Basic and Clinical Research of SARS-CoV-2: laboratory diagnosis, vaccine and antiviral developments

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Outline of the talk:

Laboratory diagnosis:

As the COVID-19 pandemic continues, the causative virus, SARS-CoV-2 continues to evolve. SARS-CoV-2 is the strain of coronavirus, a kind of RNA virus which has been known to mutate frequently. This talk will discuss viral genetic diversity and its impact on virus stability and antigenicity. First, investigation of the genomic variation of SARS-CoV-2 isolates in Taiwan and comparison of their evolutionary trajectories with the global strains will be presented. Like other isolates from different countries, D614 G change in viral spike (S) protein becomes dominant. The S-G614 variant was found to be more stable than the S-D614 variant. The spike protein of the S-G614 variant had better binding ability with ACE2 receptor than that of the S-D614 variant after storage at −20°C up to 30 days. Stability and infectivity are related to each other, and higher stability of S-G614 than that of S-D614 may contribute to fast viral spread of the S-G614 variant. Other mutations within receptor binding sites (RBD), e.g., N501Y, E484K and K417D will be discussed too regarding their changes in ACE2 binding and antigenicity.

Detection of neutralization antibodies:

A quantitative serological test for detecting neutralization antibodies of SARS-CoV-2 is critical for vaccine development. We have established standard neutralization test (NT) at BSL-3 laboratory and pseudo-virus system at BSL-2 Laboratory. Moreover, a two-variable generalize additive model analysis of binding was developed as a surrogate NT test. The coefficient of determination between predicted and NT values was as high as 0.903. This novel assay serves as an alternative to quantify SARS-CoV-2 neutralization antibody and is more accessible for research or clinical use in a general laboratory.

Dissecting viral-host interaction and development of antivirals:

Our team applied the EditCell Virology platform (genome-wide CRISPR-based system) to screen host factors that are important for RNA virus replication. We identified ACSL-4 as a crucial factor not only for coronaviruses but also for flaviviruses and enteroviruses infections. Based on this finding, we also identified two FDA-approved drugs targeting ACSL-4 protein, which are able to decrease the viral load of the above-mentioned RNA viruses, including SARS-CoV-2, the only cause of the COVID-19 pandemic.