



INFECTIOUS DISEASES

Flu from the nose: influenza A is spread from the upper respiratory tract of ferretsRichard, M. et al. *Nat Commun* **11**, 766 (2020)

As spring draws near, the flu will begin to ebb...only to flow again in the fall. Every flu season, influenza fells millions and contributes to hundreds of **thousands of hospitalizations and deaths**. Much time, money, and effort is spent combatting the flu, but still it returns.

Seasonal flu is primarily driven by two influenza virus subtypes: A & B. The latter primarily infects humans, while the various forms of the former can circulate through a number of animal hosts. It does not, however, infect lab rodents so readily.

Instead, many researchers have long turned to the ferret. Ferrets can be infected with the human virus without needing to adapt it to replicate within a mustelid host, and sick animals will exhibit similar clinical symptoms and pathologies to people. That makes them valuable models to study influenza pathogenesis and transmission, says Mathilde Richard, a virologist at Erasmus MC in Rotterdam.

In humans and ferrets, influenza A is transmitted via the air and can replicate in both the upper and lower respiratory tracts. But from where does the virus actually spread? Richard's latest work gets to the heart of that question—or rather, the nose.

To keep track of viral origins, collaborator Anice Lowen at Emory University in Atlanta had previously developed a tagging method to study re-assortment, the process by which different viruses exchange genetic material when co-infecting a host cell. “We thought this would be very interesting to use in our transmission set up,” says Richard, “And she was interested to look at whether infection in two separate parts of the respiratory tract would limit re-assortment.” Two birds, one stone, she says.

The researchers infected ‘donor’ ferrets with tagged and untagged pairs of different influenza A viruses, co-inoculating the upper respiratory tract intranasally with one variant and the lower respiratory tract intratracheally with the other

(and vice versa). Periodic nose and throat swabs were then taken from uninfected ‘recipient’ ferrets held in physically separate cages for sequencing to see what form of the virus had reached them.

“We thought that [the viruses] would mix quite fast,” says Richard, “As a matter of fact, they don’t.” Though virus replication occurred in both parts of the respiratory tract, the particles transmitted to recipient ferrets came almost exclusively from the donors’ noses.

“Common practice is that flu viruses are not transmitted beyond a meter,” she says, but, depending on the actual particle size expelled from the nose, it may be able to travel farther and linger longer in the air than previously thought. That quantification is underway.

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