A single vaccine protects against coronavirus and influenza virus in mice

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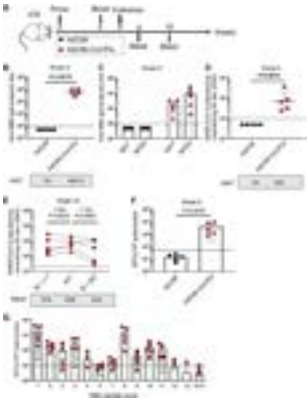
The ongoing SARS-CoV-2 pandemic posed a severe global threat of respiratory virus infections on public health, as do so by influenza viruses and other coronaviruses. The currently envisioned strategy for prevention requires comprehensive administration of vaccines tailored for individual virus. Here we present an alternative strategy by designing chimpanzee adenovirus 68 (AdC68)-based multi-immunogen vaccines universally targeting different coronaviruses and influenza viruses. The first version constructed features a fusion immunogen comprising SARS- CoV-2 receptor-binding domain (RBD), conserved stalk of H7N9 hemagglutinin (HA) and human ferritin. Its administration in mice induced neutralizing antibodies against wild-complemented with high-immunogenicity peptide from divergent coronaviruses. The broad spectrum of this improved version was demonstrated by affording protection from SHC014 attack, a bat SARS-like coronaviruses, in mouse model. Also, in order to broaden the influenza virus coverage, we constructed vaccine comprising conserved stalk of H7N9 HA and H1N1 HA. These results together support the promise of our AdC68 vectored pan- coronavirus-influenza virus vaccine and warrant its future exploration as a more effective approach toward curbing respiratory virus-causing pandemics.

Results:

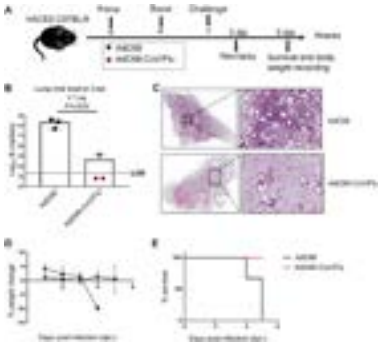
Immunogenicity of AdC68-CoV/Flu in mice



(A) Scheme of vaccination and sampling schedule (B) Serum were assessed at week 6 post prime for RBD-specific binding antibodies by ELISA. (C) Assessment of Th1 or Th2 bias in the immune response. (D) Serum neutralizing antibody titers at week 6 post prime against wild-type SARS-CoV-2 were measured by

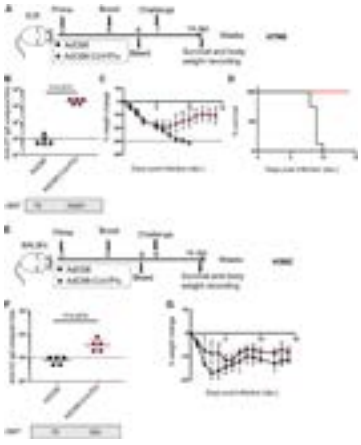
pseudovirus neutralization assays. (E) Serum neutralizing antibody titers at week 10 post prime against wild-type SARS-CoV-2 or its B.1.1.7 and B.1.351 variants were assessed by pseudovirus neutralization assay. (F and G) Assessments of RBD-specific T cell responses.

Protective efficacy of AdC68-CoV/Flu against SARS-CoV-2 challenge in mice



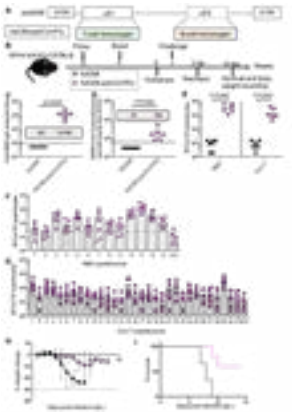
(A) Experimental schedule. (B) Lung viral loads determined by RT-PCR. (C) Representative images of H&E-stained lung sections from AdC68 and AdC68- CoV/Flu treated mice on 3 dpi.(D and E) Protection evaluated by body weight change (D) and survival (E).

Influenza-targeting immunity raised by AdC68-CoV/Flu and the afforded protection against H7N9 and heterologous H3N2 challenges in mice



(A) Experimental schedule used for evaluating AdC68-CoV/Flu-mediated H7N9 protection. (B) Serum titers of H7 HA-specific binding antibodies determined by ELISA. (C and D) Protection evaluated by body weight change (C) and survival (D). (E) Experimental schedule used for evaluating protective efficacy of AdC68- CoV/Flu against H3N2 challenge. (F) Serum titers of H3 HA-specific binding antibodies determined by ELISA. (G) Body weight change with time.

Construction of AdC68-panCoV/Flu, its immunogenicity and cross- protection against challenge of bat coronavirus SHC014 in hACE2 mice



(A) Schematic representation of AdC68 viral vaccine construct incorporating both S-protein-targeting B-cell immunogen and consensus T-cell immunogen globally covering the viral proteomes with input from all the known coronaviruses. (B) Experimental schedule. (C and D) Serum antibody responses at week 6 post prime analyzed for RBD-specific IgG antibodies by ELISA (C) and SARS-CoV-2 neutralizing activities by pseudo-virus neutralization assays (D). (E-G) Assessments of RBD and CoV-T specific T cell responses to.

Biography

Jianqing Xu, Professor at Zhongshan Hospital, Institutes of Biomedical Sciences and Shanghai Public Health Clinical Center, Fudan University. Director of the Shanghai Institute of Emerging and Re-emerging Infectious Diseases and Director of the School of Translational Medicines at Shanghai Public Health Clinical Center, Fudan University. He mainly engaged in immunology, immunotherapy and vaccinology research. He is the chief scientist of the National Science and Technology Major Special Project, the leader of the Key Project of the National Natural Science Foundation of China and the NSFC-NIH Cooperation Project. He has published 176 papers in Nature, Science, Nature Microbiology, PNAS, Nat Commun, EClinicalMedicine, Clin Infect Dis, Neurology, Biomaterials, eLife, mBio, J Infect Dis, J Immunol, AIDS, Front Immunol, J Virol , etc.

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