

Title

MAIT cells contribute to a protective antiviral innate response to influenza infection

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Abstract

Background: Mucosal associated invariant T (MAIT) cells are evolutionarily-conserved, innate-like lymphocytes which are abundant in human lungs and can contribute to protection against pulmonary bacterial infection. However, whilst they are also activated during human viral infections, it is unknown whether MAIT cells play a significant protective or even detrimental role during viral infections *in vivo*.

Aims and objectives: To determine whether MAIT cells play a significant role – either protective or detrimental – during influenza A infection *in vivo*.

Methods: We used major histocompatibility complex-related protein 1 (MR1) tetramers and intracellular cytokine staining to track MAIT cell frequencies and activation during *in vivo* murine experimental challenge with two strains of influenza A virus in immunocompetent (C57BL/6), MAIT-cell deficient (MR1^{-/-}) and immunodeficient (Rag2^{-/-}γC^{-/-}) mice.

Results: MAIT cells accumulated and were activated early in infection, with upregulation of CD25, CD69 and Granzyme B peaking at 5 days post infection. Activation was modulated via cytokines interleukin (IL)-12, -15, -18 and type I interferon, independent of MR1. MR1^{-/-} mice, which lack MAIT cells, showed enhanced body weight loss and mortality to severe (H1N1) influenza. This was ameliorated by prior adoptive transfer of pulmonary MAIT cells in both immunocompetent (Figure 1) and immunodeficient Rag2^{-/-}γC^{-/-} mice which lack T, B and NK cells.

Conclusions: MAIT cells contribute to protection during respiratory viral infections, and constitute a potential target for therapeutic manipulation.

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