Inhaled Fine Particles Induce Alveolar Macrophage Death and Interleukin 1α Release to Promote Inducible Bronchus-Associated Lymphoid Tissue Formation

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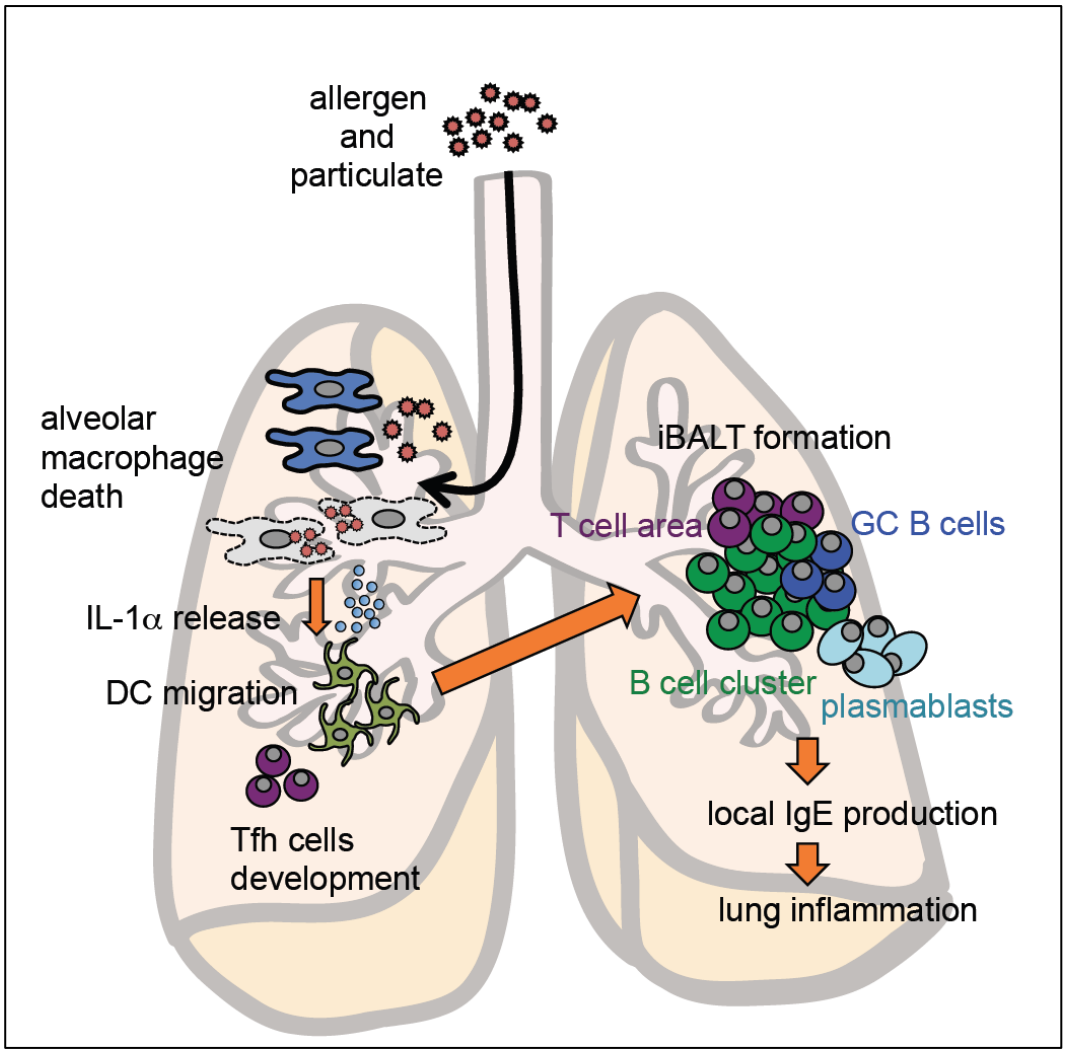
Immunity

Abstract

Particulate pollution is thought to function as an adjuvant that can induce allergic responses. However, the exact cell types and immunological factors that initiate the lung-specific immune responses are unclear. We found that upon intratracheal instillation, particulates such as aluminum salts and silica killed alveolar macrophages (AMs), which then released interleukin-1α (IL-1α) and caused inducible bronchus-associated lymphoid tissue (iBALT) formation in the lung. IL-1α release continued for up to 2 weeks after particulate exposure, and type-2 allergic immune responses were induced by the inhalation of antigen during IL-1α release and iBALT formation, even long after particulate instillation. Recombinant IL-1α was sufficient to induce iBALTs which coincided with subsequent immunoglobulin E responses, and IL-1-receptor-deficient mice failed to induce iBALT formation. Therefore, the AM-IL-1α-iBALT axis may be a therapeutic target for particulate-induced allergic inflammation.

Keywords

Particulate, IL-1α, alveolar macrophages, IgE, iBALT



Model of particulate-induced allergic inflammation in the lungs

It is known that particle pollutants (sand dust and PM2.5 etc.) trigger and exacerbate allergic inflammation. Many reports demonstrate that some particles including particle pollutants function as adjuvant and induce type-2 immune responses. However the detailed mechanisms by which particulates trigger type-2 responses are unclear

In this study, we found that inhaled fine particulates (alum and silica) are engulfed by alveolar macrophages and induce cell death. Dead cell-derived factors such as IL-1α are released and induce iBALT formation through the activation of DCs and Tfh cells. The release of DAMPs, triggered by exposure to particulates, and iBALT formation might contribute to particulate-pollution-induced allergic inflammation through antigen (allergen)-specific IgE responses.