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MERS-CoV receptor-binding domain-based vaccines and therapeutic antibodies

Middle East respiratory syndrome (MERS)-*coronavirus* (MERS-CoV), an emerging infectious *coronavirus*, was first identified in 2012 and continues to threat public health with a high mortality rate (~36%), reinforcing the urgency to develop safe, effective and innovative vaccines and therapeutic antibodies to prevent and treat MERS-CoV infection. The MERS-CoV spike (S) protein mediates virus binding to its receptor Dipeptidyl Peptidase 4 (DPP4) via the Receptor-Binding Domain (RBD) and subsequent virus-cell membrane fusion, thus serving as a key vaccine and therapeutic target. In this study, we have identified the RBD of MERS-CoV S protein as a critical neutralizing domain fragment in the development of MERS vaccines and therapeutic antibodies. Our data demonstrate that recombinant RBD vaccines induce potent and broad-spectrum neutralizing antibodies against MERS-CoV of different circulating human and camel strains, as well as antibody escape MERS-CoV mutants. In particular, a variant form of RBD vaccines with an unfavorable epitope masked in the RBD significantly enhances efficacy, completely protecting human transgenic mice from lethal MERS-CoV challenge. In addition, we have found that MERS-CoV RBD-targeting neutralizing antibodies recognize highly conserved RBD epitopes and significantly block RBD binding to viral receptor DPP4, potently cross-neutralizing antibodies protect human transgenic mice from MERS-CoV infection with 100% survival rate. Collectively, our study demonstrates the importance and feasibility for further development of RBD-based subunit vaccines and therapeutic antibodies against MERS-CoV.

Biography

Lanying Du is an Associate Member and Co-Head of Viral Immunology Laboratory at Lindsley F. Kimball Research Institute of New York Blood Center. She has over 10 years' experience in designing and developing effective vaccines against emerging infectious viruses with more than 100 papers in the related research fields.

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