Inhibition of viral replication One of the main steps in the process of viral infection is DNA and RNA genome replication of the virus.Additional examples of inhibition of viral replication by siRNA originated from the study of positive RNA viruses such as dengue (DENV), West Nile (WNV), and severe acute respiratory syndrome (SARS) [32–36].In another study, siRNA targeted to various domains of the HAV internal ribosomal entry site (IRES) induced efficient and sustained suppression of viral genome translation and replication [30].An HCV replicon is derived from an HCV consensus genome that was cloned from a viral RNA isolated from an infected human and used to construct subgenomic selectable replicons.siRNAs targeting the SARS-CoV RNA polymerase gene inhibited viral RNA replication, protein synthesis and reduced the viral cytopathic effects on Vero cells [36].Multiple siRNAs have been used to target multiple conserved viral genes that are essential for virus replication, including a long 5?- non-coding region, a short 3?-non-coding region, the viral protein VPg, the viral polymerase, and the viral capsid protein VP4.In the hepatitis A virus (HAV) replicon-based system, it has been reported that siRNAs targeting the regions coding for the non-structural proteins of the virus give rise to partial inhibition of HAV replication [28].siRNAs targeting the 3?-UTR sequence of DENV, in a region that is conserved in all the dengue serotypes, reduced viral replication and infection in dendritic cells [32].Synthetic siRNA targeted to the VP1 or to the viral polymerase showed antiviral effects in infected HeLa cells by inducing a significant reduction of viral replication [37].siRNAs targeting the viral polymerase NS5B region reduced expression of NS5B-Luc chimera in mice [27] or in the replicon system in vitro.Replication of DNA viruses can be inhibited by targeting their viral mRNA, whereas replication of RNA viruses can be inhibited by targeting either their mRNAs or their viral RNA, as was elegantly demonstrated for HIV [39].Other studies that target other regions of the HCV genome reported a significant decline in the level of HCV proteins and the level of both the sense and antisense RNA strands [25].In that study, two siRNAs specific for HAV sequences increased rather than inhibited HAV .replication