Keynote Lecture VI

Human Immune Response to SARS-CoV and Functional Analysis of SARS S-antigen

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Severe acute respiratory syndrome (SARS) is a life-threatening disease caused by the highly infectious pathogen SARS coronavirus (SARS-CoV). The spike (S) glycoprotein of coronavirus is the major structural protein responsible for induction of host immune response and virus neutralization by antibodies. Understanding the human immune response, especially the induction of neutralization antibodies (NAbs) against SARS-CoV and the antigenicity of the S protein is very important to develop strategies for treatment and prevention of SARS. We firstly incorporated the S protein from a synthetic codon-optimized gene, which could dramatically increase expression of the S protein compared with the native S gene, into the HIV cores to generate pseudotyped virus. We found this SARS/HIV pseudovirus had high infectivity on Vero E6, the host cell of SARS-CoV, and had same cell tropism with wild SARS-CoV, and its infection could be neutralized by sera from convalescent SARS patients. Based on this pseudotyped virus, we established a highly sensitive and safe neutralization assay to analyze the NAbs in serum samples from SARS patients. We found that 85.9% of serum samples contained NAbs against SARS-CoV and most NAb activities were attributed to IgG. We further studied the kinetics of NAbs and showed that they may correlate with viral load during the early stages of the disease. According to these results, we concluded that it was great possible to develop vaccines against SARS and that NAbs may be a potential strategy for treating SARS patients. To provide more clues for SARS vaccine, we analyzed the antigenicity of the S protein through testing the reactivity of sera from convalescent SARS patients against the prokaryotic expressed overlapping fragments of the S protein. We identified two linear antigenic determinants on the S2 portion, and demonstrated one of them is the immunodominant determinant, which could induce the antisera with neutralizing activity in some immunized animals. This work had implications in developing effective vaccines against SARS-CoV.