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Title: LSC 2013 abstract - The role of alveolar macrophages during the resolution of house dust mite induced allergic airways disease

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Body: Allergic asthma is a chronic inflammatory disease of the lung. Deficiencies in pro-resolving mechanisms may contribute to the persistence of inflammation in the lung. Alveolar macrophages are considered to have a critical regulatory role in the lung but their interactions in the allergic lung are not well understood. Experimental models of asthma have shown that depletion of alveolar macrophages prior to allergen sensitisation results in exacerbated disease. However, their role during resolution has not been fully examined. Using a mouse model of house dust mite (HDM) induced allergic airway disease we investigate the role of alveolar macrophages during the resolution of allergic inflammation. Disease parameters were measured at 4 hours, 7days and 13days following allergen exposure. Airway hyper-reactivity was sustained 7days post challenge compared to PBS treated controls, returning to baseline by 13 days, accompanied with concomitant levels of Th2 lymphocytes and eosinophils. Levels of neutrophils increase following HDM exposure and resolve by 7days. CD11c+ alveolar macrophage numbers increased at 4 hours and are significantly elevated at 7 and 13 days, suggesting a role during resolution. Depletion of alveolar macrophages during the resolution phase was carried out using i.t administration of clodronate encapsulated liposome. This resulted in delayed resolution of Th2 lymphocytes and airway neutrophils. However, no changes were observed in Th2 cytokines or airway hyper-reactivity. Conversely, following the adoptive transfer of alveolar macrophages during resolution, total lung tissue cell numbers and neutrophils were decreased. Levels of Th2 lymphocytes and airway hyper-reactivity remain unchanged. Levels of CD11b+ CD11c- lung tissue macrophages were reduced upon alveolar macrophage transfer suggesting a cross talk between these pulmonary subsets. These data indicate that distinct pathways are responsible for the resolution of allergic airways disease and alveolar macrophages have a specific role to play in regulating the allergic inflammatory response.