Computational Determination of Potential Talen Targets in Herpes Simplex Virus 2 Genome

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Human alphaherpesvirus 2, also known as Herpes simplex virus 2 (HSV-2), causes genital herpes and is one of the viruses that lead to chronic infections in human. Several complications occur due to this viral infection and proper medication is still not available to cure the disease. However, the modern gene editing technique, Transcription Activator Like Effector Nuclease (TALEN), has a potential to use as an alternative strategy to eradicate the disease. In this study, the potential TALEN target sites present in the genome of HSV-2 were identified using bioinformatic tools. The viral gene UL21, which is essential for the propagation of the virus, and the gene UL30 (DNA polymerase) which is essential for the viral multiplication, were selected to find targets for TALENs so that these genes can be altered to diminish the viral persistence and multiplication. We used the tool 'TAL effector nucleotide targeter 2.0' to identify the possible TALEN targets and some targets were selected based on binding efficiency and validated for the absence of off-target sites in human and murine genome and other locations of the same viral genome using the tools 'Paired target finder' and 'PROGNOS'. In addition, a rough prediction of off-targets in genomes of other organisms was performed by searching for local alignments of the TALEN target sequence using the tool 'nBLAST'. The TALEN sites with better binding affinity and null off-target effect were selected and the putative functions of the mutated protein were predicted so as to avoid the sites that lead to mutated proteins having an undesired function. Considering all these criteria, best scoring TALEN target sites were selected. The target sites selected for UL21 gene are, 5'T CACGGGCACCCGCGCCCCCA gaccgatggccgggaccg GGGCCGGGGGCGCGGGGGCC A3', 5'T GGACGCCCGCGACCGGCGC acggatgtcgtgatcacggGCACCCGCGCCCCCAGACCGA3',5'TCCGCCAGCGCGGCCTGCGG gacgtgcggcccgtggg GGAGGACGAGGTGTTCCTGG A3' and 5'TCGGGATTCTCAGCCGGGGGaaattgccaagtttgCCTGGTGGTCCGGGGGACA3'. The target sites selected for UL30 gene are 5'T CCACGACGGCCGCCTCCGGCgcgcccctaaggtgtactCGGGGGGGACGAGCGCG A3', 5'T CGCCCCGCGTTCGCTGGACG aggacgcccccgcggagcag CGCACCGGGGTCCACG A3', 5'T GCGCGCCGCCCAGCTCCACG agcgatttatggacgccatcACGCCCGCCGGGACCGTCA3',5'TGGACGCCATCACGCCCGCCG ggaccgtcatcacgc TTCTGGGTCTGACCCCCGA A3' and 5'T GGTACCGCCTCAAGCCCGgccgcgggaacgcgcCGGCCCAACCGCGCCCCCCG A3'.These potential target sites could be used to construct site specific TALENs or to construct vectors possessing the gene for TALENs which can be used as therapeutic agents for the treatment of HSV-2 infection, but the on-target and off-target effects should be further assessed by in vitro and in vivo studies. These target sites may not be universally applicable to all the strains of the virus and the off-targets may present in the genomes that are not available in the GenBank database.

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