



## INTERVIEW SPOTLIGHT

# DR. CAITLIN MULLARKEY

## VIRUSES IN THE MODERN WORLD

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This year, we had the pleasure of sitting down with Dr. Caitlin Mullarkey to hear her thoughts on topics ranging from the COVID-19 outbreak to advice for undergraduate students in STEM. Dr. Mullarkey is an Assistant Professor in the Faculty of Health Sciences who specializes in the fields of virology and immunology. A Rhodes Scholar, Dr. Mullarkey had the incredible opportunity of working on a novel influenza vaccination strategy as her PhD during her time at Oxford.

As the COVID-19 outbreak is still rapidly developing, some of the statistics quoted in the interview are no longer accurate. This interview was conducted on February 5<sup>th</sup>, 2020.

AS AN UNDERGRADUATE STUDENT AT SWARTHMORE COLLEGE, YOU WERE AWARDED THE PRESTIGIOUS RHODES SCHOLARSHIP TO STUDY AT OXFORD UNIVERSITY. WHAT WAS THAT EXPERIENCE LIKE AND HOW DID IT IMPACT YOUR RESEARCH INTERESTS?

Swarthmore College is a small liberal arts institution and I'm not going to say liberal arts institutions don't necessarily exist in Canada, but they are certainly rare. I had a broad biology education as an undergraduate and so I didn't have all these specialized courses that you have at Mac. I took cell biology, organismal and population biology, microbiology, and plant biology. So, I really had a firm understanding in diverse biological disciplines and I was very interested in the little bit of immunology and virology that I learned about in a microbiology course that I took. But I didn't feel like I had the knowledge to pursue it at a higher level. So that's what I started to study when I went to Oxford, and I really got into immunology and virology as a graduate student. I initially did a master's degree in immunology, and as a part of that master's, a short research project in a lab that worked on influenza virus vaccines, which became the focus of my career. So my experience at Oxford, as a Rhodes Scholar, really started my trajectory in virology and immunology, something that I did a master's in, a PhD, and then a postdoc, and now it's something that I love to teach to undergrads.

**AS YOU HAVE TAUGHT US IN OUR BIOCHEMISTRY AND CELL BIOLOGY COURSES THIS YEAR, VACCINATION IS THE MOST EFFECTIVE WAY TO PREVENT VIRAL INFECTION. CAN YOU TELL US ABOUT THE PROCESS INVOLVED IN DEVELOPING A NEW VACCINE?**

The process of developing a new vaccine can be very protracted; taking decades for the vaccine to reach the clinic if it even does. There are many hurdles that prophylactic vaccines need to overcome. First, you have to have in vitro, animal model, or serological evidence in humans that what you want to target on the virus or in the viral life cycle will in some way inhibit that virus from replicating. We call this proof of principle. Once you have this evidence, you need to choose how you are going to deliver your vaccine. You would do some testing again in cell culture and in vitro models first. If that looked good you would move on to animal models, assuming that there is an animal model for your particular disease pathogen. If everything looked good after testing on animal models and the vaccine was still eliciting a protective response, you would then move into human clinical trials. If you get there, there is usually another hurdle I should mention in this process; besides just having good data you also have to have money. Bringing a vaccine to the clinic takes an estimated billion dollars, and at any point, drug companies or whoever is developing, can say, “well, we’re not going to fund this anymore because it’s just too much money, and there’s not enough evidence that this is going to work or that it is going to be profitable.” We continue to monitor the safety of the vaccine and the adverse effects even after its license. In this age of vaccine hesitancy, where people may have some questions about vaccines or are reluctant to receive vaccines because they doubt their safety, we take that into consideration both before and after the vaccine is licensed. We monitor these things and if any data suggests that there are some cluster of adverse effects, this is immediately monitored by government agencies. So, the process is very rigorous and the vast majority of candidates will not make it to the clinic. The vaccines that we have are certainly safe and have gone through very rigorous testing.

**ONE OF THE BIGGEST NEWS STORIES THIS WINTER HAS BEEN THE GLOBAL THREAT OF THE CORONAVIRUS. PANIC AND FEAR HAVE SPREAD EVEN FASTER THAN THE VIRUS ITSELF AND INCREASED DEMAND FOR MASKS AND HAND SANITIZER HAVE DEPLETED STOCK EVERYWHERE. IN YOUR OPINION, IS THIS FEAR JUSTIFIED, BASED ON THE INFORMATION AVAILABLE TODAY, AND WHY OR WHY NOT?**

Is this something we should be worried about as a global scientific community? I think that there’s definitely evidence that we should have a health concern about this virus and how it’s spreading, as well as what that means for public health. Because we live in an age of global travel, this presents some challenges when we have new pathogens that arise and are transmitting in certain areas of the world. So I think as a global scientific community, should we be concerned about it? Yes. Do we need to be worried about it here at McMaster and Canada? Not yet. Coronavirus is a very large family of RNA viruses. They are responsible for 10-30% of the colds we experience over the winter. They are a pathogen that is very common to humans —

most of us will have already been infected with coronaviruses.

There have been three coronavirus outbreaks in the 21st century. The first would have been SARS (2003) which is very familiar to the Canadian population, MERS in 2012, and now this new coronavirus. There are certain features of this virus that are good, and there are certain features of this virus that are bad. And remember this is an outbreak that’s unfolding so our information is still evolving. People are publishing papers every single day with new data and information that help shape our response and our view of this outbreak. So what are some good things about this virus? If we compare it to its cousin SARS at the sequence level, it shares about 80% nucleotide homology. SARS had a mortality rate of about 10%. This new virus seems to be quite a bit lower at about 2%. So from a mortality standpoint, maybe less of a concern than SARS. However, there is higher morbidity with this virus, meaning more people are infected. SARS infected around 8,000 people. This virus has around 25,000 confirmed cases, which could be an underestimate. Some people say that over 100,000 people are affected. I’ll point out that the vast majority of deaths, 80% of the mortalities are in individuals over 65. So the virus seems to disproportionately affect older people that might have other comorbidities. There is definitely evidence that it is transmitting human to human and that there is community-acquired viral transmission.

In SARS, there were a lot of what we call “nosocomial infections,” meaning infections happening in hospitals with healthcare workers and other people that were in the hospitals. But we didn’t see a lot of community-acquired SARS. This virus looks different in that way. And in fact, even when we talk about community-acquired viruses, they resemble a little more of influenza viruses, which are spread within the community. This presents some challenges from a quarantine perspective, as it’s very difficult to stem the spread and isolate infected individuals. I would say, globally, WHO (World Health Organization) is approaching it correctly. I think health agencies around the world are, for the most part, giving it a healthy amount of concern. I don’t think we need to panic here at McMaster or in Canada —we only have four confirmed cases.

**HOW DOES THE EMERGING CORONAVIRUS PANDEMIC COMPARE WITH OTHER RECENT VIRUS OUTBREAKS, INCLUDING THE SARS CRISIS OF 2003?**

Most people that were infected with SARS experienced severe disease and were symptomatic, which means they got the virus, felt very terrible, and a lot of them showed up in hospital. Because that virus manifested with more severe disease, it allowed us to isolate individuals that presented symptoms, and what was responsible for stopping the outbreak was good isolation and quarantine measures. One of the differences with this new coronavirus is that not all people infected are experiencing severe symptoms so they are not turning up at the hospital or they might not even be staying home from work or school. This presents a problem for the current outbreak and is at least one reason why we are seeing this sustained, human-human transmission. If you don’t know you are sick, and you don’t know that you have been

in contact with somebody that has potentially been sick, it is very difficult to put into place quarantine, isolation, and contact-tracing measures. And, again, the good thing about this new virus is that it doesn't really cause, in most people, very severe disease. The bad thing is as a result, this makes it harder for us to trace and control it through traditional means.

Coronaviruses infect a very wide range of species, so their virus is familiar to humans because of the common cold that affects many individuals over cold and flu season. Coronavirus also infects many different mammals like bats, camels, and civet cats. What we know from the SARS outbreak in the early 2000s is that the virus originally came from a bat, and the bat virus infected civet cats, most likely in China's live animal markets where we bring together a whole bunch of species that are not usually used to coming into contact with each other in the wild. Civet cats are a delicacy in China that are consumed by humans, and that is how we think we got SARS from bats.

The evidence suggests that this virus looks a lot like a bat virus—it's about 96% identical. We are not exactly sure though if there's any intermediate species at play here, whether or not this virus has jumped directly from bats into humans or maybe has gone through another species along the way.

**WITH SO MUCH ATTENTION BEING FOCUSED ON THE WUHAN CORONAVIRUS OUTBREAK, LESS ATTENTION IS BEING PAID TO ANOTHER, PERHAPS MORE DEADLY VIRUS THAT HAS ALREADY KILLED THOUSANDS OF PEOPLE AND HAS INFECTED MANY MORE—THE FLU. DESPITE THE FACT THAT A FLU VACCINE IS WIDELY AVAILABLE AND ACCESSIBLE EVERY WINTER, MANY PEOPLE CHOOSE NOT TO BECOME VACCINATED. HOW WOULD YOU ACCOUNT FOR THIS UNFORTUNATE REALITY?**

The flu vaccine is unique from any other vaccine in that every year we have to reformulate it. The vast majority of vaccines you get as a child protect you for life, whereas flu vaccines we have to get a new one every year. It is a vaccine that is partially effective, and its effectiveness depends on how well the strains of the vaccines are matched to the strains that are circulating in humans. So I think part of the reason why people have been reluctant to take up the vaccine may be due to its efficacy in certain years that we have not gotten it right. It is not very efficacious and so people do not see a benefit in getting the vaccine. I think there are a lot of myths surrounding the flu vaccine that also explain why people are hesitant. People say, you know, "Oh, you can get the flu from the flu vaccine." That's not true. "I'm healthy, I don't need it." Okay. It's not just about you. It's about stemming the spread of flu within the community. It's unfortunate because if we are going to compare the flu to the ongoing coronavirus in terms of morbidity, its mortality far surpasses the outbreak of the coronavirus that's happening globally. As far as I know, there are no licensed antivirals for coronaviruses. There are some that are experimental, papers that say "XYZ" antivirals can work against coronaviruses and they're massively scrambling to try to mobilize some of those for this particular outbreak.

**IN YOUR OPINION, CAN WE LEARN ANYTHING FROM THE SUCCESS OF SCHOOL-BASED VACCINATION STRATEGIES, SUCH AS THE HPV VACCINE PROGRAM IN ONTARIO? HAS THIS APPROACH BEEN EXPLORED FOR THE FLU VACCINE?**

Nationally, there are not mandatory immunizations for school attendance. Only Ontario and New Brunswick have this policy. There are certain states that have piloted influenza vaccines in schools and are looking at the cost-benefit analysis. This is not completely applicable to Canada because the flu vaccine is paid for by OHIP. Thus, in the US, that cost benefit analysis is shaped a little bit differently in terms of who is paying for the vaccine. I think if it increases uptake, it's definitely a good idea. I think that there are some logistical challenges because, like I said, flu vaccines have to be administered every year and they change every year. Rolling this out in a school system is no small feat, but if it increases uptake, and there is definitely evidence from these US studies that it does increase uptake, I'm all for it.

**ON A DIFFERENT NOTE, WE UNDERSTAND THAT YOU TEACH AN ONLINE COURSE ENTITLED DNA DECODED. CAN YOU TELL US WHAT PROMPTED THE CREATION OF THIS COURSE? WHAT DIFFERENCES DO YOU SEE BETWEEN IN CLASS AND ONLINE LEARNING? HOW DO YOU THINK THE ONLINE FORMAT LENDS ITSELF TO EDUCATION, AND SPECIFICALLY TO THE SCIENCES?**

Online learning has experienced a huge boom in the last decade. I think people are very excited about these educational platforms in terms of changing the scope of what's accessible in higher education. I don't know if they've quite lived up to the hype, but there is certainly really rich online content now on a variety of disciplines. It's free and is taught by experts. One of the sites that hosts a lot of these massive open online courses or MOOCs as they're called is Coursera, and you can go on Coursera and take an online course and learn how to program, or learn quantum physics, and so forth. So, I think that's certainly very exciting. Who is actually accessing that information? What demographics are using these platforms? You might be surprised to learn that the vast majority of people that access these platforms already have undergraduate degrees or some level of higher education. So, is it reaching the demographics we thought it would? To some extent, but still our ability to make these online courses and reach large audiences is very beneficial. It was an exciting project to take on. So far that course has somewhere around 6000 learners that have accessed it in some capacity, so it feels good that we've been able to reach people on different continents across different age ranges and different educational levels, but it's certainly a different experience than having face time with the students.