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Aptamers: A Potential Strategy for COVID-19 Treatment

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Abstract : Respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent for coronavirus disease 2019 (COVID-19). Early evidence pointed at the angiotensin-converting enzyme 2 (ACE-2) expressed on the epithelial cells of the lung as the main entry point of SARS-CoV-2 into the cells. The viral entry is mediated by the binding of the Receptor Binding Domain (RBD) of the spike protein that is expressed on the surface of the virus to the ACE-2 receptor. As the number of SARS-CoV-2 variants continues to increase, mutations arising in the RBD of SARS-CoV-2 may lead to the ineffectiveness of RBD targeted neutralizing antibodies. To address this limitation, the objective of this study is to develop a combination of aptamers that target different regions of the RBD, preventing the binding of the spike protein to ACE-2 receptor and subsequent viral entry and replication. A safe and innovative biomedical tool was developed to inhibit viral infection and reduce the harms of COVID-19. In the present study, DNA aptamers were developed against a recombinant trimer S protein using the Systematic Evolution of Ligands by Exponential enrichment (SELEX). Negative selection was introduced at round number 7 to select for aptamers that bind specifically to the RBD domain. A series of 9 aptamers (ADI2010, ADI2011, ADI201L, ADI203L, ADI205L, ADIR68, ADIR74, ADIR80, ADIR83) were selected and characterized with high binding affinity and specificity to the RBD of the spike protein. Aptamers (ADI25, ADI2009, ADI203L) were able to bind and pull down endogenous spike protein expressed on the surface of SARS-CoV-2 virus in COVID-19 positive patient samples and determined by liquid chromatography- tandem mass spectrometry analysis (LC-MS/MS). LC-MS/MS data confirmed that aptamers can bind to the RBD of the spike protein. Furthermore, results indicated that the combination of the 9 best aptamers inhibited the binding of the purified trimer spike protein to the ACE-2 receptor found on the surface of Vero E6 cells. In the same experiment, the combined aptamers displayed a better neutralizing effect than antibodies. The data suggests that the selected aptamers could be used in therapy to neutralize the effect of the SARS-CoV-2 virus by inhibiting the interaction between the RBD and ACE-2 receptor, preventing viral entry into target cells and therefore blocking viral replication.

Keywords : aptamer, ACE-2 receptor, binding inhibitor, COVID-19, spike protein, SARS-CoV-2, treatment
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