Irreversible Pepsin Fraction (IPF) displays significant antiretroviral activity via specific novel cytokine stimulation in vitro investigation of activity on human lymphocytes

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Background

Resistance to all commercially available antiretroviral (ARV) agents within all classes has been reported. The occurrence of multi-class resistance remains high, with 20% of infected individuals developing resistance to two or more classes within six years of initiating treatment, and 10% of newly diagnosed infections already resistant to at least one class in the U.S. Multi-class resistance is even more prevalent in disenfranchised patient populations, whose rates of successful adherence to even the most simplified regimens available remains prohibitively low. Other mechanisms to treat HIV infection are sorely needed. IPF, like other natural autoantibody based fractionated proteins, has an affinity to pathogenic binding and simultaneously produces effects of immune homeostasis in the presence of replacativly competent HIV. IPF has shown significant antiretroviral activity via immune stimulatory pathways in vitro, notably helper T1 cells elaborate cytokines INFy, IL-2. These cells selectively promote cell-mediated immune responses that are disadvantageous to viral replication with selection for the pathogenesis of resistant profiles of minority subspecies.

Methods

Flow cytometric analysis of these cells was conducted using DC monoclonal antibodies and Annexin-V. A Biacore assay system that measures changes in the surface mass concentration was used to determine interactions between IPF molecules and CD4+ cells. Changes were expressed in resonance units (RU), with one RU representing a change in concentration of 1 pg/ mm. T cells were purified from peripheral blood mononuclear (PBMC) cells using anti-body coated magnetic beads.

Results

Laboratory analysis indicates that IPF is able to mediate maturation of dendrites cells in vitro, as determined by up-regulation of MHC class-II, CD86 and CD83 molecules, regulate pro-inflammatory cytokines IL-12 and INFy, and enhanced T-cells stimulatory capacity. Observable characteristics include modulation of complement activation, saturation of Fc receptors on macrophages, and suppression of various inflammatory mediators, including cytokines and chemokines. IPF demonstrated increased synthesis of Th-1 cells. IPF displayed spontaneous binding with gp41 when prepared for gel electrophoresis, and subsequent fusion inhibition of HIV with CD4+ cells and increased gp41 and gp120 antigenic activity. Virus-specific CD8 cells were stimulated. Flow cytometric analysis revealed apoptosis in CD4+ cells and stimulation of virus-specific CD8 cells.

Conclusions

IPF appears to modulate helper T1 cells' expression of elaborate cytokines INFy, IL-2, which selectively promote cell-mediated immune response and subsequently stimulate cytotoxic lymphocytes. These lymphocytes have a prominent role in the host's immunologic response to HIV infection. Proteins encoded by these pathogens enter the endogenous pathway for antigen presentation and are expressed on the surface of the infected cell as a complex with class I MHC- proteins. IPF appears to present a novel mechanism to reduce viral burden and stimulate innate immune responses to the virus for patients with significant antiretroviral resistance.

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