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MacKat and Clipper: Snipping, Trimming, and Redefining the Genome

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Nontuberculous mycobacteria (NTM) can cause highly antibiotic-resistant infections that pose a growing public health threat, especially for immunocompromised individuals. Mycobacteriophages (phages) are viruses that infect and kill a narrow host range of mycobacterial cells. Phage therapy offers treatment for these infections where few antibiotic options exist. We isolated novel phages Clipper and MacKat from soil samples collected in Orono and Palmyra, Maine, on host *Mycobacterium smegmatis* mc2155. Mackat has a 55,442-bp genome with 66.5% GC content, 93 predicted protein-coding genes, and 1 tRNA. Clipper has a 60,558-bps genome with 66.3% GC content, 103 predicted protein-coding genes, and 1 tRNA. Electron microscopy revealed that Clipper and MacKat are both *Siphoviridae* morphotype. Clipper and MacKat belong to the K1 cluster and share high sequence identity but have different life cycles. Clipper is a temperate phage, forms stable lysogens and encodes an integrase and immunity repressor. Clipper had a variable plaque morphology of both turbid and clear plaques with sizes between 1-5mm. MacKat has an approximate 5,000 base pair deletion of the genome region that encodes the tyrosine integrase (gp45) and the immunity repressor (gp47) making it only capable of fulfilling the lytic cycle and lysing the host cell. Notably, Clipper, but not MacKat, encodes a phage-encoded ESX-secreted toxin system upstream of the integrase, which potentially increases the fitness of the bacterial host. Lytic cluster K1 phages have been used in phage therapy, but more research is necessary to fully explore the differences between Clipper and MacKat.