Development of Universal Multi-Target Antibody-Like Vaccines Against the Highly Pathogenic Coronaviruses

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SARS-CoV-1, MERS-CoV and SARS-CoV-2 are highly contagious and lethal coronaviruses (CoVs). Although different forms of anti-SARS-CoV-1 and MERS-CoV vaccines have been developed, none of them is fully approved. Fc-fusion proteins, antibody-like molecules, can be engineered for vaccine development. In this research, receptor binding domain (RBD) of the spike protein of CoVs were fused with crystallizable fragment (Fc) of immunoglobin G1 (IgG1). Three versions of bispecific antibody-like vaccines were generated (BiVax). The native Fc was used in the first version as it is (BiVaxNative), while the hinge region was engineered in the second version to increase the BiVaxHinge serum stability. Finally, ABDEGTM technology was applied on BiVaxFcRn to increase the vaccine's binding affinity to neonatal Fc Receptor regardless of pH. A multi-specific RBD-Fc-based vaccine against the three CoVs (TetraVax) was generated by Knob-in-hole (KIH) technology fused with CD40L as a molecular adjuvant. The vaccines plasmids were constructed then transfected into mammalian cells. Likewise, the proteins were purified using AKTA chromatography. Additionally, vaccines purity and expression were confirmed using western blot and ELISA. Mice were vaccinated with adjuvanted vaccines. The preliminary in vivo results showed that BiVaxNative and BiVaxHinge induced a strong RBD-specific IgG titer against MERS-CoV but not SARS-CoV-2. Interestingly, BiVaxFcRn and TetraVax induced a strong RBD-specific IgG titer against the three viruses, however requiring further investigation. Together these results indicate that these constructs have the potential to act as universal vaccine against the highly pathogenic CoVs.

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