

Severe Pathogenesis of a Novel Phlebovirus is Associated with Defective B cell Immunity and Skewed Macrophage Differentiation

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Severe fever with thrombocytopenia syndrome (SFTS), an emerging infectious disease caused by a novel phlebovirus, has been on the rise and become a persistent public health threat in the East Asia due to its high fatality. The anti-viral immunity and disease pathogenesis are poorly understood. We reported that defective antibody response to SFTSV was closely associated with disease fatality and a combination of impaired B-cell dependent immunity and T-helper-related cytokines contributed to the global disruption of the anti-viral immunity, characterized by the complete absence of specific IgG response to viral nuclear capsid protein and glycoprotein, the overwhelming expansion and impaired B cell class switch off IgM-secreting plasmablasts, severe apoptosis of monocytes in the early stage of infection, impaired antigen-presentation by myeloid DCs, as well as the impeded differentiation and function of Tfh with continuous up-regulation of PD-1 expression. Besides, the significant inhibition of IL-4 and GM-CSF both in the serum and in the monocytes exacerbated the pathogenesis of the viral infection. In addition, the SFTSV infection drove macrophage differentiation skewed to M2 phenotype, facilitated virus shedding and resulted in viral spread. We identified miR-146a and b as key regulators in the skewed macrophage differentiation. Further analysis revealed that the elevated miR-146b but not miR-146a was responsible for IL-10 stimulation. We also found that SFTSV increased endogenous miR-146b-induced differentiation of macrophages into M2 cells mediated by viral non-structural protein (NSs). The M2 skewed differentiation of macrophages may have important implication to the pathogenesis of SFTS and the suppressed antiviral IgG response.

Biography:

Allen Z. Wu received his Ph.D. from The University of Edinburgh, trained as a postdoctor in New York University and worked as a faculty at Rockefeller University and The University of Pennsylvania. From 2006, Allen Wu relocated to China and founded the Center for Public Health Research at Nanjing University and has served as the director of the center since. Allen Wu's major research interest is viral infection and antiviral immunity, anti-viral mechanisms and intervention of sexually transmitted diseases. His current research interests cover HSV, HIV, EV71 and highly pathogenic acute viral infection, such as Bunyavirus.