Expression of Adhesion Molecules (ICAM-1, LFA-3) on Human Epithelial Cells (A549) after Respiratory Syncytial Virus Infection

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Key Words

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Respiratory syncytial virus (RSV) infection is the leading cause of respiratory infection in infancy worldwide. The epithelial cells of the lower respiratory tract are the primary target cells for RSV infection. After infection, RSV replicates efficiently in these cells causing cell injury by syncytium formation and direct cytopathic effects.

Recently, we have shown that epithelial cells of the human cell line A549 infected with RSV secreted interleukin (IL)-8, IL-6, and the soluble tumor necrosis factor- α (sTNF- α) in a time- and RSV-dose-dependent fashion [1]. In addition, polymorphonuclear neutrophil granulocytes synthesized proinflammatory cytokines after phagocytosis of RSV [2]. By coculturing A549 cells with peripheral blood mononuclear cells (PBMCs), we observed a synergistically increased IL-8 secretion pattern. Therefore, soluble mediators (IL-1 β , TNF- α and TNF- β) secreted by the cocultured cells themselves as well as cell-cell adhesion phenomena are involved [Arnold et al., submitted].

Next, we analyzed whether RSV-infected A549 cells show an altered adhesion molecule expression pattern

which may contribute to an enhanced direct cell-cell contact. The ICAM-1/LFA-1 and LFA-3/CD2 receptor/ligand pairing are the most important noncognate adhesive cell interactions in inflammatory and immune reactions. Therefore, the expression pattern of ICAM-1 and LFA-3 on RSV-infected epithelial cells was analyzed.

ICAM-1 and LFA-3 expression on RSV-infected A549 epithelial cells was measured by fluorescence flow cytometry 4 and 24 h after infection (MOI=1). Figure 1 shows the results of the 24-hour infection studies. As can be seen, the A549 cells expressed ICAM-1 and LFA-3 constitutively (see A1 and B1). RSV infection induced a pronounced ICAM-1 up-regulation (see A2). An increase of ICAM-1 expression was even observed after 4 h infection but was more

pronounced after 24 h (data not shown). In contrast, no alteration was measured in the LFA-3 surface expression pattern following 4 or 24 h RSV infection (see B2). In summary, the RSV-infected epithelial cells expressed more ICAM-1 than noninfected cells. Thus, the increased ICAM-1 expression profile may contribute to enhanced

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Fig. 1. Cell surface expression pattern of ICAM-1 and LFA-3 on human epithelial cells (A549). The cells were infected with RSV (MOM) and cultured for 24 h. The adhesion molecule surface expression pattern was analyzed by flow cytometry: ICAM-1 expression on noninfected cells (A1), or RSV-infected cells (A2); LFA-3 expression on noninfected cells (B1), or RSV-infected cells (B2). The results are expressed as relative cell number (y axis) versus log fluorescence intensity (x axis). The cursors were set to strengthen the altered fluorescence intensity. Nonspecific binding of the monoclonal antibodies was determined using isotype-matched irrelevant FITC-labelled mouse monoclonal antibodies (not shown). One typical experiment out of three is shown.

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PBMC-epithelial cell contact during RSV infection resulting in an increased IL-8 release. The LFA-3/CD2 interaction between epithelial cells and T lymphocytes may be possible but is not modulated via an increased LFA-3 expression pattern during RSV infection.

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References

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