O-23

Variation in parvovirus capsids controls the specific structural interactions with transferrin receptors or with antibodies, and effects host-specific infection

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Binding to receptors from different hosts are key virus:host interactions that control host range and determine the success of infection. Similarly, the binding of antibodies can lead to viral neutralization. Canine and feline parvovirus capsids bind the transferrin receptor type-1 (TfR) on host cells and enter via endocytosis to cause infection. Specific structural interactions are necessary to prepare the stable capsids for cell infection. We have defined the details of binding, competition, and occupancy of wild-type or mutant parvovirus capsids and purified receptors and antibodies. TfR/capsid binding interactions depended on the species of origin of the receptor, and varied widely. There was no direct relationship between affinity of binding and cell infection. Capsids bound feline, raccoon, and black-backed jackal TfRs at high affinity, but there were barely detectable levels of attachment to the canine TfR, which mediated infection efficiently. TfRs from different species also occupied capsids to different levels, with ~2 feline TfRs but ~12 black-backed jackal TfRs binding each capsid. Binding and competition between different TfRs and/or antibodies also showed complex relationships. Recent high resolution cryoEM structures of the capsid complexed with TfR or with monoclonal antibodies binding to different epitopes reveals the structural basis of the functional differences seen.