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Organic dust-induced activation, adhesion to substrate and expression of intercellular adhesion molecules in THP-1 monocytes

Karin Burvall, Lena Palmberg *, Kjell Larsson

The National Institute of Environmental Medicine, Lung and Allergy Research, Karolinska Institutet, Box 287, SE-171 77 Stockholm, Sweden

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Abstract

Inhalation of organic dust in a swine confinement building induces systemic reactions, increased bronchial responsiveness and intense airway inflammation in previously unexposed, healthy subjects. These effects are self-limiting, but chronic respiratory symptoms are frequently observed in swine confinement workers. The present study was aimed at investigating organic dust-induced activation of the monocytic leukemia cell line, THP-1. Unstimulated THP-1 cells proliferate in suspension but cultivation for several days in medium with complete dust or 0.22-μ-filtered suspension, caused a subset of the THP-1 cells to adhere to the substratum. As assessed by transmission light- and indirect immunofluorescence microscopy, dust-stimulated adherent THP-1 cells adopted macrophage-like morphology and expressed vimentin. Intercellular adhesion molecule (ICAM)-1 was expressed in all dust-activated adherent cells, but only in 1% of the unstimulated cells in suspension. Sialoadhesin, a macrophage marker, was detected in dust-stimulated adherent THP-1 cells but not in the parental monocytes. Serum factors were required for the dust-induced expression of sialoadhesin, but not for adhesion to substrate or expression of ICAM-1. In addition, morphology and expression of vascular endothelial growth factor (VEGF) of dust-stimulated adherent cells equalled that of PMA-differentiated THP-1 cells, but the PMA-differentiated cells exhibited weak sialoadhesin labelling. In conclusion, exposure to organic dust from a swine confinement building activated a subset of THP-1 monocytes inducing expression of intercellular adhesion molecules, which are important in inflammation. The sustained adhesion to substrate indicates that organic dust from a swine confinement building may contain agents that prevent deactivation and detachment of the cells.

Keywords: ICAM-1; Macrophage activation; Organic dust; Sialoadhesin; THP-1 monocytes

Introduction

Inhalation of organic dust in a swine confinement building induces fever, malaise and muscle pain, increased bronchial responsiveness and intense airway inflammation with an increased number of inflammatory cells and mediators in previously unexposed subjects (Malmberg and Larsson, 1993; Wang et al., 1997). The flu-like illness referred to as organic dust toxic syndrome (ODTS) is self-limited (Seifert et al., 2003), but chronic respiratory symptoms are frequently observed in swine confinement workers (Donham et al., 1995) and swine veterinarians (Andersen et al., 2004). The dust represents a complex mixture of feed, fecal particles, dander from swine, bacteria and fungi. The bacterial content includes whole bacteria and cell wall components such as lipopolysaccharide (LPS), derived from Gram negative bacteria and peptidoglycan, which is the main cell wall constituent of Gram positive bacteria.

Intercellular adhesion molecule (ICAM)-1, (or CD54), is a member of the immunoglobulin superfamily of receptors and upregulated expression of ICAM-1 has been demonstrated in chronic diseases including chronic obstructive pulmonary disease (COPD) (Papi et al., 2006; Zandvoort et al., 2006) and ulcerative cholitis (Vainer, 2005). ICAM-1 mediates adhesion by binding to the integrins CD11a/CD18 (leukocyte adhesion molecule, LFA-1) and CD11b/CD18 (Mac-1).

Sialoadhesin (Sn; Siglec-1; CD169) is the prototypic member of sialic acid-binding immunoglobulin-like lectins (Siglec) expressed by resident and inflammatory macrophage populations (Crocker et al., 1994; Crocker and Varki, 2001; Hartnell et al., 2001). In the spleen, sialoadhesin is expressed mainly on macrophages in the perifollicular zone. These cells have been implicated in specialized functions in innate and

* Corresponding author. Tel.: +46 8 52482210; fax: +46 8 300 619.
E-mail address: lena.palmberg@ki.se (L. Palmberg).

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acquired immunity, possibly in interaction with B cells (Steiniger et al., 1997). Sialoadhesin-expressing macrophages may also interact with T cells by binding to CD43, an extended molecule carrying multiple O-linked glycans (van den Berg et al., 2001). Sialoadhesin exists in two forms unmasked or masked by endogenous sialic acid, the unmasked form being available for sialoadhesin-dependent adhesive functions (Nakamura et al., 2002). Sialic acids are expressed on cell surfaces, secreted glycoproteins and in the extracellular matrix (Munday et al., 1999) and by various pathogens (Crocker and Varki, 2001).

Macrophages, which are important for the defense in normal lung, also play a role during conditions associated with chronic inflammation such as COPD (Shapiro, 1999). It has been found that patients with COPD exhibit a 5–10 fold increase of macrophages in the airways, lung parenchyma and bronchoalveolar lavage fluid (MacNee, 2005) and that the macrophage number correlates with the severity of COPD (Russell et al., 2002). Tissue macrophages are derived from monocytes, which constitute a heterogeneous population of precursor cells circulating in the blood (Kumar and Jack, 2006).

The THP-1 monocytic leukemia cell line, established from a patient with acute monocytic leukemia, expresses markers characteristic of immature cells in monocytic development. The monocytes proliferate in suspension, but can be differentiated into adherent macrophage-like cells by treatment with phorbol 12-myristate 13-acetate (PMA) (Tsuchiya et al., 1982; Abrink et al., 1994). A recent study has demonstrated LPS-induced adhesion of THP-1 monocytes to the substratum (Kounalakis and Corbett, 2006). The attachment was transient (peaking at 1 h and returning to baseline by 4 h) and a result of β2 integrin activation (Kounalakis and Corbett, 2006).

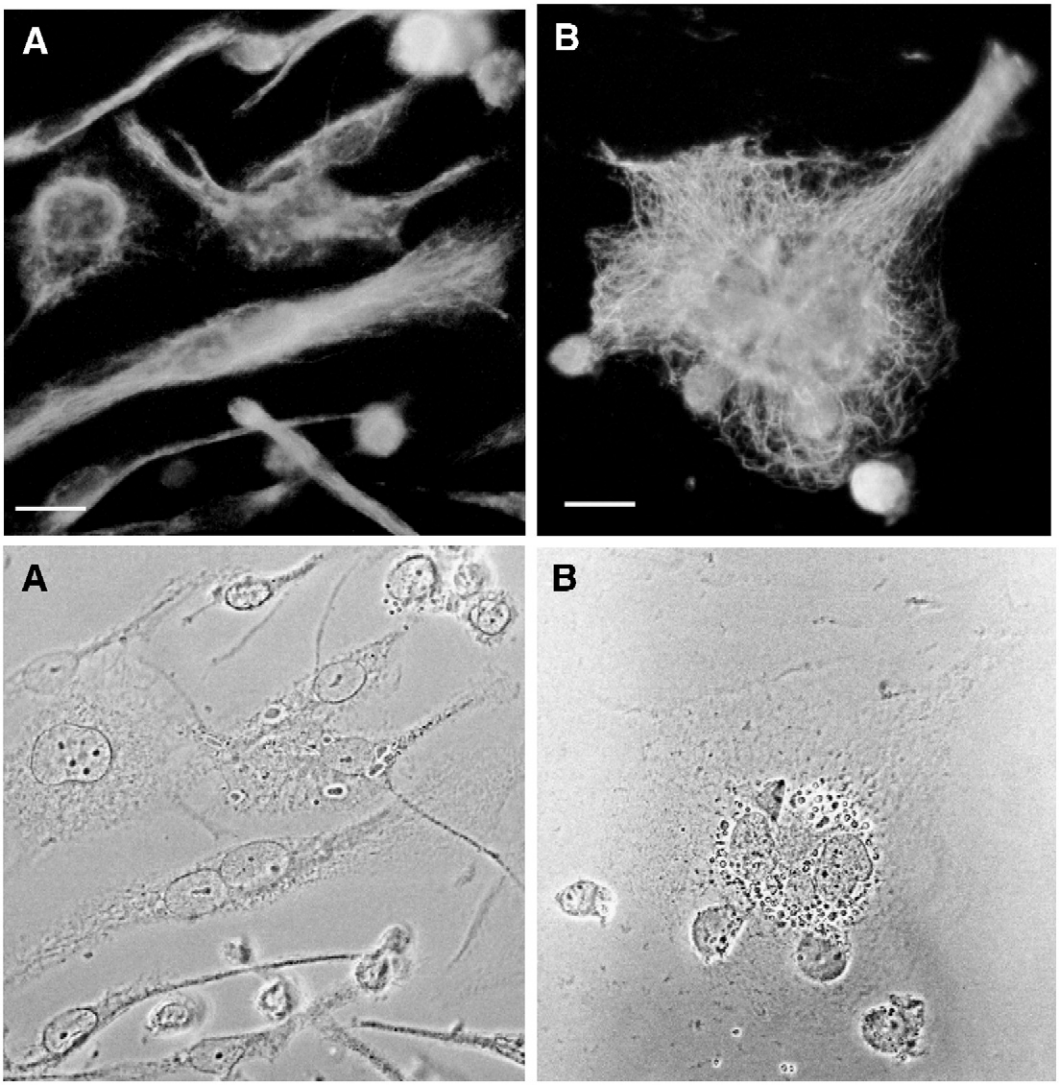

Fig. 1. Labelling of vimentin. A, Upper panel) Immunolabelling of THP-1 adherent cells after 5 days incubation in dust suspension, 5 μg/ml, followed by 2 days in RPMI-FBS when the medium was aspirated, adherent cells washed with PBS, fixed in MeOH and labelled with a monoclonal antibody against vimentin; A, Lower panel) transmission light micrograph of the same cells. B, Upper panel) Immunolabelling of adherent cells following incubation in 0.22-μ-filtered dust suspension for 7 days; B, Lower panel) transmission light micrograph of the same cells. Second Ab was Cy™2-conjugated goat anti-rabbit Ab. Visualization in a Nikon Labophot-2A fluorescence microscope. Magnification: 400×, bars 25 μm.