The viroporin function of ns12.9 in HCoV-OC43 morphogenesis and pathogenesis

With the support by the National Science and Technology Major Project, the research team led by Prof. Sun Bing (**孙兵**) from the Institut Pasteur of Shanghai, Chinese Academy of Sciences, and Prof. Xiong Si-Dong (**熊思东**) from Soochow University, found that the ns12.9 accessory protein of human coronavirus OC43 (HCoV-OC43) is a viroporin involved in virion morphogenesis and pathogenesis. This wonderful work was recently published in *Journal of Virology* (2015, 89: 11383—11395), and selected as a Spotlight Feature article.

HCoV-OC43 was first isolated in the 1960s and is a major agent of the common cold. The functions of HCoV-OC43 structural proteins have been well studied, but few studies have focused on its accessory proteins. In the present study, we identified that the ns12.9 accessory protein is a newly recognized viroporin. Then, we engineered a recombinant mutant virus lacking the ns12.9 protein (HCoV-OC43-Δns12.9) to characterize the contributions of ns12.9 during HCoV-OC43 infection, and found that HCoV-OC43-Δns12.9 presents a growth defect *in vitro* and *in vivo*. Systematic dissection of single-cycle replication revealed the important functions of ns12.9 viroporin in virion morphogenesis. Furthermore, the mice infected with HCoV-OC43-ns12.9 exhibited reduced inflammation and virulence accompanied by a lower titer in the brain than that of wild-type-infected mice, suggesting ns12.9 viroporin influences virus pathogenesis. These findings contribute to the knowledge on the functional relevance of viroporins to viral infectivity, and provide a potential target for developing antiviral drugs.

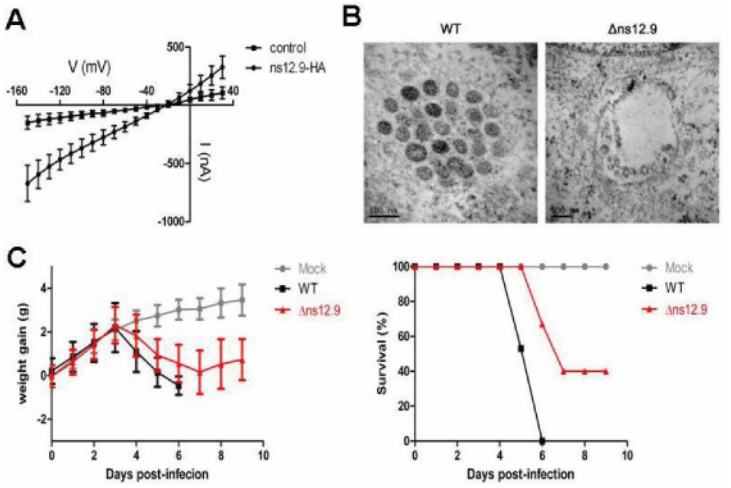

Figure The HCoV-OC43 ns12.9 protein is a viroporin involved in virion morphogenesis and pathogenesis. (A) The *I*/*V* curve of voltage dependencies of steady-state currents in control oocytes (filled squares) and ns12.9-expressing oocytes (filled circles). (B) Transmission electron micrographs of virions in the infected RD cells. (C) The weight variations and survival curves after wild type and mutant virus infection.