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Poster #2: ASO-Mediated mRNA Silencing Reveals a Link Between Tail Assembly and Genome Packaging in Phage ΦKZ

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The P. aeruginosa infecting jumbo bacteriophage ΦKZ encodes 371 predicted genes, most of which are of unknown function. This limited characterization is partly attributable to its classification within the Chimalliviridae, a family of phages that assemble a nucleus-like compartment within the bacterial host. The phage nucleus encloses the viral genome to protect it from host defense systems such as restriction nucleases, thereby rendering the phage highly recalcitrant to traditional genetic manipulation.

To overcome this limitation, we established a platform for programmable antisense oligomer (ASO)-mediated gene silencing, enabling the targeted knockdown of essential genes in genetically intractable phages. This approach allows phenotypic characterization of phage mRNA knockdowns during infection. For example, knockdown of transcripts encoding the essential tail sheath and tail tube proteins resulted in a distinct phenotype. Fluorescence microscopy revealed atypical DNA signals in the cytoplasm, consistent with defects in virion assembly. To date, the mechanism by which the phage genome is exported from the phage nucleus and packaged during virion assembly remains unknown.

Future studies will investigate the coupling between tail assembly and genome packaging and determine whether defects in structural protein expression result in impaired DNA encapsidation or accumulation of unassembled genomic material.

Reference #1

Gerovac, M., Buhlmann L. et al. Programmable antisense oligomers for phage functional genomics. Nature 646

Reference #2

Reference #3

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