S29 MANNOSE BINDING LECTIN DEFICIENCY IN CHILDREN WITH RESPIRATORY INFECTION

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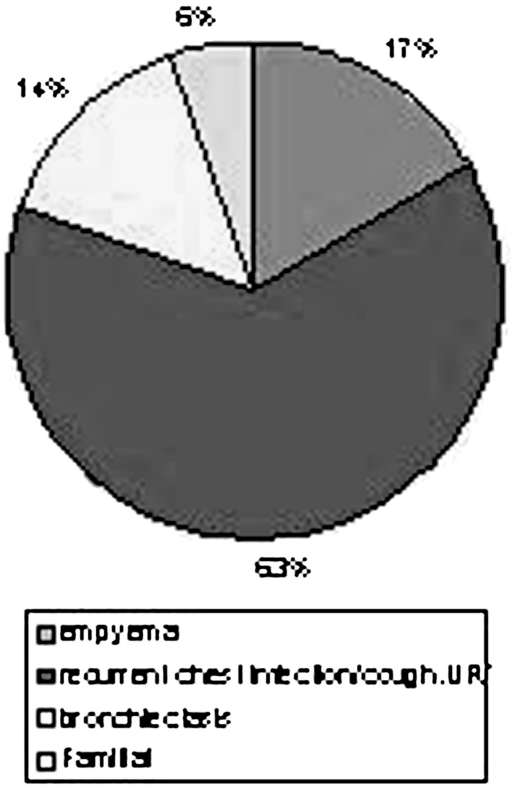
Introduction Mannose binding lectin (MBL) plays a crucial part in innate immunity by activating the complement pathway. MBL deficiency is common, it has been associated with pulmonary disease, but low levels may also be found in otherwise normal individuals. Little is known about the importance of MBL deficiency as a risk factor for recurrent upper and lower respiratory tract infections.[1 2] We describe our experience of measuring MBL levels in children with recurrent upper and lower respiratory tract infections.
Methods MBL levels and clinical data were extracted from immunology laboratory records, of children being investigated for acute or chronic recurrent respiratory tract infections between November 2008 and February 2010. MBL deficiency was defined as a level <75 ng/ml.
Results 489 children had serum MBL measured during this time period. 199 had recurrent respiratory infections and of those 36 were positive for MBL deficiency (Abstract S29 Figure 1). Deficiency was found in 29% of positive boys and 14% of positive girls. 20% of positive patients were <2 years, 16% 2–5 years and 28% >5 years at the time of investigation.
Conclusions MBL deficiency is common in our population. The true significance of this abnormality as a risk factor for respiratory infection in children remains to be determined. Case–control studies will be required to evaluate the relative importance of this abnormality in different subgroups of patients.



Abstract S29 Figure 1 The distribution of clinical problems of MBL deficient children.

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Linking airways inflammation and remodelling

S30 TRUSS IS A REGULATOR OF TNFα-TNF-R1 INDUCED NF-κB ACTIVATION

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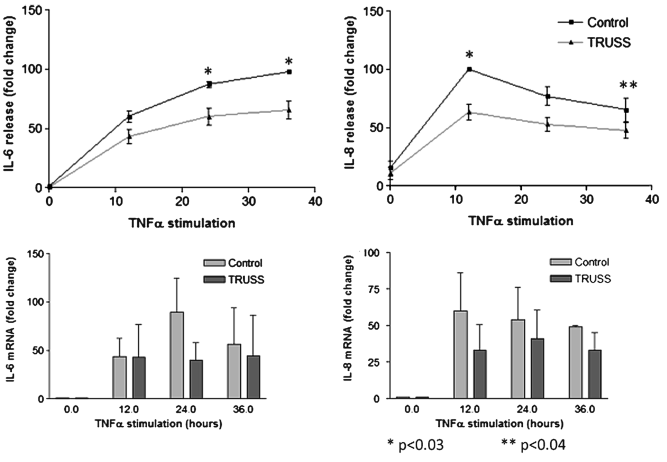
Introduction TNFα is a pleiotropic cytokine that can exert opposing biological actions, either pro-inflammatory or pro-apoptotic, through interaction with its cognate receptor TNF-R1. How this balance is regulated remains to be elucidated. One possible regulator is the novel TNF-R1 interacting protein TRUSS (TNF-R1 ubiquitous signalling and scaffold protein). Ectopic expression of TRUSS activates the transcription factors NF-κB and AP-1.
Aims To determine the physiological role of TRUSS in TNFα-TNF-R1 signal transduction.
Methods Human epithelial (A549) cells were transfected with human TRUSS siRNA and responses to TNFα stimulation were assessed by RT-PCR, ELISA, immunoblotting and confocal microscopy.
Results TRUSS knockdown impaired secretion of the inflammatory chemokines IL-6 and IL-8 following prolonged TNFα stimulation. The maximal reduction of IL-8 mRNA and protein occurred after 12 h of TNFα incubation in the TRUSS deficient cells ($p<0.03$), whereas the IL-6 responses were decreased after 24 h ($p<0.03$) (Abstract S30 Figure 1). Furthermore, these effects were abrogated by cycloheximide or the NF-κB inhibitor Bay11-7085, indicating that the inflammatory chemokines were newly synthesised in response to TNFα stimulation via an NF-κB dependent pathway. The upstream signalling molecules TNFR1, TRADD, TRAF2 and RIP were unaffected by TRUSS deficiency. However, phosphorylation of the p50 precursor p105 was augmented in the cytosolic fraction of TRUSS knockdown cells whilst total p50 in the nuclear fraction was reduced by TNFα stimulation. This was associated with impaired nuclear translocation of the activated NF-κB subunit p65 and enhanced JNK phosphorylation.



Abstract S30 Figure 1

Conclusions Our data suggest TRUSS is integral to TNFα-TNF-R1 mediated NF-κB activation. We propose that TRUSS functions as a