Protective effect of intranasal regimens containing peptidic MERS-CoV fusion inhibitor against MERS-CoV infection

With the support by the National Natural Science Foundation of China and the Ministry of Science and Technology of China, Prof. Jiang Shibo's laboratory at the Basic Medical College, Fudan University, reported the *in vivo* efficacy of anti-MERS-CoV peptide, HR2P-M2 in mouse model, which was published in *Journal of Infectious Diseases* (2015, Jun 8, pii: jiv325, [Epub ahead of print]).

To gain entry into the target cell, Middle East respiratory syndrome coronavirus (MERS-CoV) utilizes its spike (S) protein S2 subunit to fuse with the plasma or endosomal membrane. We previously identified a peptide derived from the HR2 domain in S2 subunit, HR2P, which potently blocked MERS-CoV S protein-mediated membrane fusion. Here, we tested an HR2P analogue with an improved pharmaceutical property, HR2M6, for its inhibitory activity against MERS-CoV infection *in vitro* and *in vivo*. HR2M6 was highly effective in inhibiting MERS-CoV S protein-mediated cell-cell fusion and infection by pseudoviruses expressing MERS-CoV S protein with or without mutation in the HR1 region. It interacted with the HR1 peptide to form stable α-helical complex and blocked the 6-HB formation between the HR1 and HR2 domains in the viral S protein. Intranasally administered HR2M6 effectively protected Ad5-hDPP4-transduced mice from infection by MERS-CoV strains with or without mutations in the HR1 region of S protein, with > 1,000-fold reduction of viral titers in lung, and the protection was enhanced by combining HR2M6 with interferon ß (IFN-ß). These results indicate that this combinational regimen merits further development to prevent MERS in high-risk populations, including healthcare workers and patient family members, and to treat MERS-CoV-infected patients.

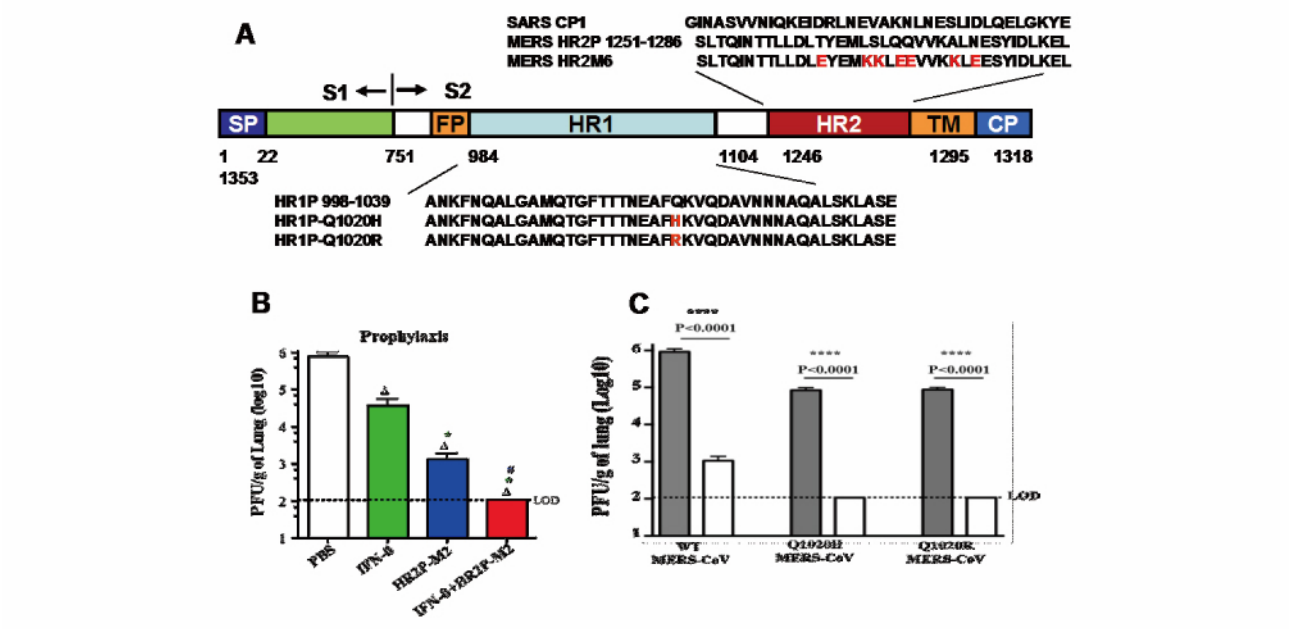

Figure The sequence of HR2P-M2 and its anti-MERS-CoV activity. A, Sequences of the peptides derived from the HR1 and HR2 domains of MERS-CoV S protein S2 subunit. B, Inhibition of MERS-CoV infection in Ad5 hDPP4-transduced mice by intranasal application of HR2P-M2 peptide, alone or in combination with IFN-ß, before viral challenge. C, Inhibition of MERS-CoV infection in Ad5 hDPP4-transduced mice by intranasal administration of HR2M6 alone before viral challenge (blank bars).