

P0405

Paper Poster Session

Viral pathogenesis and treatment targets

Pneumovirus-induced lung disease in mice is independent of neutrophil driven inflammation

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Background: Respiratory syncytial virus (RSV) infection is a common and deadly disease in young children. Neutrophil recruitment in the lungs is a hallmark of RSV infection and massive neutrophil recruitment has been proven detrimental in numerous diseases, including acute respiratory distress syndrome. Yet, the contribution of neutrophils to disease severity in RSV infection is unknown. Gaining insight in the role of neutrophils during RSV infection and pathogenesis will help to determine the relevance of potential neutrophil targeting therapies.

Material/methods: We implemented antibody (1A8)-mediated neutrophil depletion in a mouse pneumovirus model using pneumonia virus of mice (PVM). PVM is a host specific murine virus closely related to RSV, which reproduces the robust clinical symptoms, high viral replication and strong neutrophil recruitment as seen during RSV disease. Clinical disease and markers of lung inflammation and injury were studied in PVM-infected C57Bl6 and BALBc mice treated with either 1A8 or isotype control antibodies.

Results: Neutrophil depletion in blood and lungs by 1A8-antibodies was efficient and significant throughout the disease. However, there was no difference in clinical disease severity (fig. 1A-B) or survival between neutrophil-depleted and control mice. In line with this observation, there was no difference in histopathological lung injury and lung permeability (fig. 1C) nor in lung viral loads between the groups (fig. 1D-E).

Conclusions: Our study shows that neutrophil recruitment to the lungs does not affect disease outcome or viral clearance during PVM infection in mice. As such, it does not support the notion that neutrophils play a key role in RSV disease.

Figure 1:

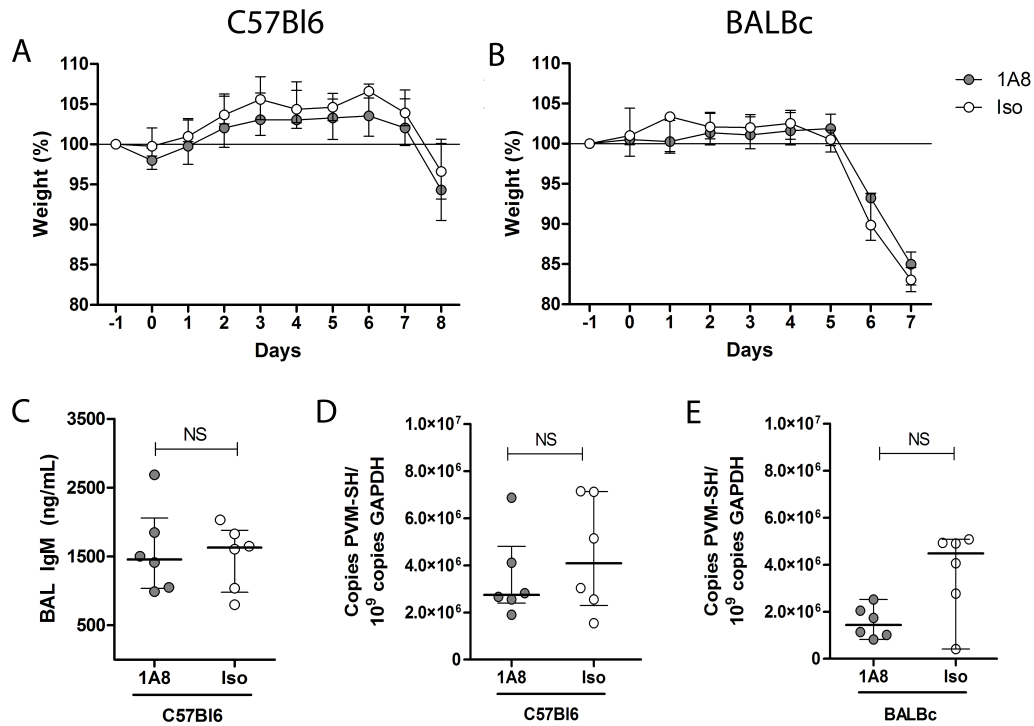


Figure 1: (A + B) Disease severity as measured by percentage weight loss since start of the study (day -1) in C57Bl/6 and BALB/c mice during PVM infection. 1A8 = neutrophil depleted mice (grey circles), Iso = isotype control treated mice (white circles). **(C)** Lung permeability as measured by IgM concentration in broncho-alveolar lavage (BAL) in C57Bl/6 mice on day 8 **(D+E)** Lung tissue viral load in C57Bl/6 (day 8) and BALB/c mice (day 7). NS; not significant