S97 MAIT CELLS CONTRIBUTE TO A PROTECTIVE ANTIVIRAL INNATE RESPONSE TO INFLUENZA INFECTION

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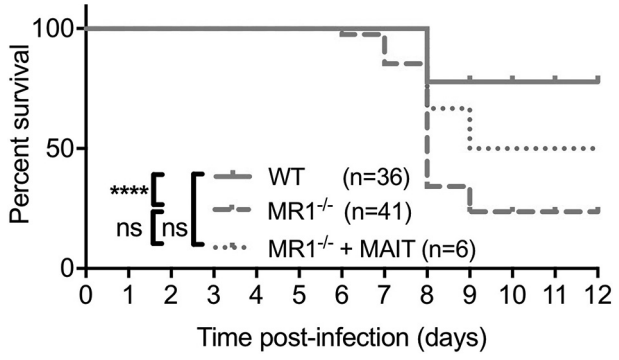
Background Mucosal associated invariant T (MAIT) cells are evolutionarily-conserved, innate-like lymphocytes which are abundant in human lungs and can contribute to protection against pulmonary bacterial infection. However, whilst they are also activated during human viral infections, it is unknown whether 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 ($Rag2^{-/-}gC^{-/-}$) 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 $Rag2^{-/-}gC^{-/-}$ mice which lack T, B and NK cells.



Abstract S97 Figure 1

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

S98 PELLINO-1 REGULATES THE RESPONSES OF THE AIRWAY TO VIRAL INFECTION

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Introduction and objectives Exposure to respiratory pathogens is a leading cause of exacerbations of airway diseases such as asthma and chronic obstructive pulmonary disease (COPD). We have shown that Pellino-1, an E3 ubiquitin ligase, is involved in viral-induced TLR3 signalling; thus we sought to describe the role of Pellino-1 in the host response to viral stimulation of the airway.

Methods Pellino-1 expression was examined in bronchial sections from patients with GOLD stage 2 COPD (n=7) and healthy controls (n=8). Primary bronchial epithelial cells (PBECs, n=5) in which Pellino-1 expression had been knocked down using siRNA, were extracellularly challenged with the TLR3 agonist poly(I:C). C57BL/6 *Peli1*$^{-/-}$ mice and wild type littermates were subjected to intranasal infection with the clinically-relevant respiratory viruses rhinovirus (RV1B) and influenza A, and responses monitored up to 8 days later.

Results We show that Pellino-1 is expressed in the airways of normal subjects and those with COPD. In the absence of Pellino-1, PBECs showed significant reduction in proinflammatory cytokines, including CXCL8 and IL-6, upon TLR3 activation. Surprisingly however, knockout of Peli1 in the murine lung resulted in increased production of the proinflammatory cytokines IL-6 and TNFα with viral infection. This was accompanied by an enhanced recruitment of immune cells to the airways in these animals, including a population of innate B cells, without loss of viral replication.

Conclusions We conclude that Pellino-1 functions as a positive regulator for antiviral responses in isolated bronchial epithelial cells and in systemic responses to TLR3 activation, but it has the opposite effect in the lung. Here, Pellino-1 has a distinct function in the down-regulation of antiviral inflammation; a role dissociated from viral replication. Our data therefore suggest that Pellino-1 may offer therapeutic potential to limit viral inflammation in COPD and asthma.

S99 POINT OF CARE TESTING FOR RESPIRATORY VIRUSES (RPOCT): A NOVEL SERVICE TO FACILITATE APPROPRIATE DISCHARGE AND INFECTION CONTROL MEASURES AND IMPROVE ANTIMICROBIAL STEWARDSHIP

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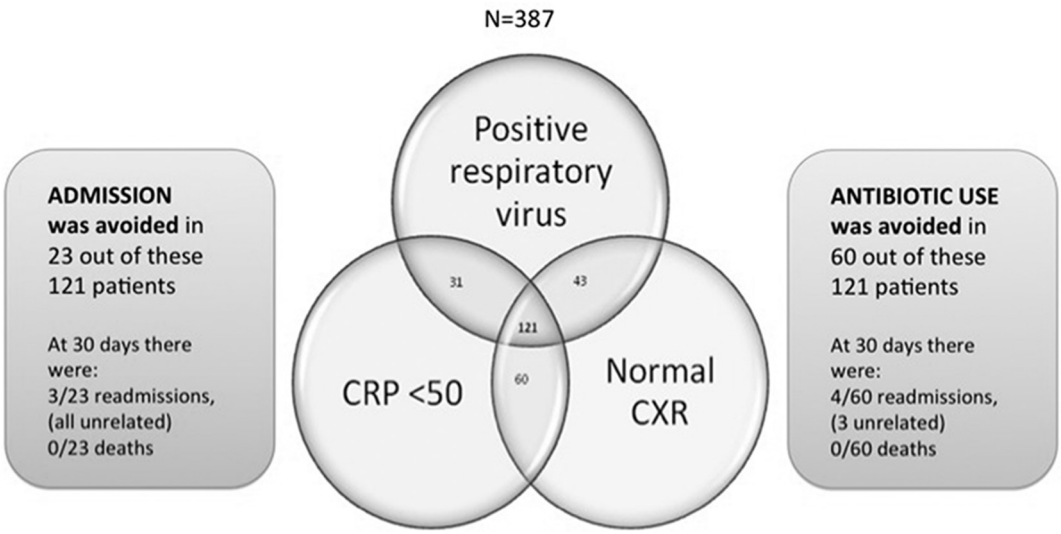
Introduction Respiratory infection, predominantly due to viral pathogens, poses a huge burden on the NHS especially during



Abstract S99 Figure 1

winter. An earlier definitive microbiological diagnosis should allow more rapid clinical decision-making on aspects of care, including hospital admission (versus discharge) and antibiotic use, and prevention of nosocomial infection.

We hypothesised that use of RPOCT would improve the quality of service by guiding early management plans, improving bed flow and infection control within the Trust and reducing morbidity associated with empirical antibiotic prescribing.

Objectives To investigate whether an RPOCT service in ED/AAU would result in:

1. Earlier definitive microbiological diagnosis
2. Improved antimicrobial stewardship
3. Early safe discharge (in appropriate cases)
4. Reduced nosocomial infection and bed closures for infection control purposes.

Methods We present 1075 patients who underwent RPOCT (BioFire Film Array, Biomerieux Inc.) from 15 January to 1 May 2018 when presenting with respiratory and/or generalised viral symptoms.

Results

1. A positive viral result was noted in 61% of tests, of which only 56% were positive for Influenza and the rest for other viruses.
2. Time from ED admission to result was significantly shorter with RPOCT versus conventional laboratory methods (6.5 versus 44.4 hours: $P<0.001$).
3. RPOCT findings were integrated with other key clinical indices (figure 1) and clinical outcomes shown. 121 patients were identified as potentially suitable for discharge without antibiotics (normal CXR, low CRP in absence of bacterial infection).
4. Of 50 influenza cases, 22 who had been tested in ED had no subsequent bed moves as opposed to 28 tested outside ED where there were 14 bed moves some resulting in closure of bays or beds ($P<0.001$).

Conclusions We have demonstrated that RPOCT permits more informed early decision-making, likely to improve the patient journey and was associated with avoidance of bed and ward closures with potential reduction in nosocomial transmission of infection.

Integration of RPOCT results with other clinical information can help identify cohorts among whom some patients may be appropriate for avoidance of antibiotic use and/or avoidance of hospital admission – patients considered suitable for these approaches had good outcomes at short term follow-up.

S100 IMPACT OF INFLUENZA NEAR-PATIENT TESTING ON ADMISSIONS AND ANTIMICROBIAL USE: A SINGLE SCOTTISH CENTRE EXPERIENCE

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Introduction Seasonal influenza leads to an increase in acute presentations to hospital. The infectious nature of influenza mandates source isolation of confirmed and suspected admitted cases, and national guidelines recommend antiviral use in confirmed influenza. Early diagnosis of influenza using near-patient testing (NPT) should optimise use of limited infection-control resources as well as improve antimicrobial use.

Methods NPT using a real-time PCR (polymerase-chain reaction) system was trialled at our centre between December 2017 and April 2018. A retrospective analysis of cases identified as Influenza A/B positive was performed using data from electronic records. Characteristics of the entire trial population were analysed, with a more detailed analysis of two samples (first 100 cases (cohort 1); final 100 cases (cohort 2)). In addition, a retrospective analysis of lab-confirmed influenza cases (n=98) from the same period during 2016–2017 was performed to assess the impact of NPT.

Results 2205 tests were performed during the trial period, with 710 (32%) positive tests. 446 (21%) of samples were positive for Influenza A, 220 (11%) were positive for Influenza B. Comparison with the previous year showed clear improvement in admission characteristics and antimicrobial prescribing (see table 1). Over the course of the trial, there were also positive changes in admission rates and antibiotic prescribing. Only 5.8% of NPT-positive samples were sent for confirmatory conventional lab PCR, all of which were positive. An additional 39 cases were identified with lab testing –