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Perspectives

# Innovation and Expanding Horizons within Research at the University of Manitoba

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## 1 Introduction

The University of Manitoba is at its peak in novel research discoveries eliminating any shrouds of ambiguity that permeate its walls.

## 2 Discussion

Diversity and inclusivity are the driving forces behind the cutting-edge research at the University of Manitoba. This innovation extends to all levels of academia, from undergraduate through to post-graduate studies. Dr. Jason Kindrachuk from the Department of Medical Microbiology & Infectious Diseases and Dr. Mojgan Rastegar from the Department of Biochemistry and Medical Genetics are two of the many research supervisors at University of Manitoba's Bannatyne Campus currently addressing issues associated with human health. Dr. Kindrachuk's research centres on the mechanisms of Ebola virus transmission, pathogenesis and persistence while Dr. Rastegar's research centres on the neurological disorder, Rett syndrome.

### 2.1 Dr. J Kindrachuk's Research Lab

Dr. Kindrachuk places a large emphasis on understanding the intersection of basic and clinical research in emerging viruses not only in terms of the physiological repercussions that result from infection but the role they play at the level of individual tissues and cells. He stresses the importance of "understanding how these viruses usurp and undermine our own defense systems," as well as the lasting effects these diseases may have at the molecular level. To accomplish these tasks, Kindrachuk and his students employ various complex lab techniques. An area of interest to Kindrachuk are methods for evaluating the maintenance of blood-tissue barriers, including the blood-testis barrier. This interest stemmed from Kindrachuk's experience in West Africa when he and his fellow colleagues learned that male Ebola virus disease survivors can still carry the virus within their testicular tissue after recovery.

Furthermore, testing these patients with current diagnostic methods lead to a negative result. This is of great concern according to Kindrachuk as "patients that have been released to the general public have been shown to be able to spread the disease sexually and carry high amounts of virus, in the absence of disease.

[Thus] we can start to use systems like blood-testis barrier or our kinome platform within our labs to better understand how these viruses are able to do this." The persistence of this virus within the human body raises many more questions than we currently have answers for. Kindrachuk recalls another patient who relapsed twice due to viral penetration into and out of the central nervous system. Kindrachuk believes the virus gained entry, laid dormant, and then resurfaced in the blood.

To further elucidate, what really allowed the virus to transverse the barrier in the first place? Furthermore, what caused the essential breakdown of the barriers and allowed for virus transmission across these internal physiological barriers within the human body? Interestingly, research within Kindrachuk's lab has shown that bilateral navigation of Ebola virus is not seen across the blood-testis barrier. This was reflected in one of their subjects that had 10,000 times higher concentrations of virus in semen than was found during peak Ebola virus infection in the patient. Kindrachuk hopes to dissipate the enigma of Ebola virus's mechanisms within the body and hopes to answer many unanswered questions including why the virus can only enter the blood-testis barrier in one direction but can easily traverse across the blood-brain barrier in both directions.

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*— Dr. Jason Kindrachuk, Department of Medical Microbiology & Infectious Diseases*

### 2.2 Brayden Schindell & Ebola survivors

PhD student Brayden Schindell from the Department of Medical Microbiology & Infectious Diseases has worked in the emerging and re-emerging virus's laboratory since January 2018. He was intrigued with the research conducted on Ebola virus and began pursuing his PhD degree in Dr. Kindrachuk's lab in January of 2018. He studies how Ebola virus persists in the reproductive

tracts of male and female survivors and how these patients maintain the virus despite remaining largely asymptomatic. Currently the lab is focused on utilizing polymerase chain reaction based diagnostics similar to those employed during Ebola virus disease outbreak. Kindrachuk states that it is "much more sensitive than an ELISA (enzyme linked immunosorbent assay) and is capable of sensing very remote traces of the virus." The issue with this technique arises when the virus is housed in a more precarious location such as the brain or the testes where the immune system is more limited in its ability to initiate a response. Schindell and Kindrachuk believe responses to current outbreaks is a top priority.

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The goal of Schindell's project involves studying the mechanisms of establishment of persistent infections in the reproductive tracts of males and females. He is also collaborating with researchers in West and Central Africa to study the long-term reproductive health effects on survivors of Ebola virus disease. He will be studying the reproductive health effects by working with cohorts of survivors in Sierra Leone conducting survey-based analysis and sample analysis. Currently there are two vaccines for Ebola in clinical trials.

## 2.3 Research Opportunities in Winnipeg

Part of Winnipeg's flourishing research opportunities can be attributed to the National Microbiology Laboratory located in Winnipeg that provides students with direct lines to many lead researchers in many viral and bacterial fields. The facility houses several classes of containment laboratories as well as the only containment level four laboratory in Canada. Having this facility in such close proximity to the University provides students with the opportunity to conduct novel experiments and analysis on high containment viruses such as Ebola virus. "The work environment is very supportive and extensively collaborative," Schindell states. He also believes the University houses a world-class facility in conjunction with the heavy focus on community engagement locally and abroad. "It allowed me to venture beyond what I believed I was capable of accomplishing and has allowed me to gain new perspectives on my research with Ebola virus."

## 2.4 How Integrating Labs can Facilitate Change and Innovation

The collaborative nature of the Bannatyne campus allows for students with a myriad of different strengths and backgrounds within the field of science to share their ideas and innovations to formulate new discoveries. The Regenerative Medicine unit and the Department of Medical Microbiology and Infectious Diseases are indicative of this breadth of cooperation as well as the collaborations between community groups that directly translate research to the community. A great example of this collaboration is reflected in the work of Dr. Keith Fowke's laboratory (Medical Microbiology and Infectious Diseases) with the community organization Sunshine House. Sunshine House supports the largely underserved groups including those affected by HIV/AIDS, those who use substances, those exploring gender and sexual identity and those experiencing homelessness. They provide a community drop-in and resource centre that promotes harm reduction and social inclusion by providing programs, which fulfils social, health, and recreation needs of the community.

In 2005, Sunshine House reached out to the Fowke lab because the community wanted to understand the effects of solvent use on the body. In collaboration with Sunshine House, the Fowke lab has uncovered novel findings about the impact of solvent use on some aspects of the immune system. The study results have been discussed with community members to arrive at a collective understanding and interpretation of the findings. This work has resulted in not only answering the communities initial question, but has sparked new discussions and new questions leading to new projects that involve more researchers at the University of Manitoba and from other institutions.

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*— Brayden Schindell PhD, Department of Medical Microbiology & Infectious Diseases*

Dr. Mojgan Rastegar joined the University of Manitoba in 2009 as the primary member of the Regenerative Medicine program, at the Rady Faculty of Health Sciences. Since then, she has built a strong research program on epigenetics, stem cells, and neurodevelopmental disorders. Apart from running her own research laboratory and training of graduate and undergraduate students, she is the director of multiple courses at the graduate level, while teaching undergraduate courses. At the University of Manitoba, she is a member of the Senate, and Senate Committee on Admis-



sion, Senate Committee on Planning and Priorities, as well as Faculty and College Executive member.

### 2.5 Novel Techniques

Dr. Rastegar's research program is focused on the role of epigenetics in neural stem cell self-renewal and differentiation and their abnormalities in X-linked neurodevelopmental disorders such as Rett Syndrome. In these regards, her lab uses a combination of *in vitro* and *in vivo* approaches, using different types of stem cells, primary brain cells, human cell lines, and transgenic mice. Her lab pioneered the research on developing tools and reagents to study different protein variants of the MeCP2E1 and E2, in the brain. Dr. Rastegar has now taken a leadership role in Canadian research on Human Rett Syndrome Brain Tissues. Earlier this year, she received an award from the Ontario Rett Syndrome Association (ORSA) to establish the "Human Rett Syndrome Brain Bio-Repository Laboratory" in Manitoba that is currently located at the Children's Hospital Research Institute of Manitoba (CHRIM).

The grand opening of this laboratory was September 2019, which was well attended by Rett Syndrome parents (from Ontario, British Columbia, Manitoba) and the president of ORSA. This new laboratory is a unique resource in Canada. Dr. Rastegar is now studying the molecular basis of intellectual disability in neurodevelopmental disorders, aiming to use cutting edge techniques in stem cell biology, epigenetics, genomics, and drug repurposing to find potential novel avenues for devastating diseases that currently have no cure, such as Rett Syndrome.

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## 3 Conclusion

Compared to other research laboratories across the province, Dr. Rastegar believes the University of Manitoba has an extremely strong and diverse research team with scientists from all across Canada with her lab specifically bringing expertise from Europe, United States, and Canada. Despite the various challenges encountered working with neural stem cells for Dr. Rastegar and the strenuous experimental procedures required for Ebola research for Dr. Kindrachuk, both research labs are continually inspired and face these inevitable road blocks with an open approach and an equally open mind.

## 4 Acknowledgements

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