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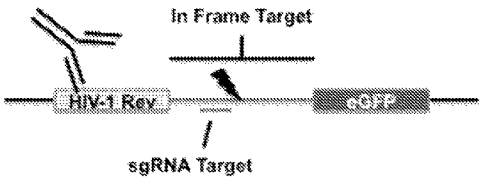
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(54) **Title**: COMPOSITIONS FOR THE INACTIVATION OF VIRUS REPLICATION AND METHODS OF MAKING AND USING THE SAME

Fig. 1A



(57) **Abstract**: Provided herein are recombinant constructs, vectors and expression cassettes including a first promoter which is suitably a tRNA promoter operably connected to a first polynucleotide encoding a first single guide RNA and a second promoter operably connected to a second polynucleotide encoding a Cas9 polypeptide. The first single guide RNA includes a first portion complementary to a strand of a target sequence of a DNA virus and a second portion capable of interacting with the Cas9 polypeptide. Also provided are codon optimized Staphylococcus aureus derived Cas9 polynucleotides and polypeptides with nuclear localization signals and optionally an epitope tag. Also provided are constructs for production of sgRNAs including a tRNA. Methods of inhibiting viral replication, inhibiting expression of a target sequence from a virus or treating a viral infection or viral induced cancer using the compositions are also provided.

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