عنوان مقاله:

Developing oncolytic Herpes simplex virus type 1 through UL39 knockout by CRISPR-Cas9

محل انتشار:

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خلاصه مقاله:

Objective(s): Oncolytic Herpes simplex virus type 1 (HSV-1) has emerged as a promising strategy for cancer therapy. However, development of novel oncolytic mutants has remained a major challenge owing to low efficiency of conventional genome editing methods. Recently, CRISPR-Cas9 has revolutionized genome editing.Materials and Methods: In this study, we aimed to evaluate the capability of CRISPR-Cas9 to manipulate the UL39 gene to create oncolytic HSV-1. Herein, three sgRNAs were designed against the UL39 gene and transfected into HEK-293 cell line followed by infection with HSV-1 KOS.Results: After three rounds of plaque purification, several HSV-1 mutants were identified by PCR analysis and sequencing. One of these mutations in which 55 nucleotides were deleted resulted in a frameshift mutation that in turn produced a truncated protein with only 167 amino acids from 1137 amino acids. Functional analysis in Vero and primary fibroblast cells revealed that viral replication was significantly lower and plaque size was smaller in the HSV-1 mutant compared with HSV-1 KOS. Moreover, the relative amount of viral genome present in the supernatants of infected cells (Vero and primary fibroblast cells) with HSV-1 mutant was significantly decreased compared with those of HSV-1 KOS.Conclusion: Our data revealed that targeting UL39 with CRISPR-Cas9 could develop oncolytic HSV-1.

کلمات کلیدی:

CRISPR-Cas9, Herpes simplex virus type 1, Oncolytic virus, Ribonucleotide reductase, UL39