Feline virus, antiviral drug studied to understand drug resistance

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Researchers at Ohio State will spend the next two years testing their theories about just how an AIDS-like virus in cats is able to resist the powerful medicines that are thrown against it.

It's one of the latest efforts at understanding one of the leading problem areas in medicine today -- antimicrobial drug resistance. When bacteria or viruses become resistant to drugs, they become more difficult, or even impossible, to treat.

The project, funded by the National Institute on Drug Abuse, could reveal how some viral infections become able to withstand antiviral medications and even thrive in the presence of some drugs.

If successful, the research might pave the way to smarter, more effective treatments for a host of pathogens that have learned to resist most therapeutic efforts.

The project grew from important discoveries made five years ago as part of a controversial research program investigating the impact of methamphetamine on feline immunodeficiency virus (FIV) – one of only three animal viruses that can be used to mimick HIV (human immunodeficiency virus) infections in humans.

Surprisingly, that project showed that the virus was able reproduce itself 15 times faster when methamphetamine was present.

The work also showed that FIV mutated rapidly to adapt to grow in astrocytes, the dominant cell type within the brain, and that this phenomenon was accelerated by exposure to methamphetamine.

That observation led to an epiphany of sorts, explained Lawrence Mathes, professor of veterinary biosciences and associate dean for research and graduate studies in the College of Veterinary Medicine and principal investigator on the project.

“If the virus becomes drug-resistant as it routinely mutates into this new form, would that drug resistance occur earlier if methamphetamine were present?” he asked.

After an initial phase five years ago that used cats as the animal model for the study, research shifted to more refined work with cell cultures of astrocytes grown in the laboratory, focusing on the changes taking place in individual cells. Mathes reasoned that the same mutated form of FIV would probably be present in the brains of infected cats.

He and his colleagues turned to tissue stored from another decade-old unrelated project that looked at how the virus suppressed the animals' immune systems.

“We went back to those tissues and, in fact, found that the same virus mutations we saw in the cultured cell experiments were present in that brain tissue but only after long-term infection,” he said.

The new research grant will use tissue culture methods to look specifically at how the presence of methamphetamine may increase the virus' ability to resist anitiviral drugs, in this case, a powerful AIDS drug called azidothymidine, or AZT.

“We know a lot about AZT, how it works and what mutations it causes

in the virus," he said. The researchers will treat FIV-infected cell cultures with low concentrations of AZT, forcing it to develop a resistance to the drug, repeating the procedure in the presence of methamphetamine.

"We know how long it normally takes the mutation to appear in the virus. We predict that it will appear earlier in cells exposed to both AZT and methamphetamine," he said.

Mathes said that the first year of the project is focused on continued in vitro studies using both FIV and cat cell lines as well as parallel experiments with HIV in human cell lines.

If the results are promising, the researchers will test the drugs' interactions with the virus in a small study using two dozen cats in the second year.

Source: Ohio State University