels that their passions lie outside of academia.

For the final question, when you're not in the lab, how do you like to spend your free time?

I'm a mom, and my natural inclination and priority is to be with my children. I have two kids that are 18 months apart, and when I had my first child, I remember speaking to my mom and being conflicted about staying at home or going to work, but I knew that staying home wasn't for me. When I spend time with my children, I am with them 100% and do my best to make it quality time. So, with my free time, it's about trying to spend time with my kids. It's such a pleasure to see them growing, learning, and becoming individuals!

Note: *A preliminary version of this interview was inadvertently published on March 20, 2023, and replaced on March 27, 2023.*

Reference

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