the VAP and non-VAP groups (Abstract S77 Figure 1). Soluble TREM-1 levels were not significantly different between the groups. There was no difference in peripheral blood white cell count, CRP, expression of CD11b, L-selectin and inflammatory cytokines between VAP and disease controls.

Conclusion The BALF/blood ratio of monocytic surface TREM-1 discriminates between the VAP and non-VAP groups. Measurement of surface TREM-1 using a two-compartment index may have utility in diagnosing VAP.

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S78 DETERMINANTS OF MACROPHAGE RESPONSES TO *STREPTOCOCCUS PNEUMONIAE*

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Introduction and Objectives *Streptococcus pneumoniae* is the commonest cause of pneumonia and associated with marked inflammatory responses that underpin its immunopathogenesis. Surprisingly little is known about the molecular determinants of host–pathogen interactions that mediate these responses. We have studied the role of the pneumococcal capsule and surface lipoproteins in innate immune responses by macrophages that comprise the first line of cellular immune defence within the lung.

Methods Human macrophage responses to wild type *S pneumoniae* (TIGR4) and isogenic mutant strains deficient in capsule (P1672) or surface lipoproteins (Δlgt) were investigated at the level of intracellular signalling, genome-wide transcriptional profiling and at protein level by cytokine ELISA.

Results Unencapsulated bacteria invoked greater activation of the classical NFkB pathway, suggesting that the capsule may serve to inhibit some innate immune host pathogen interactions. In contrast, the Δlgt strain showed attenuated activation of NFkB, suggesting that lipoproteins are important ligands for innate immune recognition of pneumococci. Transcriptional responses to both unencapsulated and Δlgt strains showed marked differences to wild type pneumococci. However, quantitatively, major gene expression changes were preserved in the mutant strains. Despite the divergent effects on NFkB activation, both unencapsulated and Δlgt strains showed attenuated responses amongst these genes, although some key responses such as upregulation of TNFα were equivalent in all strains. Transcription factor enrichment analysis was conducted for the list of genes up-regulated by each strain to obtain new insight into the different pathways by which pneumococci may activate inflammatory responses. As expected, genes up-regulated by the wild type strain were enriched only for the NFkB family. In keeping with the signalling data, the Δlgt strain was not enriched for NFkB but only the PPARγ-RXR transactivator, and the unencapsulated strain was highly enriched for NFkB and a raft of other transcription factors.

Conclusion Pneumococcal capsule and lipoproteins are important determinants of inflammatory responses to pneumococci. Our data suggest that the capsule inhibits multiple innate immune signalling pathways and that lipoproteins are critically important for activation of the canonical NFkB pathway. TNFα responses are independent of capsule and lipoproteins.

S79 POTENTIAL DIAGNOSTIC SIGNIFICANCE OF NEUTROPHIL PROTEASES IN VENTILATOR-ASSOCIATED PNEUMONIA

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Introduction and Objectives The clinical diagnosis of ventilator-associated pneumonia (VAP) remains notoriously difficult, as several non-infective conditions mimic VAP. Microbiological confirmation of the diagnosis using conventional cultures typically takes 48–72 h. Identification of molecules measurable within a short time frame and closely associated with microbiologically confirmed VAP is therefore highly desirable. VAP is associated with significant influx of activated neutrophils into the alveolar space. We postulated that extracellular neutrophil proteases in bronchoalveolar lavage fluid (BALF) may reliably identify VAP in suspected cases.

Methods Fifty-four intubated and mechanically ventilated patients in the intensive care unit developed clinically suspected VAP and were recruited. Bronchoalveolar lavage (BAL) was performed using a standardised protocol. An aliquot of BALF was sent to the diagnostic microbiology laboratory for quantitative culture, with confirmation of VAP defined as growth of a pathogen(s) at $>10^4$ colony forming units/ml. Remaining BALF was centrifuged. The following neutrophil-specific proteases were assayed in cell-free BALF supernatant—matrix metalloproteinase (MMP)-8 and MMP-9 by Luminex assay, and human neutrophil elastase (HNE) by enzyme-linked immunosorbent assay. Urea was simultaneously measured in serum and BALF, and used to correct for the dilution of epithelial lining induced by BAL. Receiver operating characteristic (ROC) curves were constructed and optimal specificity and sensitivity for each marker calculated.

Results Eleven patients (20%) had confirmed VAP. For HNE (cut off 670ng/ml) the ROC area under curve (AUC) was 0.87 ($p<0.0001$), sensitivity 93%, specificity 79%. For MMP-8 (13 ng/ml), ROC AUC was 0.81 ($p<0.005$), sensitivity 91%, specificity 63%. For MMP-9 (22 ng/ml), ROC AUC was 0.79 ($p<0.005$), sensitivity 82%, specificity 63%.

Conclusions Neutrophil proteases are strongly associated with confirmed infection in cases of suspected VAP. The values for HNE, in particular, compare extremely favourably with any previously published equivalent values. These data suggest that neutrophil protease concentrations in BALF deserve further attention as potentially diagnostic markers for VAP. They further suggest that neutrophil proteases, inappropriately released into the extracellular space, may contribute to the pathophysiology of VAP.

S80 THE ROLE OF MYD88 IN RHINOVIRUS 1B INFECTION

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Introduction Rhinovirus (RV) are major triggers of acute asthma exacerbations and result in innate immune cell infiltration into the airways. Viral recognition by TLRs results in activation of pathways mediated by the adaptors MyD88 and TRIF, which predominantly control the production of proinflammatory cytokines and interferons respectively. We have previously shown that addition of the cytokine IL-1 (which also signals via MyD88) potentiates responses to the viral mimic Poly (I:C),[1] which acts in a MyD88-independent