Antibody Dependent Enhancement of SARS-CoV Infection is Mediated by the Antibodies against Spike Proteins

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Background/Objective

Severe acute respiratory syndrome coronavirus (SARS-CoV) had an outbreak in 2003. Even though SARS-CoV now remains in the natural bat reservoir, it still has the reemergence threat. Antibody-dependent enhancement (ADE) is a mechanism by which viruses such as, dengue virus, feline coronavirus, and HIV, as alternative strategies, apply to infect host cells to gain entry into the target cells by taking advantage of anti-viral humoral immune responses. The ADE effect of SARS-CoV infection is controversial.

Method

SARS-CoV TW1 strain (AY291451) was obtained from Taiwan CDC and SARS-CoV pseudotyped virus particles harboring the SARS-CoV S protein with HIV core structure virus were constructed for infectivity assay. The anti-SARS CoV infected patient’s sera and generated monoclonal and polyclonal antibodies against spike proteins were used for virus infectivity, neutralization and ADE evaluation. Immunofluorescence staining and TEM assays were used to confirm ADE phenomenon of SARS-CoV.

Result

We found that SARS-CoV uses ADE to enhance its infectivity towards a human promonocyte cell line-HL-CZ. Quantitative-PCR and immunofluorescent staining indicated that SARS-CoV can replicate in HL-CZ and display virus-induced cytopathic effect as well as increased TNF-α, IL-4 and IL-6 two days postinfection. Results from flow-cytometry indicate HL-CZ cells express angiotensin converting enzyme 2 (ACE2), a SARS-CoV receptors and higher level of FcrRII receptors. Our data demonstrated that higher diluted sera from SARS-CoV infection patients promote SARS-CoV infection and induced higher level of apoptosis. Infectivity assay demonstrated that ADE of SARS-CoV is majorly mediated by diluted antibodies against envelope spikes rather than nucleocapsid proteins. We further generated monoclonal antibodies against spike proteins of SARS-CoV and found that most monoclonal antibodies promote SARS-CoV infection.

Conclusion

We suggested that antibodies against spike proteins of SARS-CoV may cause ADE effect. This data raises reasonable concern regarding the use of SARS-CoV vaccine and shed light on some roles in SARS pathogenesis.