Abstract 21:

Understanding viral resilience to promote host resilience: A study on coronavirus endoribonuclease nsp15 as a viral antagonist of host immune responses

Xiaoqian Gong[1, 2], Bo Gao[1], Christine Jansen[2], Edwin Tijhaar[2], Huub F.J. Savelkoul[2], Maria Forlenza[2]* and Ying Liao[1]*

[1] Department of Avian Diseases, Shanghai Veterinary Research Institute, P. R. China
[2] Cell Biology and Immunology Group, Wageningen University & Research, The Netherlands
* Corresponding author. E-mail: liaoying@shvri.ac.cn; maria.forlenza@wur.nl.

The outcome culminating coronavirus infection is determined by mutual interactions between the viruses and the hosts. Host cells possess elaborate immune responses, such as interferons that play a central role, and stress granules that function as signalling platforms. To maintain viral replication, coronaviruses have correspondingly evolved various counterstrategies, that we refer to as 'viral resilience'. To assist the hosts to survive viral infection, it is essential to develop anti-viral therapeutics. We refer to curing a viral infection via anti-viral therapeutics as 'host resilience'. Designing appropriate targets is critical to anti-viral therapeutics, and requires understanding the mechanism of viral counterstrategies. To put it another way, improving 'host resilience' requires knowledge of 'viral resilience'. In my PhD thesis, we studied the counterstrategies of coronavirus-encoded endoribonuclease nsp15. After infection of wild type and nsp15 endoribonuclease-deficient avian coronaviruses (IBV) in chicken and mammalian cells, we found that endoribonuclease nsp15 antagonizes interferons but also stress granules during IBV infection. Further analysis showed that this antagonism is mediated by nsp15's regulation of double-stranded RNAs. In addition, we observed a crosstalk between IFNs and SGs during IBV infection. Moreover, we provided evidence that nsp15 of IBV interferes with formation of chemically-induced SGs. And this activity of nsp15 is conserved among different genera of coronaviruses. Collectively, my PhD thesis work provides a better understanding of the 'viral resilience', the counterstrategy of coronavirus endoribonuclease nsp15, and thereby promote the 'host resilience', the exploitation of this enzyme for anti-viral therapeutics.