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IDENTIFICATION OF POSSIBLE PHAGE QUORUM SENSING SYSTEMS

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Quorum sensing is the production of group behavior in bacterial cells through the release of extra-cellular chemical autoinducers. When autoinducers reach a certain concentration, cells will sense this and engage in coordinated gene expression resulting in a change in group behavior. Well known examples include the production of flagella, toxins, and formation of biofilms. In a recently published paper, it was reported that bacteriophage also communicate with each other using quorum sensing systems to regulate phage lysis versus lysogeny (Erez et al, 2017). The authors named these “Arbitrium” systems in bacteriophage and described the key genetic elements involved in the Bacillus phage Phi3T. The authors showed that the gene for a small, secreted protein, arbitriumP (aimP) that functions as the extra-cellular autoinducer, follows the gene for an intracellular peptide receptor helix-turn-helix (HTH) protein (aimR). High concentrations of aimP cause aimR to dimerize and bind to a DNA regulatory site just downstream of the aimR gene, resulting in increased transcription of a downstream aimX protein, which down regulates lysis through an unknown mechanism. To find similar genetic elements in *Actinobacteria* phage, we searched annotated genomes in PhagesDB looking for HTH protein genes followed by a gap region. We hypothesized that the small aimP protein genes may not have been annotated, but might be found in the gap region along with the DNA regulatory sites for aimR binding, followed by a putative aimX gene. Most phage did not have the genetic pattern described. However, of the 50 *M. smegmatis* cluster C1 phage (all myoviruses) currently in GenBank, all 50 contain HTH protein genes followed by a gap containing one or more small, un-annotated ORFS with strong N-terminal secretory signals. Further, we identified 33 out of 70 phage in the Bacillus cluster C (myoviruses) with similar HTH/gap patterns, containing small, un-annotated ORFS in the gap regions. Curiously, none of the *Bacillus* phage small ORFS had N-terminal secretory signals, but instead had internal type VII secretory signals. No type VII secretory signals were found in the *M. smegmatis* cluster C1 phage small ORFS. We speculate that these may represent phage-encoded quorum sensing genes.