Title:	A Mouse Model of PPRV Infection for Elucidating Protective and Pathological Roles of Immune Cells
Authors:	Sharma, Yashu (/jspui/browse?type=author&value=Sharma%2C+Yashu) Sarkar, Roman (/jspui/browse?type=author&value=Sarkar%2C+Roman) Jain, Ayush (/jspui/browse?type=author&value=Jain%2C+Ayush) Singh, Sudhakar (/jspui/browse?type=author&value=Singh%2C+Sudhakar) Shekhar, Chander (/jspui/browse?type=author&value=Shekhar%2C+Chander)
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Abstract:	The study was aimed at developing an accessible laboratory animal model to elucidate protective and pathological roles of immune mediators during Peste des petits ruminants virus (PPRV) infection. It is because of the critical roles of type I IFNs in anti-viral defense, we assessed the susceptibility of IFN receptor knock out (IFNR KO) mice to PPRV infection. IFNR KO mice were exceedingly susceptible to the infection but WT animals efficiently controlled PPRV. Accordingly, the PPRV infected IFNR KO mice gradually reduced their body weights and succumbed to the infection within 10 days irrespective of the dose and route of infection. The lower infecting doses predominantly induced immunopathological lesions. The viral antigens as well as the replicating PPRV were abundantly present in most of the critical organs such as brain, lungs, heart and kidneys of IFNR KO mice infected with high dose of the virus. Neutrophils and macrophages transported the replicating virus to central nervous system (CNS) and contributed to pathology while the elevated NK and T cell responses directly correlated with the resolution of PPRV infection in WT animals. Using an array of fluorescently labeled H-2Kb tetramers, we discovered four immunogenic epitopes of PPRV. The PPRV-peptides interacted well with H-2Kb in acellular and cellular assay as well as expanded the virus-specific CD8+ T cells in immunized or infected mice. Adoptively transferred CD8+ T cells helped control PPRV in infected mice. Our study therefore established and employed a mouse model for investigating the pathogenesis of PPRV. The model could be useful for elucidating the contribution of immune cells in disease progression as well as to test anti-viral agents.
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