

SOME COVID-19 NEUTRALISING ANTIBODIES MAY WORSEN THE DISEASE

A series of neutralising antibodies against SARS-CoV-2 that potently block binding to the host receptor ACE2 are found to either enhance or inhibit virus spike-mediated membrane fusion and the formation of tergetmax(2p) 009(())=tb1(29)032(b)82((t)-6.6gi)215(ctpp)rtQ(iesco) p0ebi3e[6(e):602(i)2rt09,anfenine:etmatisgetiocry use as early COVID potency remain unknown.

SARS-CoV-2 neutralizing-antibodies modulate syncytic



chnology andeResearchet(A*STAR), in QCRG) at University of California San aboratories discovered that while some nhance it. The researchers discovered a series of human antibodies that all potently block ACE2 binding yet exhibit divergent neutralisation efficacy against live virus. Strikingly, these neutralising antibodies can either inhibit or enhance spike-mediated membrane fusion and formation of syncytia, which are associated with chronic tissue damage in COVID-19 patients.

Cryogenic electron microscopy reveals differential antibody-viral spike binding modes leading to different biological consequences. The distinct binding modes not only block ACE2 binding, but also alter the spike protein conformational cycle triggered by ACE2 binding.

The study shows that stabilisation of different spike conformations leads to modulation of spikemediated membrane fusion, with profound implications in COVID-19 pathology and immunity.

Dr Wang Cheng-I, senior principal investigator at A*STAR's Singapore Immunology Network and last author of the study said, "This is the first time that a neutralising antibody can either inhibit or enhance syncytia is discovered and described. The discovery has a profound implication in how the therapeutic antibodies against COVID-19 should be designed. Better understanding of the mechanism of neutralising is critical for better treatment design, given the ever-mutating nature of the COVID-19 virus."

"The project was made possible by the remarkable progress that has been made in cryo EM in ways that could not be imagined before," said Yifan Cheng, Ph.D., professor of biochemistry and biophysics at University of California, San Francisco.

Charles Craik, Ph.D., professor of pharmaceutical chemistry at Univeror f,2(t)-6.0 Tw 0.m0.38.8(.3(a6(t)-

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