How viruses expand their host range: Insights from parvoviruses in domestic and wild carnivores

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Tentative novel route of cross-species parvovirus transmission among wild carnivores. Based on phylogenetic analysis and the field evidence shown here with puma carnivory on raccoons, predation and/or scavenging of infected animals may provide an alternate pathway for cross-species parvovirus transmission, in addition to the prototypical fecal-oral route found in domestic systems Credit: Ashley Gramza, Colorado State University, CC-BY 4.0

Virus multiplication continually generates new variants at a rate that is much faster than their hosts. One consequence of their higher mutation

rate is that many viruses can rapidly adapt to new hosts. A study published on November 6th in *PLOS Pathogens* reports on the systematic analysis of the host range of canine parvovirus (CPV) and reveals different factors that determine which carnivores the virus can infect.

"Parvo" as it is known to dog owners, is a virus that was first seen in domestic dogs in the late 1970s and rapidly spread around the world. CPV is thought to have evolved from a closely related cat virus called feline panleukopenia virus (FPV), which infects domestic and wild cats, along with other related species in the order Carnivora.

To define the natural host range of viruses related to CPV and FPV, Andrew Allison, from Cornell University in Ithaca, USA, and colleagues tested samples from over 850 individual wild carnivores from 18 species, including foxes, coyotes, raccoons, otters, martens, wolves, bobcats, and pumas, for the presence of parvoviruses. The results showed that these viruses were much more widespread in North American carnivores than previously thought. In addition, infection in some species such as coyotes and raccoons was very common, making it likely that transmission occurs not just sporadically from domestic animals but also between wild animals, and possibly between many different wild species.

To explore how viruses adapt to alternative hosts, the researchers selected three different parvovirus variants (one isolated from domestic dogs and two from raccoons) and infected cultured cells from six different carnivore host species (domestic dog, domestic cat, domestic ferret, American mink, gray fox, and raccoon). They then allowed the viruses to multiply over several rounds of cell culture infection for 20 weeks (likely over 100 viral generations), then characterized any genetic changes that occurred after these passages, and compared them to the sequences of viruses recovered from hosts in the wild. The rationale was that mutations that are consistently associated with specific hosts in both

natural systems and after experimental cell passage are likely to influence host range.

The researchers focused their analysis on the gene coding for VP2, a protein in the outer shell of the virus capsid that interacts with a protein called transferrin receptor type-1 (TfR) on the mammalian host cells (this "docking" process is the first step of infection). They found that passage of the viruses in cell cultures of different hosts results in mutations at many of the same positions in VP2 that also vary in nature. This suggests that as these DNA viruses transfer between different hosts they encounter barriers to infection that can be overcome by only a few mutations in the virus that likely alter the specific interaction between VP2 and the TfR.

The researchers conclude that "parvoviruses may cross species barriers to infect less susceptible hosts through single or only a few mutations, and that differences in the genetic background, host range, and/or evolutionary history of the viruses influence their propensity to jump hosts". Overall, they say, their findings "will help reveal the mechanisms that control host switching and viral emergence.

More information: Allison AB, Kohler DJ, Ortega A, Hoover EA, Grove DM, et al. (2014) Host-Specific Parvovirus Evolution in Nature Is Recapitulated by In Vitro Adaptation to Different Carnivore Species. *PLoS Pathog* 10(11): e1004475. DOI: 10.1371/journal.ppat.1004475

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