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A possible host cell-binding protein in cluster EK phages

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Among actinobacteriophages, those with podoviral morphology are considerably less common than long-tailed siphoviruses. Despite excellent model podoviruses that infect other kinds of bacteria, including *Enterobacteriaceae* phage T7, *Salmonella* phage P22, *Shigella* phage Sf6, and *Staphylococcus* phage P68, the podoviruses of actinobacteria are less well-understood at the genetic level. *Microbacterium foliorum* bacteriophage clusters EK, EM, and GI consist of podoviruses. The interaction of model podoviruses with the host cell is mediated by an assortment of tail proteins with architectural similarities but distinct organizations and interactions with both the bacterial surface and the rest of the capsid. For example, in phage Sf6, trimers of tail spike proteins associate with both tail hub proteins and O-antigen on the *Shigella* outer membrane. In phage P68, the comparable tail fiber protein is also organized in trimers, but are linked to the capsid through proteins completely dissimilar to those present in phage Sf6. The Sf6 tail hub protein, to which the tail spike proteins are attached, consists of a lamin B1-like domain and a distinctive beta-propeller domain. No similar functions are assigned to any of the genes of actinobacterial podoviruses. In annotating the genome of subcluster EK2 phage Moleficent, a student in Miami University's 2023 Bacteriophage Genomes class noted that gp45, highly conserved in EK phages but assigned no function, had strong predicted similarities with parts of other podovirus proteins when analyzed by HHpred. Further analysis of this protein using Alphafold revealed the prediction of a long protein with four distinct domains, from end to end: a lamin B1-like domain, a beta-propeller, an unknown domain, and a beta-barrel with strong similarity to polysialic acid-binding domains of other phage proteins. We propose that Moleficent gp45 represents a host cell surface-binding protein in cluster EK that has evolved by fusion of an Sf6 tail hub-like or P68 tail fiber-like protein with a domain, positioned distally, that promotes adherence to some host cell surface carbohydrate.