Using Ferret Models to Study the Pathology of SARS-Cov-2 and General Vaccine Development

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Dr Alyson Ann Kelvin is an assistant professor at Dalhousie University and a scientist with the Vaccine and Infectious Disease Organization at the University of Saskatchewan. Born into student life and watching her parents work in academia, she developed an early interest in research. After completing her undergraduate degree in Canada, she decided to travel to Europe to learn how science is conducted in other countries and cultures. She received her PhD from Queens University in Belfast. Her research primarily focuses on emerging viruses, such as influenza viruses and the novel SARS-CoV-2, and vaccine development against these threats.

Dr. Alyson Ann Kelvin

Here she discusses the effectiveness of using ferret models to study the pathology of SARS-CoV-2 infection and the development of vaccines against this virus. Identifying the next "pandemic virus" and developing measures to mitigate its effect has always been a pertinent part of virology and global health. Like Dr Kelvin, many scientists have studied the patterns of emerging viruses, reservoir species and the mechanisms behind these pathogens, but it remains an ever-evolving area of study. Dr Kelvin started her journey in emerging viruses by working on influenza viruses in Italy to identify how avian influenza outbreaks occur. However, the following "pandemic virus" was influenza A subtype H1N1, originating from swine which spilled over instead, causing a pivot in her research. She became more interested in understanding the difference in disease severity and how H1N1 affects diverse populations, stating .

This led her to refine the ferret model to allow the investigation of age and previous infection as host-risk factors. Ferrets are naturally susceptible to human clinical isolates of many different viruses, including Ebola, influenza viruses, coronaviruses (CoV) and Respiratory Syncytial Virus (RSV) rendering them an appropriate model for also studying the effects of age or previous infections. In 2008, she was a part of a team that published work demonstrating the efficiency of the CXCL10 ferret model to understand the biology of ferrets during severe acute respiratory syndrome (SARS-CoV) (2). Ferrets were chosen as a model organism due to the similarities in lung infection patterns observed in SARS-CoV patients. Due to its efficiency in modelling viral infections in human, the ferret model enabled future studies to investigate intersections between certain

"H1N1 was causing more severe disease in infants and possibly the elderly. I became very interested in knowing why certain people are more susceptible to severe disease"

variables, such as age, pre-existing conditions and sex, as well as the severity of viral infection. For example, Dr Kelvin used a pregnant ferret model to study why pregnant individuals were more susceptible to Zika than other groups (4).

When studying SARS-CoV-2, she could use the readily available ferret models and apply them to this new virus. The objectives of this new work were to use the ferret models to better understand the pathogenesis of SARS-CoV-2 and why the older population as well as males were more susceptible to severe disease than younger people. Experiments were conducted to study the impact of age and sex on the severity of SARS-CoV-2 infections. Aged male ferrets exhibited prolonged viral replication and virus shedding compared to young female ferrets; this is possibly because the female ferrets had a higher interferon response than the males (3). This study shows that older males have a decreased antiviral response to SARS-CoV-2 compared to other populations. Therefore, the ferret model is essential for understanding the pathogenesis of SARS-CoV-2 across various conditions.

The ferret model can also be used for vaccine and therapeutic evaluations. A 2012 paper reveals that the ferret model is a great candidate for developing influenza A subtype H5N1 vaccines because it shows immunological memory and cross-protective immunity (1). These features are ideal, especially when it comes to testing the safety and efficacy of human vaccines. In addition to her work in older male ferrets, Dr Kelvin also developed and applied a similar ferret model to evaluate and test the efficacy of potential SARS-CoV-2 vaccines. Currently, she is working with multiple groups throughout Canada including Entos Pharmaceuticals, Immovaccine, and researchers at the Canadian Center for Vaccinology (CCfV) towards developing various types of vaccines. An essential goal is to develop a more broadly reactive vaccine, to curve the impact of emerging virus strains.

Overall, Dr Kelvin's work using the ferret model to study emerging viruses, including SARS-CoV-2, has largely impacted the field. This use of this model has the potential to make further significant strides in vaccine development.

References

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