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Features of the interaction of human piRNAs with the SARS-CoV-2 coronavirus genome

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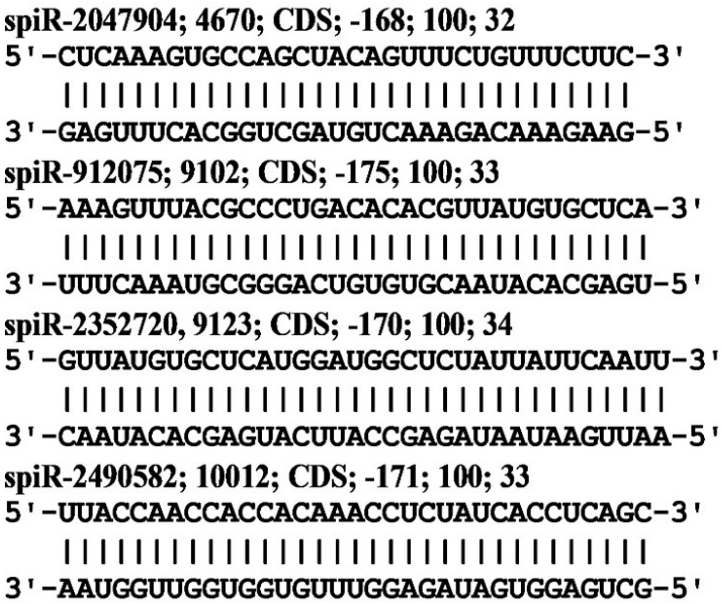
Motivation and Aim: The prolonged COVID-19 pandemic, with numerous human casualties, requires a rapid search for remedies against various strains of SARS-CoV-2. We investigated the interaction of over eight million molecules of piRNAs (PIWI-interacting RNA) with the genomic RNA (gRNA) SARS-CoV-2 (NC_045512.2). Completely complementary binding of piRNAs to mRNAs of several human protein-coding genes has been shown, indicating the biological function of piRNAs as regulators of gene expression.

Methods and Algorithms: The nucleotide (nt) sequences of SARS-CoV-2 genome was taken from NCBI. The nucleotide sequences of 200000 piRNAs were taken from Wang et al [1]. The piRNA binding sites (BSs) in the mRNAs of genes were predicted using the MirTarget program [2]. This program defines the following features of piRNA binding to mRNA: a) the initiation of piRNA binding from the first nucleotide of the mRNAs; c) the schemes of nucleotide interactions between piRNAs and mRNA; d) the free energy (ΔG, kJ/mol) of the interaction between piRNA and the mRNA; e) the ratio ΔG/ΔGm (%) is determined for each site (ΔGm equals the free energy of piRNA binding with its fully complementary nucleotide sequence).

Results: More than 200 piRNAs can inhibit protein synthesis and simultaneously inhibit viral gRNA replication. Regions of gRNA with overlapping nucleotide binding sites (BSs) of many piRNAs, which we called clusters, were revealed. A 28 nt cluster of 70 piRNAs BSs was identified in the SARS-CoV-2 gRNA region encoding the LETIQITIS oligopeptide of the ORF1ab protein. The second cluster of 39 piRNAs BSs of 31 nt lengths in the gRNA region encodes the RATLQAIASEF oligopeptide of the ORF1ab protein. The third cluster of 24 piRNA BSs of 31 nt length encodes the oligopeptide PKLQSSQAWQP of the ORF1ab protein. Twelve piRNAs were identified that strongly interact with the gRNA single sites of the virus from 4670 to 29024 nt. These endogenous piRNAs can be used in higher concentrations to suppress coronavirus multiplication. Synthetic piRNAs (spiRNAs) based on these endogenous piRNAs can be used to rapidly suppress coronavirus multiplication by replacing non-canonical nucleotide pairs with canonical pairs.

The schemes of spiRNAs interaction with CDS gRNA SARS-CoV-2 from 4670 nt to 29475 nt



The spiRNAs will inhibit the coronavirus multiplication even more strongly. These spiRNAs and selected endogenous piRNAs have little effect on human 17494 protein-coding genes, indicating a low probability of side effects. We assume that endogenous piRNAs can protect humans from mass infection with coronaviruses. The spiRNA and piRNA kits are proposed to suppress SARS-CoV-2 strains. The piRNA and spiRNA selection methodology created for the control of SARS-CoV-2 can be used to control all strains of this coronavirus.

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