

International Research Center for Infectious Diseases

Department of Special Pathogens

高病原性感染症系

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The aim of this laboratory is to launch an interdisciplinary research platform to comprehensively understand the behavior of viruses from macroscale to microscale. COVID pandemic alarmed the importance of understanding viral transmissibility and spreading pathway. These knowledges are brought from epidemiology and public health (science at macroscale). Viral surveillance, molecular phylogenetic and bioinformatics provide information of the variant currently spreading (science at macroscale). "Science at mesoscale", the use of animal models and cell cultures, performing experiments, and assessing clinical data, provide the knowledge of viral pathogenicity, features and drug efficacy. When certain variants that are resistant to antivirals or vaccines emerged, the molecular mechanisms of actions should be understood. For that, the understanding based on structural biology is essential (science at micro scale). Our study will launch the platform to perform multiscale investigation of viruses.

1. Virological characteristics of the SARS-CoV-2 XBB variant derived from recombination of two Omicron subvariants

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In late 2022, SARS-CoV-2 Omicron subvariants have become highly diversified, and XBB is spreading rapidly around the world. Our phylogenetic analyses suggested that XBB emerged through the recombination of two cocirculating BA.2 lineages, BJ.1 and BM.1.1.1 (a progeny of BA.2.75), during the summer of 2022. XBB.1 is the variant most profoundly resistant to BA.2/5 breakthrough infection sera to date and is more fusogenic than BA.2.75. The recombination

breakpoint is located in the receptor-binding domain of spike, and each region of the recombinant spike confers immune evasion and increases fusogenicity. We further provide the structural basis for the interaction between XBB.1 spike and human ACE2. Finally, the intrinsic pathogenicity of XBB.1 in male hamsters

is comparable to or even lower than that of BA.2.75. Our multiscale investigation provides evidence suggesting that XBB is the first observed SARS-CoV-2 variant to increase its fitness through recombination rather than substitutions.

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