AMs enter the G1 + M phase of the cycle following exposure to GM-CSF, the local production of this cytokine is likely to play a role in the events leading to the expansion of AMs. Since GM-CSF has chemotactic properties for neutrophils, it is also possible that this cytokine may account for the mechanisms leading to the BAL neutrophilia characterizing the advanced phases of the infection.

Resting and LPS-stimulated AMs from patients with HIV-1 infection synthesize and secrete increased amounts of IL6 as compared to normal subjects. This cytokine behaves both as a growth stimulatory and differentiation factor for B cells, thus inducing immunoglobulin synthesis. Inasmuch as HIV-1 infection is characterized by a polyclonal hypergamma-globulinemia, and B lymphocytes isolated from the BAL fluid of HIV-1 infected patients spontaneously produce immunoglobulins, our findings suggest that the local production of IL6 is likely to play a role in the events leading to the aforementioned polyclonal B cell activation.

Abnormalities of pulmonary function tests are frequently present not only in HIV-seropositive patients with diffuse lung disease but also in individuals with few or no respiratory symptoms and normal findings on chest radiograph. Considering that TNFα is able to alter the lung endothelium causing edema and interstitial damage, the release of this cytokine is likely to contribute to the decline of the lung function characterizing the AIDS-associated interstitial lung disease. Another issue that remains to be established is whether TNFα participates to the mechanisms governing the accumulation of immunocompetent cells in the lower respiratory tract.

It has been reported that proinflammatory cytokines (IL1, IL6, and TNFα) and GM-CSF increase HIV-1 expression in primary mononuclear phagocytes. In particular, TNFα is known to cause a superinduction of HIV-1 enhancer binding proteins (NFκB), whereas GM-CSF and IL6 mediate HIV-1 expression via nontranscriptional mechanisms. Studies should be planned to analyze the mechanisms which control HIV-1 replication in the lung and to determine whether opportunistic pathogens eliciting the release of TNFα, IL6, and GM-CSF activate the transcription and the spreading of new HIV-1 virions. Whether these cytokines might synergize in the induction of HIV-1 replication in the respiratory tract is another point that deserves further investigation.

In conclusion, our study suggests that an upregulation of the physiologic activation state of AMs occurs during HIV-1 infection. The increased expression of accessory molecules and the in vitro release of cytokines are consistent with this interpretation. The release of TNFα, IL6, and GM-CSF in the pulmonary microenvironment might play a crucial role in controlling the activity of lung immunocompetent cells, and in turn, the spreading of HIV-1 infection.

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HIV Impairs Alveolar Macrophage Mannose Receptor Function Against Pneumocystis carinii*

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The host factors responsible for development of Pneumocystis carinii (PC) pneumonia in human immunodeficiency virus (HIV) infection are incompletely understood. Normal alveolar macrophages (AM) are capable of binding, *From New England Deaconess Hospital (Drs. Koziel and Rose), and Children's Hospital Medical Center (Drs. Kruskal and Ezekowitz), Harvard Medical School, Boston. Dr. Koziel is a Parker B. Francis Foundation Pulmonary Research Fellow.

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internalizing, and destroying PC in vitro.1 The AM mannos receptor (MR) plays an important role in mediating this interaction, presumably by recognizing the mannos residues on the surface of PC.2 Human AM from HIV-infected individuals demonstrate an impairment in the ability to bind and internalize PC.3 We postulated that alterations in the expression or function of MR may be responsible for this observation. Our goals were to determine the effect of HIV and its components on MR, and to quantitate the expression of MR on AM from HIV-infected individuals.

The MR binding was quantitated with the aid of 
$^{125}$I-mannosyl-bovine serum albumin ( 
$^{125}$I-Man-BSA). The amount of nonspecific ligand binding to AM monolayers was estimated by the addition of yeast mannan (1 mg/ml). Normal AM demonstrated binding of 
$^{125}$I-Man-BSA of which up to 90% was inhibited by mannan. Addition of HIV p24 core protein (10 ng/ml) had no significant effect on total binding. However, addition of the mannose-rich HIV gp120 envelope glycoprotein (10 μg/ml) reduced AM total binding of 
$^{125}$I-Man-BSA by approximately 60%.

Although normal AM and AM from asymptomatic HIV-seropositive volunteers had comparable total binding of 
$^{125}$I-Man-BSA, only approximately 50% of binding was inhibited by mannan in the HIV-infected group. The AM obtained from HIV-seropositive individuals with PC pneumonia demonstrated total binding of which only approximately 10% was inhibited by mannan.

These observations support an important role for the AM MR in the impaired response of HIV-infected subjects to PC. Quantitative or qualitative alterations in MR and presence of competitive inhibitors may account for the inability of AM from HIV-infected individuals to adequately defend against this organism.

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