

Cancer remains the second leading cause of death in the US. To overcome this problem, new treatments are sorely needed. A promising approach to cancer treatment is the use of oncolytic viruses engineered to selectively replicate in tumor cells while leaving healthy cells unharmed and express genetic payloads. We aim to take a systematic approach to identify host factors involved in the maturation of an oncolytic virus in mammalian cells for improved spread throughout a tumor. Specifically, we propose the use of CRISPR-based systems for genome-wide activation or knockout of the expression of over 18,000 human host cell genes by incorporating the Agilent SureGuide gRNA template libraries into the oncolytic virus. Oncolytic viruses more capable of infecting cancer cells in tissue culture will be enriched, and this enrichment will be detected via next generation sequencing of the gRNAs. Identification of host modifications conferring improved cell-to-cell spread will ultimately inform the heterologous cargo to include in a novel oncolytic virus strain with improved cell-to-cell spread among tumors.