COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

Development Of Rapid Therapeutics Platform Against Emerging Infectious Virus

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The COVID-19 virus, which was first confirmed to be infected in Wuhan, China in December 2019, had become a global pandemic virus disease.
This resulted in great social and economic losses. As synthetic biology develops, it is possible to manufacture artificial viruses in the laboratory, which could pose a threat to humanity. In addtion, experts warn that unknown viruses will become another threat to humanity due to climate change. Therefore, it is essential to develop a papid therapeutic platform to quickly respond to the pandemic of emerging and new variant viruses in the future. In this project, two types of therapeutic platforms were developed to prepare for unknown viral threats.

The first therapeutic is an antisense oligonucleotide (ASO) platform. To improve cell permeability, olipass peptide nucleic acid (OPNA), a subtype of ASO, has been created.
The purpose of this work is to evaluate OPNA's ability to break the Hantaan virus's RNA genome by attaching a cationic lipid moiety to the PNA oligomer backbone's nucleonase.
Vero E6 cells were exposed to 2.5uM antisense HTNV OPNAs upon viral challenge, and the levels of viral RNA were quantified using RT-qPCR.

Among the tested HTNV OPNA, OPNA29, targeting the nucleocapsid protein (NP) of HTNV, reduced viral RNA levels to less than 50% of the control level.
Furthermore, OPNA 56, which targets the glycoprotein (GP), showed a 71% reduction in the expression levels of viral genes.
This sutdy provides insight into the development of OPNA, characterized by exceptional chemical stability, high binding affinity and enhanced cellular permeability.
These findings suggest the potential of OPNA as a promising plaform for antiviral agents against furture pandemic disease.
The second therapeutic platform is an antibody-mRNA platform. A spike-delta protein of SARS-CoV-2 was produced as an antigen in order to set up the antibody-mRNA platform.

After the synthesis of IVT-mRNA, LNP-mRNA was formulated.The LNP-mRNA antigen was injected into mice to stimulate the development of antigen-specific antibodies. Subsequently, a total of eight antigen specific novel antibody candidates were selected by antigen specific memory B cell isolation using FACS sorter and their nucelotide sequences were obtained. The mRNA for the eight novel antibody candidates were synthesized and each LNP-mRNAs were manufactured. By in vitro and in vivo test, the final candidates showed neutralizing effect against SARS-CoV-2. These results suggest that it is possible to obtain the novel antibodies in about 60 days after antigen inoculation. As a result, it is validated that the fast antibody detoxification platform technology in this project enables quick response to novel viruses by creatively reducing the production time of nucleic acid medicines.

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