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RESEARCHER PURSUES ONE HEALTH VISION

Dr Nicola Fletcher, Assistant Professor and Ad Astra Fellow at UCD School of Veterinary Medicine, discusses her exciting career path encompassing research work on human and animal disease. We also look at her groundbreaking work on the first deer herd in Europe to be infected with the COVID-19 virus

Nicola Fletcher grew up in Dublin but moved to Wicklow with her family when she was a teenager. She recalls: "We traded city life for a smallholding that quickly filled with horses, sheep and a medley of homeless animals that we were delighted to take in, and I thrived in the rural setting. While I sometimes got side-tracked from my studies, I developed a strong interest in science during my secondary school years. In 1996, I began my academic journey with a BSc in Equine Science from the University of Limerick. I enjoyed my undergraduate years and made the most of the freedom university life offered including an eight-month trip to Kentucky to work at a thoroughbred horse stud."

A passion for research

Although she initially did not envisage a future in research, her love of the laboratory classes at university led her to a job at the Irish Equine Centre's virology department. "I gained invaluable experience and developed a passion for the study of viruses. While at the Irish Equine Centre, there was an influenza outbreak that I worked on, and we isolated and characterised the virus using a range of techniques. This piqued my interest in research, prompting me to start a PhD at UCD under the

mentorship of Professor Sean Callanan and Professor David Brayden back in 2002.

"My doctoral research focused on developing an in vitro blood-brain barrier for studying feline immunodeficiency virus (FIV) neuropathology. It was an incredible experience, and I even had the opportunity to travel to the Glasgow Veterinary School under a Royal Academy Scholarship and continue the project with my first postdoctoral position investigating FIV neurotropism, funded by Science Foundation Ireland and mentored by Professor Callanan."

Nicola wanted to gain experience in human virology after her PhD. This led her to the University of Birmingham in 2009 for a postdoctoral research position, where, under the mentorship of Professor Jane McKeating, she discovered that hepatitis C virus (HCV) is capable of infecting the blood-brain barrier, which was the first demonstration that HCV replication is not restricted to the liver. Nicola subsequently identified a novel mechanism by which viruses can hijack the inflammatory microenvironment to promote their own infection.

Nicola commented: "I thoroughly enjoyed my time at the University of Birmingham, where I honed my skills as a research scientist. I saw the impact that translational research can have while working with clinicians in the liver transplant unit at Queen Elizabeth Hospital. I realised the impact that a One Health approach to research could bring, so in 2014 I moved back to UCD to complete a degree in veterinary medicine. After qualifying as a veterinary surgeon in 2018, I moved to the Animal and Plant Health Agency (APHA-Weybridge) in the UK as a research pathologist, where I conducted research studies on important infectious diseases such as rabies, African swine fever, hepatitis E virus, and tuberculosis, and began specialty training in veterinary pathology."

Lifelong dream

Nicola continued: "In January 2020, I realised a lifelong dream when I joined the School of Veterinary Medicine as an Ad Astra Fellow, meaning that I could build a research team focused on a One Health approach to zoonotic viruses and teach veterinary students across the veterinary programme, from first year physiology to final year pathobiology."

The COVID-19 pandemic meant that her research took a different direction to the one originally planned, but she established the first laboratory in Ireland for SARS-CoV-2 culture, at the UCD Veterinary Medicine Biosafety Level 3 Laboratory, and obtained funding to investigate a range of projects including neurological disease associated with COVID-19, wastewater surveillance, antiviral therapies and the first discovery of European deer with anti-SARS-CoV-2 antibodies, in the fallow deer population at the Phoenix Park.

"Currently, I lead a dynamic team of researchers comprising two postdoctoral fellows, a research assistant, two PhD students, and honorary member, Noodle the poodle!

"Together, we adopt a One Health approach to investigate the complexities of hepatitis E virus, an emerging zoonotic viral disease gaining significance. What makes our work exciting is the array of cutting-edge technologies we employ, most of which are available at UCD. From soft X-ray microscopy to novel 3D cell culture techniques and high throughput sequencing methods, we use a diverse toolkit to answer our research questions. This interdisciplinary approach allows us to gain comprehensive insights into the virus and its interactions within the ecosystem. If you are interested in working with us or have a project idea, we are always looking for new team members."

Outside of work, Nicola says she fully embraces her "inner nerd". "I'm an avid astronomer and own a collection of telescopes. I also seek out adventurous experiences around the globe. Whether it is embarking on a safari in Tanzania, horseback riding in Arizona, or taming camels in Egypt, I relish the opportunity to explore and immerse myself in new cultures and landscapes.

DUBLIN DEER HERD FIRST IN EUROPE TO BE INFECTED WITH COVID-19

Dr Fletcher was a key member of the team of UCD scientists who discovered that deer at the Phoenix Park in Dublin were the first in Europe to be infected with the COVID-19 virus, most likely a result of regular human contact. The research was highlighted by *Science* in 2023 in the article "First Eurasian cases of SARS-CoV-2 seropositivity in a free-ranging urban population of wild fallow deer".

Nicola had been monitoring the Phoenix Park deer for the presence of SARS-CoV-2 (the virus that causes COVID-19) since 2020. "Our study revealed that in 2022, 57 per cent of the animals we tested had antibodies to SARS-CoV-2. This is the first time European deer have been demonstrated to have anti-COVID antibodies and the first deer species, apart from US white-tailed deer, with demonstrated previous exposure to SARS-CoV-2."

The team's research indicated a change in host tropism as new variants emerged in the human reservoir. This underlines the importance of continued wildlife disease monitoring and of limiting human-wildlife contacts.

Nicola warns: "Animals with anti-SARS-CoV-2 antibodies were known to take food from people who visit the Phoenix Park. This highlights the importance of people not feeding these deer, due to the risk of 'reverse zoonosis' – transmitting diseases from humans to animals which could then transmit back to people."

The study was a collaboration between Dr Fletcher's laboratory at UCD School of Veterinary Medicine, and Dr Simone Ciuti's team at UCD School of Biology and Environmental Science who have been studying the behaviour of the Phoenix park deer for many years. Researchers at the UCD National Virus Reference Laboratory, UCD Centre for Experimental Pathogen Host Research (CEPHR) and UCD Conway Institute also contributed to the findings.

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