Neonatal CD8⁺ T cells demonstrate PD-1 dependent impairment following human metapneumovirus (HMPV) infection

Taylor Eddens[1], Olivia Parks[2], Yu Zhang[3], John Wiliams[3,4*]

[1]UPMC Children's Hospital of Pittsburgh Allergy/Immunology Division; [2]University of Pittsburgh Medical Scientist Training Program;

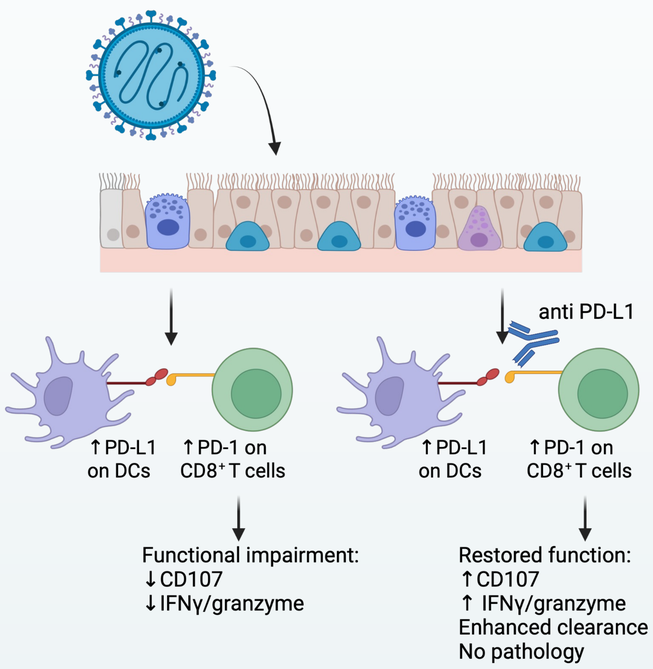
[3]UPMC Children's Hospital of Pittsburgh; [4]University of Pittsburgh School of Medicine, Division of Infectious Diseases

Introduction

Human metapneumovirus (HMPV)

- In children <5years globally:
  - 14.2 million acute LRTIs
  - 500,000 hospitalizations
  - ~11,300 deaths
- Worse outcomes in infants/neonates

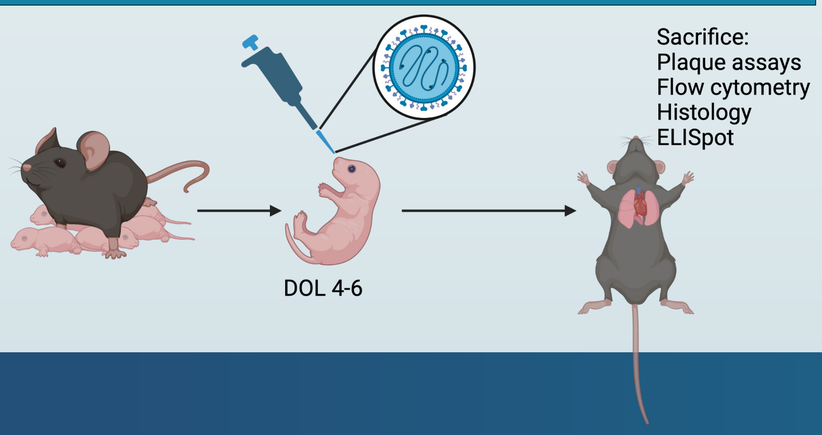
Functional impairment of CD8⁺ T cells in adult mice:



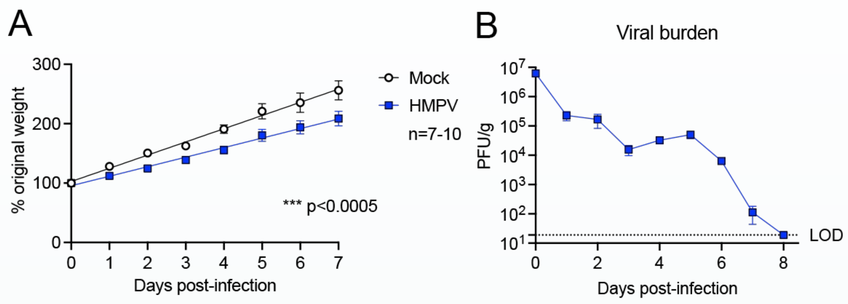
Neonatal lung immunology

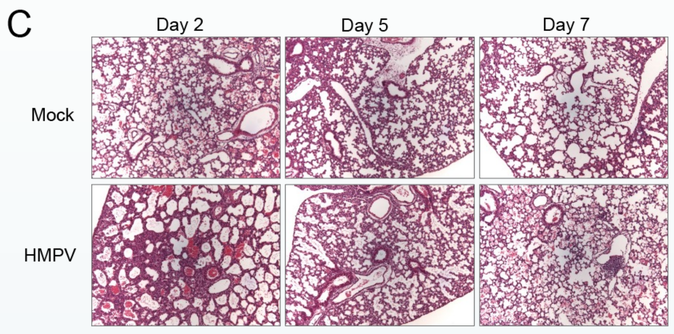
- Murine lungs continue to develop (e.g. alveolarization) until day of life 28
- Neonatal lungs have anti-inflammatory and tolerogenic properties due to multiple mechanisms, including an increase in PD-L1 expression within the first week of life
- Neonatal CD8⁺ T cells demonstrate alternative functions, such as reactive oxygen species generation

Methodology



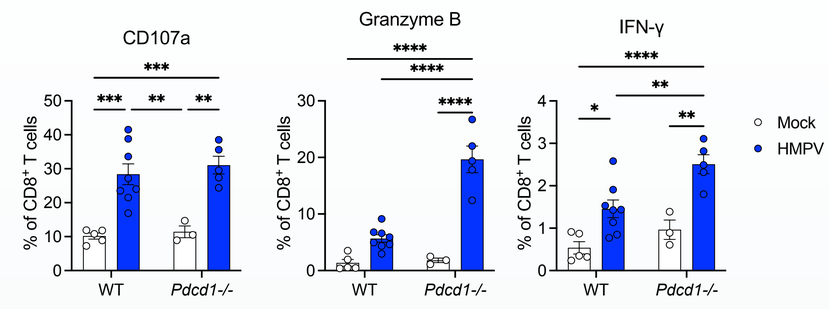
Neonatal HMPV model



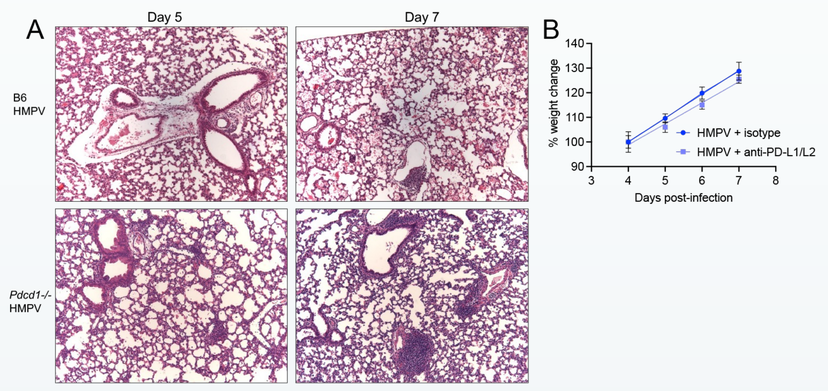


Neonatal CD8⁺ T cells ↑ inhibitory receptors

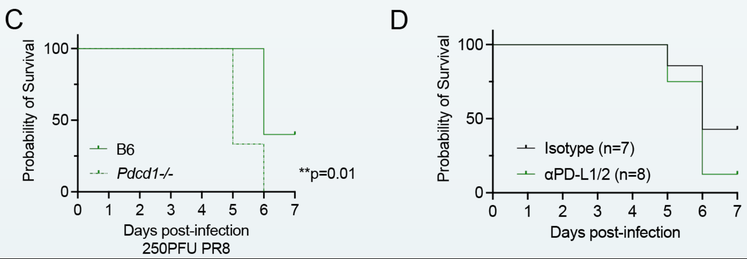
Pdcd1-/- mice have ↑ CD8⁺ function



Pdcd1-/- mice have ↑ pathology



Lethal influenza PR8 model:



Conclusions

- Neonatal mice clear HMPV infection
- Neonatal CD8⁺ T cells upregulate inhibitory receptors following HMPV
- PD-1 mediated inhibition of neonatal CD8⁺ T cells limits effector function
- Absence or blockade of PD-1 leads to increased pathology/mortality

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