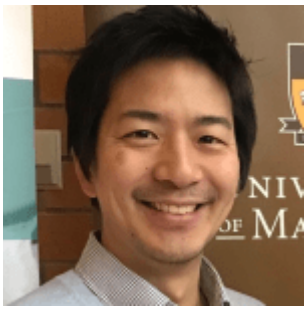
Thomas Murooka



Thomas Murooka, PhD
Associate Professor, Departments of Immunology and Medical Microbiology and Infectious Diseases Department

Education: Postdoctoral fellowship, Massachusetts General Hospital, Boston (2009-2014)
Ph.D (Immunology), University of Toronto, Canada (2002-2008)
B.Sc (Microbiology & Immunology), University of British Columbia, Canada (1997-2002)

I am also an active member of the Canadian HIV Cure Enterprise (CanCURE), which is a research collaboration focused on studying HIV persistence and developing strategies towards a functional HIV Cure.

Tell us about yourself and your career?
I obtained my Bachelor's degree at the University of British Columbia (UBC) in Microbiology & Immunology. My first experience with research was when I entered the co-op program there and worked at two biotech companies as my work terms,

where I learned many cellular and molecular techniques I continue to use today. I was also fortunate to have a supervisor who gave me free reins to experiment with anything I wanted in the cancer biology field, and I started to play around with a new fluorescent microscope that no one was using at the time. I started to make videos of cancer cells dying when applied with various drugs, which was my first appreciation of cell biology and the mechanisms that control cell survival and death.

I went on to do my PhD at the University of Toronto in Immunology, and then a postdoctoral fellowship at Massachusetts General Hospital (MGH) in Boston. I stuck with my strong interest in microscopy and learned how to perform imaging directly in living tissues, called intravital two-photon microscopy (IVM). There, I was the first to image HIV-infected T cells in the lymph node and to describe how infection altered the behaviors of immune cells. I have continued to use similar techniques and tools in my lab as Principal Investigator at the University of Manitoba since 2014, where we are interested in how microbial infections alter the immune response at various tissue sites.

What is the main interest and research in your lab? And what influenced your research focus?

My lab utilizes a visualization-based approach to understand how pathogens infect healthy tissues, and how host immunity responds to those infections. In most cases, the infection is cleared by our immune system, but sometimes pathogens can circumvent host responses and establish infections that are not cleared. We are particularly interested in the latter, whether they are parasitic, bacterial or viral infections, and use a microscopy-based approach to provide unique perspectives on host-pathogen interactions at relevant tissue sites. This is an interest I developed very early on in my career and continue to develop innovative tools that allow us to “see” the immune system. I continue to train students that have

similar interests in my lab.

What is your scientific background? Why did you decide to pursue immunology as your research interest?
I'd always been interested in Immunology during my undergraduate studies, especially how immune cells were able to move towards the site of infection. I realized early on the importance of studying microbial infections in the context of the whole body, rather than just studying the microorganism in isolation. This is because the ensuing tissue damage can be the result of an aggressive immune response that can cause significant collateral damage that is often worse than the damage caused by the microorganism itself. My PhD thesis was based on deciphering the signals that controlled T cell migration towards a stimuli, and we described a previously unappreciated role of the mTOR pathway that controlled protein expression required for efficient cell motility. While these studies were primarily done in cell culture systems, I was really keen on learning a novel technology at the time, where immune cell behaviors were being imaged directly in tissues in response to a wide range of insults. There was an explosion of interest in intravital microscopy, which peaked my interest and decided to pursue this approach during my postdoctoral studies. What's really clear now is that the immune system, previously thought of primarily in the context of microbial infections, is implicated in several diseases outside of the infectious disease field, including obesity, atherosclerosis and cancer. I think it's important for everyone to gain a strong foundation in Immunology.

What interesting discoveries has your research group made and how has it impacted the field of immunology. What do you consider the most important findings in your research?
Our most important observation is that the context in which HIV infection occurs matters a lot. Infection studies in T cells and macrophages have mostly been done using purified, single cell suspensions, which is convenient to study the

various steps in the HIV life cycle. However, HIV does not infect purified T cells in tissues: in fact, there are a number of barriers in place that prevent HIV from infecting T cells and other immune cells. For example, HIV can't "move" on its own, so the virus must be creative in accessing tissues where the preferred target T cells are located. When HIV infection studies are performed in 3D cultures that mimic lymphoid tissues, or directly in the lymph node *in vivo*, the dynamic nature of the infection changes dramatically, and reveals ways this virus takes advantage of normal immune cell behaviors to establish a chronic infection. We have pioneered HIV imaging studies in the field, and will use similar technologies to understand why HIV can establish a pool of infected cells that seem to persist in the body. Again, we feel that the context in which HIV-infected T cells reside, and access signals from their surroundings, has a big impact on these mechanisms. We are also interested in host immunity against other microbial infections, but guided by the same principles that the tissue environment in which infections occur, plays a critical role in successful immunity. Complex 3D and tissue model systems need to be used to confirm observations made using simple, cell culture systems.

What have been your biggest difficulties conducting research?
The research focus in any lab is guided by the data obtained. While my lab is rooted in using a microscopy-based approach to study fundamental host-pathogen interactions and the immune evasion mechanisms utilized by various pathogens, there are a number of unexpected, but really interesting observations being made by my trainees. The most difficult aspect of leading a research group is deciding which observation(s) are worth pursing and investing resources into, and which observations to keep in the background. With a finite amount of funding and time to dedicate to various projects, I find it critically important to pursue projects that are likely to make the most impact in the field, and one that can lead to more funding and collaborative opportunities. This requires a

good understanding of the field, and what the major questions are that can only be addressed by my lab. As a PI, my job is to guide students towards success, and deciding where to invest time and resources is critically important towards this goal and sometimes keeps me up at night.

What do you hope to achieve once you decide to hang up your lab coat?

I've always wanted to run a lab where all of my trainees reach their potential as scientists. My job is to guide students towards projects that are most likely to have success, and establish a positive, supportive environment that will contribute to success. This can be in the form of establishing required infrastructure, securing funding or making collaborative contacts. I hope that my trainees will continue to find their calling long after they leave my lab, armed with the skills and knowledge gained from training here. It will be very rewarding to witness my trainee's career trajectory, knowing that I played a small role in that process.

What is your advice for graduate students who aspire to be immunologists?

Be involved in several different projects. Have a curious mind and strive to contribute to studies other than your own, because it allows you to gain additional skills and learn from your colleagues. You want to graduate with your advanced degree armed with many skills, because they will come in handy in the next stage of your training, even if it doesn't seem obvious at the time. As you move up the academic ladder and slide into a leadership position, you want to make sure you can provide training in a number of techniques to your students. It's important to pay attention to seminars and learn from your fellow student presentations, and ask questions along the way!

Interview by Faisal Nuhu