JEM Journal of Experimental Medicine

PEOPLE & IDEAS

Kazuyo Moro: Building relationships is essential for gaining both speed and opportunities in research

Montserrat Cols[1]

Professor Kazuyo Moro holds dual appointments as a team leader for the Laboratory for Innate Immune Systems at RIKEN IMS as well as Osaka University Graduate School of Medicine. Her lab conducts multifaceted research on type 2 innate lymphoid cells (ILC2), from ILC2 differentiation, activation, suppression, and transcriptional control mechanisms, as well as basic research and drug discovery. The research from Prof. Moro lab aims to build new models and therapies for related immune diseases such as allergies, fibrosis, and metabolic diseases.

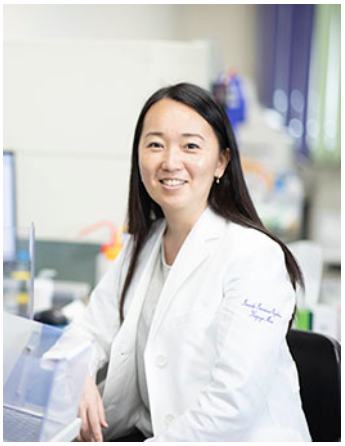
Please tell us a little about yourself and how you first became interested in science.

I grew up in Tochigi, a rural area north of Tokyo that's rich in natural beauty. In Japan, it's common for kids to attend cram schools early on to prepare for competitive high schools and universities, but my childhood was more carefree and unstructured. I spent my days playing in the garden, and exploring insects and plants. I didn't develop a real interest in science until I started my graduate school research, although I've been told I was a child who asked relentless questions, enough to wear out the adults around me. My original plan was to become a dentist, as I graduated from a dental school. However, when I graduated from university, I realized that I wanted a career where I could make brand-new discoveries that would change medicine rather than simply administering prescribed treatments as a clinician.

Tell us about your career trajectory and what led you to becoming a group leader. How did you end up having two appointments?

After graduating from dental school, I immediately entered a PhD program. However, after 2 years, I left my first lab due to dissatisfaction with its top-down research structure and joined a new one. In this second lab, I was free to choose my own research theme, so I spent 6 months exploring different ideas until I eventually discovered the cell that is now known as ILC2. The publication of this work in *Nature* in 2010 was a turning point for my career. Until then, I'd never been selected for oral presentations at conferences, and few people even stopped by my poster presentations. But top-journal publications have an extraordinary influence, and suddenly I found myself in the spotlight. It felt unsettling to see how dramatically external perceptions shifted, even though my research itself hadn't changed before or after publication.

For the first year after earning my PhD, there were no available positions at the university, so I covered my own salary from my research funding. Then I moved to RIKEN, where I worked as a senior researcher for 3 years before becoming independent in 2015. RIKEN is Japan's top research institute, and I was fortunate to have a supportive environment and wonderful colleagues there. However, RIKEN lacks an affiliated hospital, which posed a challenge for my lab as we aimed to translate basic research into clinical discoveries. So, in 2018, I was thrilled when I got the chance to establish another lab in Osaka University School of Medicine. Having dual labs at RIKEN and Osaka University enabled our research to encompass both mouse models and human disease, creating a more comprehensive approach. Although the two labs are 500 km apart, I travel to both each week.



Kazuyo Moro.

How did you first become interested in working in the immunology field and ILC2s specifically?

My interest in immunology comes from a simple idea—the immune system. With its many "characters" of cells, it reminds me of a complex human society. When

[1]Senior Scientific Editor, *JEM*, Rockefeller University Press, New York, NY, USA.

Correspondence to Montserrat Cols: mcols@rockefeller.edu.

https://doi.org/10.1084/jem.20242176

each person does their job and takes breaks when needed, society runs smoothly. But if someone disrupts others' work or confuses friends for enemies, things fall into chaos. Immune disorders work in a similar way: if we can fully understand the unique roles of each cell and support them to function properly, I believe we can prevent disease.

The discovery of ILC2s happened by coincidence. One day, I treated mesentery with collagenase and performed flow cytometry with T cell, B cell, and natural killer cell markers. I found that 20–30% of cells in the lymphocyte gate are negative for all lymphocyte markers. Even after testing hundreds of antibodies available in our lab, I couldn't understand what kind of cells they are. This sparked my interest in this population. For the first 2 years, I believed they are lymphoid progenitors based on their Lin-c-kit^{+}Sca-1^{+} phenotype and conducted almost 400 experiments to prove this hypothesis. However, in every experiment, this cell did not differentiate into any known lymphocyte, and ultimately, we concluded that it was a new type of lymphocyte. This new shift in perspective propelled the research forward, leading to important discoveries about the cell's remarkable ability to produce type 2 cytokines and its role in defending against parasitic infections.

What are you currently working on, and what projects are you most excited about?

In our lab, we study the roles of ILC2s in various diseases, including allergies, fibrosis, infections, and colitis, as well as ILC2 signaling and regulatory mechanisms. Recently, my focus has shifted toward understanding individual differences—why some people develop diseases and others don't, and why treatments work for some but not others. This led us to explore wild immunology. Standard specific pathogen–free (SPF) mice lack genetic diversity and haven't been exposed to the infections or diseases that humans typically encounter throughout their lives. Since ILC2 activation is regulated by a variety of biological factors, we came to believe that truly understanding ILC2 requires analyzing cells from wild mice that have been exposed to many environmental stimuli rather than studying ILC2s that have never encountered such stimuli.

Please tell us about some work in your field that you are currently interested in. (For example this could be a lab, an early career researcher, or perhaps a future direction you think the field is going in.)

Similar to my answer to question 4, I believe "wild immunity" will become increasingly important globally. Some argue that the discoveries made in mice have limited applicability to understanding human diseases, and I suspect this stems from researchers' reliance on SPF mice. SPF mice live in a sterile environment, and their immune systems are said to resemble those of human fetuses. It's hard to imagine that immune mechanisms derived from such underdeveloped mice would help us understand human diseases. Research using wild mice presents challenges, such as difficulty in achieving statistical significance and complexities in managing housing conditions and infection risks. However, I believe that to bridge mouse studies more effectively with human disease understanding, this is a field that researchers should increasingly engage in.

When you first became a group leader, how did you gain confidence in your new role, and was the transition to independence easy to achieve?

Setting up my lab went smoothly, thanks to the unwavering support of my wonderful colleagues and students. In Japan, principal investigators (PIs) tend to gain independence later than in other countries, often starting with larger groups, which can be quite demanding. In my case, I already had over 20 members in my lab. I was fortunate that most of them were not new members but colleagues I had worked with in the lab before becoming independent. Their trust has always been a source of confidence for me. One of the biggest challenges, however, was securing funding to support the experiments conducted by such a large team. To address this, I put significant effort into mentoring lab members in grant writing, helping both myself and my team secure funding. Once we were able to secure funding, everyone could fully focus on the research they were passionate about. Watching my team actively engage in their experiments gave me the confidence to continue thriving as a PI.

What are some of the qualities that you learned during your graduate studies or postdoc that you maintain and foster in your own lab?

I have always placed great importance on fostering respect and appreciation among lab members. During my time in graduate school, I was able to do good work because I had a supportive advisor and colleagues who stood by me through challenging times. Daily research can often be done independently, but the process from generating research ideas to writing papers requires the support of many people. Building strong relationships is key to making this process smooth and stress-free, and I believe mutual respect and gratitude naturally cultivate such connections. When I first started my research career, I believed that simply working diligently at the lab bench alone was enough to succeed. However, I now realize that building relationships is essential for gaining both speed and opportunities in research.

Mentorship in science is extremely important. What are some qualities that students and postdocs should look for in potential mentors?

Since I changed mentors during my PhD, I deeply understand the importance of finding the right mentor. The most crucial factor is determining whether the mentor can offer what you need. There's no "best" mentor for everyone; it's all about compatibility. Some students prefer top-down guidance, others value autonomy, and some want just enough research experience for future employment, while others want rigorous training for an academic career. When students come for an interview, I always ask my colleagues to honestly share both my strengths and weaknesses. This is to ensure that students are not disillusioned by a gap between their expectations and reality if they join the lab. I want students to have a clear image of what they are looking for in a lab and to evaluate whether my approach aligns with their expectations. The kind of lab I'd want to avoid is one that doesn't support the research I'm passionate about,

lacks opportunities for international collaboration, or has a PI without big aspirations.

Where do you find inspiration for your work, and what motivates you as a group leader?

New project ideas often come to me while listening to presentations at conferences or during progress meetings where lab members share their work. Learning about phenomena that clinicians understand through experience but lack scientific explanation inspires me, as a basic researcher, to investigate further. In progress meetings, many of my ideas stem from negative data, as it often raises new questions. Some might think that focusing only on obtaining desired results speeds up research, but I believe unexpected discoveries often lie hidden within negative data—even ones I could never have predicted.

It's a tough question to answer—what drives me as a group leader? Honestly, being a PI is nowhere near as fun as the days when I was hands-on in the lab. It makes me feel a bit sad to think that I might never again experience the excitement I felt when I was doing experiments. Still, I continue in this role because I believe that one day, I'll get to relive that excitement from the other side—when a student or postdoc bursts into my office to share their groundbreaking discovery, just like I used to do with my own supervisor. That's why my office door is always open, waiting for someone to come running in with exciting news.

While not in the lab, how do you like to spend your time, or alternatively, how would you like to spend your time?

It's often said that Japanese people work hard, and it's true—we work too much. I stay in the lab working until 10:30 at night, and when I finally get home, I have a cup of tea with my husband, take a bath, and go to bed. So, my days off are like a machine with a dead battery. I get up, settle on the couch, play app games on my phone, watch TV absentmindedly, and relax with my husband as we cook simple meals. I do minimal chores like laundry and cleaning and enjoy an hour-long bath. With frequent business trips, I don't have much desire to travel, and after a week of all-consuming research, I prefer to spend my weekends completely disconnected—no emails, no lab thoughts, just unwinding. People might wonder why I don't just take it easier during the weekdays instead of spending my weekends like that. Sometimes, though, it feels like working is almost a hobby ingrained in the DNA of Japanese people.