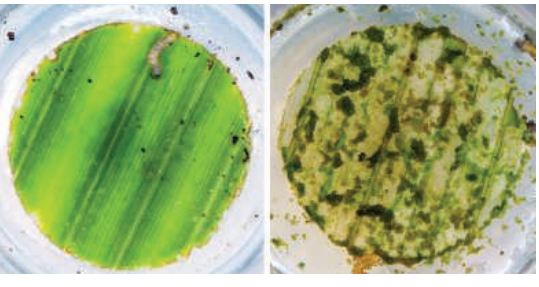
Co-author Megan Maher, a structural biologist at the University of Melbourne, and colleagues solved the structure of one variant. They found that it resembles the Bt proteins used as insecticides, except it has just two major active parts, whereas Bt proteins have three. Bt proteins work by puncturing the insect gut. The researchers think the fern proteins do, too, but because the active part missing in fern proteins is the one Bt proteins use to bind receptors on the cell membranes, the fern proteins may bind different receptors. "The hope is the new fern proteins can be Goldilocks insecticides—similar enough to Bt to be safe and effective yet different enough to kill insects that evolved resistance to Bt," Tabashnik says.

When the Corteva team transferred the genes for the most effective IPD113 versions into maize, leaf damage from key pests such as fall armyworm and corn earworm fell to at most 30% compared with more than 50% in unmodified maize. The fern proteins also worked against insect strains resistant to Bt proteins. The paper "is an excellent advance and establishes ferns as a repertoire of new molecules," Singh says.

These successes will likely attract interest from other research groups, says Georg Jander, a chemical ecologist at the Boyce Thompson Institute. And he thinks other companies are quietly casting an even wider net for new insecticidal proteins. Jander and Boyce Thompson fern biologist Fay-Wei Li, for example, are looking into defense compounds of primitive plants called liverworts. And Sepčić is evaluating mushroom-derived compounds that kill insects by a different mechanism. Instead of binding protein-based receptors on the cell membrane as the fern proteins do, they bind the lipids the membranes are made of. Because these lipids are conserved across the tree of life, Sepčić thinks insects will not easily evolve resistance.

If such compounds prove effective against Bt-resistant pests, proteins from some of the earliest land organisms may help ensure the future of food security. ■



In lab tests, corn earworms usually devour maize leaf samples (right), but one carrying a newly identified fern protein was protected.

PHOTOS: CORTEVA AGRISCIENCE

INFECTIOUS DISEASE

Novel coronavirus blamed for Cyprus cat deaths

Coopted dog virus sequences may have boosted the strain

By **Catherine Offord**

When thousands of cats started to get sick and die in Cyprus this year, the crisis made international news. Symptoms such as fever, a swollen belly, and lethargy pointed to feline infectious peritonitis (FIP), a common condition caused by a cat coronavirus—but scientists struggled to explain the surge in cases. Now, researchers have identified a possible culprit: a novel feline coronavirus that has borrowed key RNA sequences from a highly virulent dog pathogen called pantropic canine coronavirus (pCCoV). The findings, posted on 9 November as a preprint on bioRxiv, could help explain how severe illness spread so widely.

"They've done a great job in identifying what looks to be a very interesting and concerning virus," says Gary Whittaker, a virologist at the Cornell University College of Veterinary Medicine. Although canine-feline coronavirus crossovers have been reported before, this is the first documented case of a cat coronavirus combining with pCCoV, apparently leading to a "perfect storm of both disease and transmissibility."

Veterinarians in Cyprus raised the alarm early this year about increased cases of FIP, which is not related to COVID-19 and does not affect humans. By July, media outlets reported nearly 300,000 cat deaths, though local veterinarians revised that to about 8000. In August, the Cypriot government greenlighted the veterinary use of SARS-CoV-2 medication molnupiravir, which blocks coronavirus replication and appears to be an effective treatment for FIP.

The explosion in cases presented a puzzle. Most feline coronaviruses infect the gut, causing mild infections that don't escalate to FIP. Strains sometimes mutate into a form called FIP virus (FIPV) that infects immune cells and triggers serious disease. But unlike intestinal strains, which spread easily through feces, FIPV typically isn't transmitted between cats.

To learn more, researchers ran RNA sequencing on fluid from the abdomens and spines of sick cats in Cyprus. They found a previously undescribed feline coronavirus, which they dubbed FCoV-23, that contains a chunk of RNA from the dog virus pCCoV. (The "pantropic" in its name means that, unlike regular intestinal canine coronaviruses, pCCoV infects many tissues.)

FCoV-23 seems to have arisen when a feline coronavirus encountered pCCoV in an unidentified animal host and coopted the latter's spike protein—the structure coronaviruses use to gain access to host cells. Study co-author Christine Tait-Burkard, a virologist at the University of Edinburgh's Roslin Institute, says this and other genetic tweaks may have allowed FCoV-23 to cause FIP while still infecting the intestines and spreading through feces. The team speculates that the spike protein changes could also help stabilize FCoV-23 outside an animal host, increasing chances of transmission via contact with contaminated feces. It's unclear how far FCoV-23 has spread, though the team identified one case in the United Kingdom in a cat imported from Cyprus. The general risk to cats outside the island remains low, Tait-Burkard says.

Margaret Hosie, a virologist at the University of Glasgow, says that although it's exciting to see virological data emerging from the Cypriot population, there remain many open questions. More data are needed to confirm FCoV-23 is transmitted directly among cats through feces, she says.

Increased awareness could explain some of the apparent rise in FIP cases this year, she adds. Without historical case numbers, "we can't say there's been a huge outbreak." Feline coronaviruses and pCCoV have coexisted in the Mediterranean region for years, so it's possible that the genetic crossover happened some time ago.

Tait-Burkard and colleagues are collaborating with researchers in Cyprus to test local cats for FCoV-23 and get better estimates of its prevalence and fatality rate. They also want to investigate whether unique features of FCoV-23 explain the resulting disease's apparently high rate of neurological symptoms—twice that of typical FIP.

In the meantime, the discovery of this mixed cat-dog coronavirus highlights the importance of taking a cross-species approach to understanding viral evolution, Whittaker says. "This feline coronavirus has got huge potential for us to understand what goes on in general in coronavirus virology." ■

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