

Inhibitory mechanism of synthetic humates in HIV-1 infection.

Schneider J, Werner A, Weis R, Manner C, Seubert B, Riede U; International Conference on AIDS.

Int Conf AIDS. 1993 Jun 6-11; 9: 33 (abstract no. WS-A17-2).

Institute of Medical Microbiology, Freiburg.

OBJECTIVE: Polymeric phenolic compounds with structures similar to those of natural humates have been described as efficient inhibitors of HIV-1. They block the infectivity of the HIV-1 virion and virus-induced syncytium formation at nanomolar conc. with a selectivity index of about 1000. We have studied the mechanism of inhibition at the molecular and cellular level. **METHODS:** Metabolically labelled gp120 and virus were prepared in H9/HIV-1 cell cultures. Binding of humate to gp120 was detected by affinity chromatography of gp120 on humate-sepharose. Binding of virus to the receptor was studied with radiolabelled virus to several cell lines. Inhibition of cell fusion was determined in virus-free cocultures of HeLa/CD4 cells with uninfected, env protein expressing CL-4 cells (V. Bosch et al. in press). The influence of the inhibitor on proteolytic cleavage of the gp120 V-3 loop, observed after binding of soluble CD4 to highly purified virus (Werner et al. in press), was evaluated by immunoblotting. **RESULTS:** Gp120 specifically bound to and was eluted from humate-sepharose, allowing enrichment of gp120 from culture fluids. However, humate did not prevent binding of gp120 to soluble CD4. Attachment of virus to CD4-positive cells was only partially inhibited by humate, but humate prevented the cleavage of virion gp120 in the V-3-loop, that is normally observed after binding to the receptor protein. Furthermore, humate completely blocked the HIV env protein-induced cell fusion in our virus-free system. **CONCLUSION:** Our experiments support the hypothesis, that humate blocks the infectivity of HIV by attachment to gp120. Since this interaction does not prevent binding of gp120 to CD4, the inhibitor most probably interferes with a step in the fusion reaction, that occurs after binding of virus to the receptor.

Publication Types:

Meeting Abstracts

Keywords:

Acquired Immunodeficiency Syndrome

Anti-HIV Agents

Antigens, CD4

CD4-Positive T-Lymphocytes

Cell Fusion

Cell Line

Gene Products, env

HIV

HIV Antibodies

HIV Envelope Protein gp120

HIV Infections

HIV Seropositivity

HIV-1

Receptors, HIV

Recombinant Proteins

SK&F 106528

Virion

immunology

Other ID:

93334693

UI: 102204067

From Meeting Abstracts