**INVASION VERSUS OVERGROWTH: UNDERSTANDING SUPPRESSION OF MACROPHAGE INFLAMMATORY RESPONSES TO Streptococcus pneumoniae BY REGULATORY T CELLS**


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**Background**

The highly inflammatory immune response to *Streptococcus pneumoniae* infection can result in complications such as sepsis and Acute Respiratory Distress Syndrome. Macrophages are an important source of the inflammatory cytokines that activate epithelial and endothelial cells, resulting in a loss of barrier integrity. Regulatory T cells (Tregs) are a population of anti-inflammatory cells that modulate macrophage activity and are protective against invasive pneumococcal disease in mice.1,2

**Aims**

To characterise the *in vitro* effects of Tregs on the macrophage inflammatory response to *S. pneumoniae* and to observe Treg recruitment to the site of intradermal injection of UV-killed *S. pneumoniae* in a human model.

**Results**

Preliminary data suggest that co-culture of human monocyte-derived macrophages (MDMs) with CD4+CD25+ Tregs reduced MDM TNFα production by at least 45% (One-way ANOVA p<0.01) and IL-6 production by at least 52% (One-way ANOVA p<0.01) 72 hours after initial infection with *S. pneumoniae* TIGR4 strain (MOI of 2, ratio of 1 Treg to 3 MDMs). Separation of Tregs from the MDMs during co-culture using transwell inserts prevented the suppressive effects of the Tregs. Using a novel human model of *S. pneumoniae* challenge involving intradermal injection of UV-killed *S. pneumoniae* into the forearm of healthy volunteers, we demonstrated that Tregs accumulated at the site of injection within 48 hours, increasing from undetectable Treg population at 4 hours to constituting approximately 33% of CD4 cells by 48 hours.

**Conclusion**

Preliminary data suggest that Tregs modulate the MDM inflammatory response to *S. pneumoniae* in a contact-dependent manner, and track to the site of intradermal injection of the UV-killed bacteria in human volunteers.

**REFERENCES**


Lung cancer screening has arrived

**IDENTIFICATION AND ATTENDANCE OF A HIGH-RISK COHORT IN A LUNG CANCER SCREENING DEMONSTRATION PILOT**

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Introduction Lung Cancer screening by Low-Dose CT (LDCT) has been shown to reduce mortality, though exactly how best to implement this is unclear. Uptake to screening trials has generally been low, particularly in those at highest risk of lung cancer. The Lung Screen Uptake Trial is a UK based dual centre LDCT randomised controlled screening trial of a modified invitation strategy versus a standard approach in a population with high levels of socioeconomic deprivation.

Methods Patients were identified as ‘high-risk’ primarily by age and smoking history on a predesigned EMIS-Web search and subsequently invited on behalf of their general practitioner (GP) to a ‘lung health check’ appointment. Those attending were offered enrolment into the study and a LDCT if they met the required threshold of lung cancer risk. This abstract focuses on the mode of recruitment via general practice.

Results Potentially eligible participants were recruited from 16 GP surgeries serving a population of 155,034. Of these, 8.7% were in the required age range of 60–75% and 98.9% of those had smoking status recorded. A mean of 32.2% (SD 3.8) of those aged 60–75 had been recorded as a current smoker in the preceding 15 years. A total of 1997 patients, who had been recorded as current smokers within the past 5 years were invited. Uptake to the study was 50.3% (n=1005) of all those invited. 765 underwent a LDCT examination (figure 1). In 10.3% of patients the smoking history was confirmed to be too light for CT screening, despite GP records suggesting otherwise.

Conclusions Smoking status was found to be very well recorded in primary care records, providing a feasible method for initial selection of those eligible for screening. However we also showed the importance of confirmation of smoking history, something that might be done prior to invitation in screening programmes. This study observed a high rate of attendance when compared to previous LDCT screening trials. The explanation for this observed difference is likely to be multifactorial, though one key factor, unique to this study, is that the invitation to participate came from patients’ own GP.

**THE LIVERPOOL HEALTHY LUNG PROJECT (LHLP) – SEEKING OUT LUNG DISEASE**

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Introduction Liverpool has high respiratory morbidity with double the national lung cancer incidence, particularly in lower socioeconomic groups. To tackle this health inequality Liverpool CCG with the primary and secondary care sectors, Public Health and Liverpool University commenced a 3 year LHLP. The project cost £600 k in the first year. It was adopted by the national ACE program, and we report the first year results.

Methods Firstly, a series of coordinated focused public engagement events are arranged in areas with a high lung cancer incidence, aiming to promote positive messages around lung health, and address the fear and fatalism surrounding lung cancer, called ‘Healthy Lung Events’ Secondly, from GP records all aged 58–70 with COPD, who smoke, or have asbestos exposure are invited to a face to face lung health check by a respiratory nurse who promotes positive lifestyle messages and calculates a 5 year personal lung cancer risk.

Abstract S11 Figure 1 Flow chart illustrating the numbers of individuals invited, recruited to the study and undergoing LDCT screening.